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Dadabhay, Zeenat

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The knowledge of South African Venous thromboembolism: Prophylactic and therapeutic practice guidelines of registrars in anaesthesiology and orthopaedic surgery at the University of the Witwatersrand

Zeenat Dadabhay

A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in partial fulfilment of the requirements for the degree of Master of Medicine in the branch of Anaesthesiology

Johannesburg, 2018

Declaration

I, Zeenat Dadabhay, declare that this research report is my own, unaided work. It is been submitted for the degree of Master of Medicine in the branch of Anaesthesiology at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other University.

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28 February 2018

Acknowledgments

Thank you:

To my husband, for help and support throughout this degree,

To my supervisors for patiently bearing with and guiding me,

To my mentor for encouragement, advice and support,

To my kids, always.

Abstract

Background: The South African Venous thromboembolism: Prophylactic and therapeutic practice guideline has been developed to aid clinicians with the correct administration of thromboprophylaxis. This can reduce the incidence of venous thromboembolism (VTE) and thus the associated morbidity, mortality and socio economic implications. However, studies have shown that without other interventions, adherence to clinical guidelines is poor.

Method: A prospective, contextual, descriptive study was undertaken to determine the knowledge of registrars in anaesthesiology and orthopaedic surgery of the Venous thromboembolism: Prophylactic and therapeutic practice guideline (2013). A self---administered questionnaire was developed in consultation with experts. Convenience sampling was used and all registrars present at departmental academic meetings were invited to participate.

Results: Of the participants only 12 (12%) obtained the specified pass mark of greater than or equal to 80%. Of the participants 10 (14%) of the anaesthetic registrars and 2 (7%) of the orthopaedic registrars achieved the required pass mark. Anaesthetic registrars achieved a mean score of 56% . Orthopaedic registrars achieved a mean score of 44%. Two junior registrars (4%) and 10 senior registrars (18%) achieved the required pass mark. Senior registrars scored significantly (p=0.002) higher than their junior colleagues (56% vs 48%)

Conclusion: Knowledge of The Guideline amongst registrars was poor and room for improvement and intervention in order to improve practices relating to VTE at teaching hospitals associated to Wits exist.

iv

Contents

LIST OF FIGURES VII

LIST OF TABLES VIII

LIST OF ABBREVIATIONS IX

SECTION 1: LITERATURE REVIEW 1

1.1 Introduction 1

1.2 Pathophysiology of VTE 1

1.3 Incidence of VTE 2

1.4 Prophylaxis of VTE 5

1.5 Knowledge and implementation of guidelines 10

SECTION 2: AUTHORS GUIDELINES 21

SECTION 3: DRAFT ARTICLE 24

SECTION 4: APPENDICES 37

SECTION 5: PROPOSAL 41

5.1 Introduction 42

5.2 Problem Statement 43

5.3 Aims 44

5.4 Objectives 44

5.5 Research assumptions 44

5.6 Demarcation of the study field 45

5.7 Ethical considerations 45

5.8 Research methodology 46
5.8.1 Study design 46
5.8.2 Study population 46
5.8.3 Study sample 47
5.8.4 Data collection 47
5.8.5 Data Analysis 48

5.9 Significance of study 49

5.10 Validity and reliability 49

v

5.11 Potential limitations **50**

vi

List of figures

Figure 1.1: Number of hospitals with VTE protocol 13

Figure 3.1: Percentage of correct answers by speciality 29
Figure 3.2: Percentage of correct answer by experience 29

List of tables

Table 1.1: Drugs acting on coagulation 6

Table 3.1: Percentage of correct answers by question 28

List of abbreviations

The Guideline: The South African Venous thromboembolism: Prophylactic and therapeutic practice guideline

VTE: Venous thromboembolism

Wits: University of the Witwatersrand

USA: United States of America

EU: European Union

Section 1: Literature review

1.1 Introduction

Concepts regarding venous thromboembolism (VTE) are reviewed in this literature review. In the first section a brief overview of the pathophysiology is given. In the second the incidence and complications related to VTE are discussed. The third section considers prophylaxis of VTE, and the fourth the knowledge and implementation of various thromboprophylaxis guidelines.

1.2 Pathophysiology of VTE

The key to understanding the pathophysiology of clotting has long rested on an understanding of Virchow's triad, first described by the German pathologist Rudolph Virchow in 1856. The proposal is that thrombosis is a multifactorial event due to changes in: blood flow, the state of the vessel wall, or the composition of blood (1, 2).

Further understanding of the microvasculature has allowed the expansion and explanation of Virchow's model. It is now known that the vessel wall and underlying endothelium are critical to the maintenance of a patent microvasculature (3). The endothelium contains three essential thromboregulators: nitric oxide, prostacyclin, ectonucleotidase CD39. Collagen is an essential facilitator in thromboregulation. When the endothelium is disrupted, collagen and tissue factor are exposed and thrombus formation is initiated (3).

Using this model, various risk factors for hyper---coagulability have been identified. These may be inherited or acquired. Identified risk factors include: cancer, age, critical care admission, thrombophilias, obesity, significant medical comorbidities, family history, use of hormone replacement therapy, use of

oestrogen containing contraceptive and varicose veins (4). Risk factors for the development of VTE form a part of most thromboprophylaxis guidelines (4---6).

Recent research particularly in the fields of genetics and cellular biochemistry attempts to expound on the understanding of VTE and explain conundrums not adequately explained by simply referring to Virchow's triad. These conundrums include: why some patients first develop deep vein thrombosis (DVT) and some pulmonary embolus (PE), the presence of classical signs of inflammation and the role of platelets (2).

Developments include the discovery of thrombus associated single nucleotide polymorphisms, which have been proposed as possible biomarkers. The role of hypoxaemia in the development of thrombi has also been studied. In 2004 neutrophil extracellular traps were first described, it is thought that these along with other innate immune cells may also play a role in the pathogenesis of venous thrombosis (2).

1.3 Incidence of VTE

VTE is a common and important health care challenge. Significant morbidity, mortality and expenditure can result from VTE. Almost all hopitalised patients have at least one VTE risk factor (5). Studies describing the incidence of VTE are often hard to compare due to different study populations, methodology and reporting.

In 2003, White (7) reviewed the literature related to the epidemiology of DVT in the United States of America (USA) and quoted a first time incidence of symptomatic DVT as 71 – 117 cases per 100 000 population. In this review, the author concludes that DVT is more common in the Caucasian population. However, most of the studies reviewed were done in predominantly Caucasian American cohorts, thus it is difficult to make definite conclusions about other population groups. From the literature however, higher rates are seen in Caucasians and Africa Americans than Hispanics and Asian---Pacific Islanders.

Another limitation is that many of the studies in this review had data collection periods in the 1980's. The change in epidemiology and also diagnosis may mean that these are not fully representative of the current incidence. In this review, it is stated that DVT results in death in approximately 6% of cases and PE results in death in approximately 12% of cases within the first month from diagnosis. Predictors for early mortality include: presentation as PE, advanced age, underlying malignancy and cardiovascular disease (7).

In 2005, it was reported in the United Kingdom that an estimated 25 000 people die annually from preventable hospital---acquired VTE (4).

During 2006/2007 the Epidemiologic International Day for the Evaluation of Patients at Risk for Venous Thromboembolism in the Acute Hospital Care Setting (ENDORSE) (8) study was carried out across 358 hospitals in 32 countries. Patients were assessed for risk of VTE and whether they were receiving recommended prophylaxis according to the 2004 ACCP guidelines (9). A total of 30 827 surgical patients were enrolled in this study (8) and 64.4% of surgical patients were reported to be at risk of VTE according to ACCP guideline criteria (9).

In 2007 Cohen et al (10) aimed to estimate the extent of VTE within the European Union (EU). This study used six member states as a representation of the 28 EU states. The heterogeneity of the sample states was considered and individual models were developed for each state in the study. Their findings indicated 465 715 cases of DVT, 295 982 cases of PE and a total of 370 012 cases of VTE---related deaths. The authors concluded that VTE poses a significant health problem in the EU and this could have important implications for the allocation of healthcare resources and concurred with other studies that as effective VTE prophylaxis is available many of these events could have been prevented (10).

In 2007 Anderson et al (11) conducted a study designed to estimate the number of hospitalised USA patients at risk for VTE using the 2004 ACCP guideline criteria (9): 7 786 390 surgical patients were included in the study; of these 15%

were considered moderate, 24% high and 17% highest risk for VTE. These patients were eligible for VTE prophylaxis (11).

In 2009 in Australia, it is estimated that 2000 deaths are annually related to VTE (12). A retrospective study in Tasmania conducted between June 2007 and June 2009, (13) examined the records of 300 patients (150 each for hip and knee arthroplasty), and found an incidence of symptomatic VTE within 90 days of surgery of 2.7%. A total of three patients in this study experienced PE. Some limitations of this study (13) were that readmission for VTE may occur in medical wards and may not be at the same institution where the original surgery took place. Additionally, some patients may be treated for DVT by their general practitioners, thus there may be an under---recording of the number of VTE related incidents.

In 2015, Heit quoted an incidence of 104 − 183 per 100 000 person years in a Caucasian population (14). It is estimated that this may be higher in some African American populations and lower in Asian and Native American populations. The incidence of PE associated with DVT is quoted as 29 − 78 per 100 000 population (14).

The *Registro Informatizadoa de Enfermedad TromboEmbolica* (RIETE) (15) is a multicenter, international, ongoing prospective registry started in 2004 in which consecutive patients presenting with symptomatic, acute DVT or PE confirmed by testing (venography, ultrasonography, pulmonary angiography, computed tomography scan) are enrolled. Countries involved are: Spain, France, Italy, Israel, Switzerland, Greece, Czech Republic and Republic of Macedonia. This registry has provided data for many studies related to VTE. One such study, published in 2012 explored silent PE in patients with proximal, lower limb DVTs (16). Of the patients included 35% were considered to have silent PE, and these patients were shown to have an increased incidence of symptomatic PE events in the first 15 days.

There is evidence that between 5 – 10% of in---hospital deaths are a direct result of PE (17). In addition there may be significant morbidity associated with a thrombotic event. The most notable complications are post---thrombotic syndrome and pulmonary hypertension. The cost of treating these complications should also be considered (11).

The costs related to VTE are also difficult to estimate and compare. These include costs of treating the condition, treating associated complications and loss of productivity. It has been estimated that the associated costs of VTE in the USA range between $3.2 – $15.5 billion (1992 dollars) annually (18). Grosse et al (19) estimated the cost of incidental VTE in the USA to be between 7 – 10 billion dollars annually.

1.4 Prophylaxis of VTE

VTE prophylaxis consists of both mechanical and pharmacological methods. Mechanical methods are specific non---pharmacological measures to improve venous outflow and/or reduce stasis in the lower limb. These include graduated compression stockings, intermittent pneumatic compression devices and venous foot pumps (8).

There are various different antithrombotic drugs, acting at different sites on the clotting cascade. These drugs are summarised in Table 1.

Table 1.1
Drugs Involved in coagulation (20)

Classification	Mechanism of action	Examples
Anticoagulant drugs	Antagonism of vitamin K dependent factors	Warfarin
	Binding to antithrombin 111	• Heparin • Low molecular weight heparin (LMWH) (mainly Xa): Enoxaparin, dalteparin, nadroparin
	Factor Xa inhibition	• Pentasaccharides: Fondaparinux • Xabans: Rivaroxaban • Tick anticoagulant peptide: Antistatin
	Factor 11a inhibition • Direct • Indirect: Recombinant factors	• Direct: Bivalent: Hirudins Univalent: Argatroban. Dabigatran • Indirect: Antithrombin 111, protein C, heparin co---factor 11
Antiplatelet drugs	COX inhibitors	• Aspirin • Non steroidal anti---inflammatory drugs
	Thromboxane inhibitors	• Thromboxane synthase inhibitors: Daxoxiben • Receptor antagonists • Tissue factor---pathway inhibitor
	Phosphodiesterase inhibitors	Dipyridamole
	Prostoglandin analogues	Iloprost, prostacyclin, trepostinil
	ADP receptor/P2Y12 inhibitors	• Thienopyridines: clopidogrel, ticlopidine • Nucleotide or nucleoside analogues
	Glycoprotein 11b/111a receptor antagonists	• Abciximab, eptifibatide, tirofiban • Peptides and peptimimetics • Snake venom polypeptides • Synthetic antiplatelet peptides and non peptides
	Other	Dextrans

Sehgal et al (21) systematically reviewed the literature relating to the use of the new oral anticoagulants (NOAC) in anaesthetic practice. Some salient points were discussed: NOACs are easier to administer and require no routine monitoring, however no antidote is available for these drugs and drug interactions also need to be considered. For example Rivaroxaban is contraindicated with protease inhibitors (21).

As guidelines are part of the prophylaxis of VTE they are now discussed. The high incidence and relative importance of VTE has resulted in the development of numerous guidelines internationally and nationally. The development of clinical based guidelines aims to develop evidence---based practice. Evidence based guidelines aim to improve patient care, yet individual patient consideration is also required (22).

One of the most comprehensive and cited thromboprophylaxis guidelines is the ACCP evidence---based clinical practice guideline (5, 9, 23, 24). A similar, comprehensive set of guidelines, the National Institute for health and clinical excellence (NICE) clinical guideline 92, was released for use in the National Health Service in England and Wales (4).

The ACCP guidelines are comprehensive and published with an executive summary for ease of clinical reference. Recommendations are provided on different topics. Recommendations are classified as strong (Grade 1) and weak (Grade 2) based on high, moderate or low quality evidence (Grade A, B or C respectively). Only general recommendations and sections pertinent to orthopaedic surgery will be discussed here.

A Grade 1A recommendation is made that every general hospital should have a formal, active strategy addressing the prevention of VTE. Various strategies are recommended (Grade 1A – 1C) including formal policies, computer decision support systems, periodic audits and feedback. Numerous other studies have

also accessed the effectiveness of various implementation strategies (25---28). These are discussed in more detail in section 1.5, Implementation.

General principles include the correct use of mechanical prophylaxis. Mechanical prophylaxis may be the primary modality in patients at high risk of bleeding. Aspirin alone as thromboprophylaxis is not recommended in any patient group (Grade 1A) (23). A Grade 1A recommendation is made with regards to neuraxial techniques: "For all patients undergoing neuraxial anesthesia or analgesia, we recommend appropriate patient selection and caution when using anticoagulant thromboprophylaxis." The same cautions should be applied to deep peripheral nerve blocks (Grade 1C) (23).

The ACCP guidelines (23) for orthopaedic surgery are divided into: Total hip replacement (THR), total knee replacement (TKR), knee arthroscopy, hip fracture surgery, spine surgery and isolated injuries distal to the knee. Trauma surgery may also relate to orthopaedic surgery (major trauma and pelvic and femoral fractures). For all major trauma patients, routine thromboprophylaxis is recommended if possible (grade 1A). For major trauma patients thromboprophylaxis should be continued until discharge (grade 1C) or longer in patients with impaired mobility.

According to the NICE guidelines (4) for orthopaedic surgery, LMWH should be started post operatively, with patients covered by mechanical measures pre operatively. The NICE guidelines (4) differ from the ACCP guidelines (5, 23) with regards to lower limb plaster casts, according to the NICE guideline pharmacological prophylaxis should be offered until cast removal after discussion with the patient. The NICE guidelines also differ from others in that clear recommendations are made for discharge planning. These refer mainly to patient education regarding signs and symptoms of DVT and PE. The last update to the NICE Guidelines in 2015 left sections pertaining to risk factors and thromboprophylactic options in major orthopaedic surgery unchanged.

The most recent South African guideline is published in the South African

Medical Journal in April 2013 (6). The guideline is similar in many respects to the international guidelines discussed above. The guideline is evidence based and multi disciplinary. Represented specialities were: anaesthesiology, cardiology, clinical haematology, critical care, obstetrics and gynaecology, haematopathology, internal medicine, neurology, orthopaedic surgery and pulmonology. It had been reviewed by international experts, preventing local bias. Drug use is based on Medicines Control Council registration at the time of publication (6).

With regards to surgical patients, the guideline assesses risk of developing a DVT based on patient related and procedure related risk factors. These are summarised in table 1. Prophylaxis is prescribed depending on the risk category the patient is assigned to (6). Noted in the guideline is that timing of prophylaxis remains controversial. It is recommended that prophylaxis be started 6 – 12 hours post operatively. Generally accepted European practice is to begin thromboprophylaxis 10 – 12 hours prior to surgery, while in the USA it is usually commenced 12 – 24 hours post---operatively (5).

Orthopaedic and trauma surgery are considered very high risk procedures, and mechanical prophylaxis should be considered along with one of the pharmacological options listed (6):

- enoxaparin 40 mg subcutaneously daily
- nadoparin weight adjusted dose of 38 anti---Xa units/kg subcutaneously (sc) 12 hours pre operatively and repeated 12 hours after end of surgery and daily on days 1 – 3, with 57 anti---X1 units/kg daily from day four for a minimum of ten days.
- dabigatran (THR and TKR) 110 mg four hours after surgery followed by 150 mg daily in special populations including moderate renal impairment, patients on amiodarone, elderly patients.
- rivaroxaban (THR and TKR) 10 mg daily starting six hours after surgery

- fondaparinux 2.5mg daily sc (THR and TKR, administered after surgery).

Recommendations with regards to neuraxial anaesthesia in the setting of prophylactic doses (6)

- neurological monitoring is mandatory for a minimum of 12, and ideally 72, hours
- extreme caution in patients on other haemostatically active agents
- **LMWH:**
    - no catheter placement or removal within 12 hours of dose
    - LMWH not to be commenced within 2 hours of insertion or removal of catheter
    - commencement should be delayed for at least 24 hours if blood in needle or catheter during insertion
- **fondaparinux:**
    - limited data available, no definitive recommendations
    - neuraxial catheter should not be removed within 36 hours of cessation
- **NOACs:**
    - catheter removal may take place 22 −26 hours after last dose
    - after removal: next rivaroxaban dose six hours after removal, next dabigatran dose one hour after removal.

Unlike the ACCP guidelines (5, 23) the recommendations are not individually graded, making it hard for the clinician to gauge the strength of the evidence.

1.5 Knowledge and implementation of guidelines

The publication of a guideline is not enough to ensure its translation into clinical practice (22). There are numerous studies that highlight the gap between guidelines and implementation, even in academic institutions. A few studies that

highlight this gap as it translates into thromboprophylaxis as well as studies exploring the knowledge of clinical guidelines will be discussed.

An Australian study published in 2004 found recommended prophylaxis prescribed for only 51.5% of hip or knee arthroplasty patients at two academic centres (27). The study was a prospective cohort study, with data collected in 2002 and patients followed up after three months. The study included 396 patients at two academic centers. Prophylaxis was continued after discharge in 56.6% of patients but after excluding patients who were already taking Warfarin or aspirin at the time of admission, only 18.9% were maintained on prophylaxis after discharge. However, 95.7% of patients did receive some form of prophylaxis. This seems to indicate that most practitioners acknowledge the need for prophylaxis, however the knowledge of accepted guidelines may be lacking (27, 29).

In a large retrospective study published in 2007, Yu et al (18) used the HealthFacts database to examine the records of all patients 40 years or older admitted between January 1 2001 and March 31 2005 (18). After applying various exclusion criteria, 123 304 patients were included in this study, and only 16 444 patients received prophylaxis conforming to ACCP guidelines. This study used the 2001 ACCP thromboprophylaxis guidelines as a reference (30).

Of the 2 324 orthopaedic surgery patients included in the study by Yu et al (18), 52.4% received ACCP compliant prophylaxis. Of those deemed to have received inadequate or noncompliant prophylaxis, most received either an inadequate duration or no prophylaxis. This despite the fact that those orthopaedic patients discharged before the full course of recommended prophylaxis would have been complete, were deemed to have received an adequate duration if the correct prophylaxis was continued throughout the hospital stay. Only 4.4% of the 7 469 trauma patients received compliant prophylaxis. The major challenges of this study were its retrospective nature and heavy reliance on the correct use of diagnostic coding (18).

The ENDORSE study (8) found that 58.5% of at risk surgical patients received recommend ACCP VTE prophylaxis (9) . Only 39.5% of at risk medical patients received ACCP recommended prophylaxis (8).

Anderson et al (26) studied 81 USA hospitals between September and November 2006 to determine compliance to the 2004 ACCP guidelines (9). The participating hospitals spanned 37 USA states and included 14 teaching hospitals. The characteristics of the hospitals with better guideline compliance were studied. The study took the form of a retrospective chart review. A major drawback of the study is that only the type of prophylaxis was considered (i.e. if the right type of prophylaxis was prescribed, regardless of dose and duration, the chart was considered compliant with recommendations.) The lead investigator in each centre was asked not to let prescribing doctors know about the audit until after charts were collected. Thus trying to minimise the changing of prescribing behaviour. Feedback was given to the hospitals concerned, and after one year they were once again audited and had to complete a questionnaire to determine what measures to improve practice were implemented. 79 of the 81 hospitals participated in the feedback (26).

It was found that a total of 59% of surgical patients received the recommended prophylaxis. This ranged from 36% for the 20 hospitals in the lowest quartile to 74% for the 21 hospitals in the highest quartile. Characteristics of hospitals in the highest quartile included: bigger size, academic affiliation and the presence of a formal, hospital wide thromboprophylaxis protocol (26). The study by Yu et al (18), discussed earlier, also found better thromboprophylaxis prescribing patterns at academic institutions.

In the follow up survey an improvement was seen across all quartiles, with the highest quartile demonstrating persistently better use. The number of hospitals with a formal VTE protocol improved across all quartiles as indicated in Figure 1. The follow up survey was not reported on in as much detail as the original survey (26).

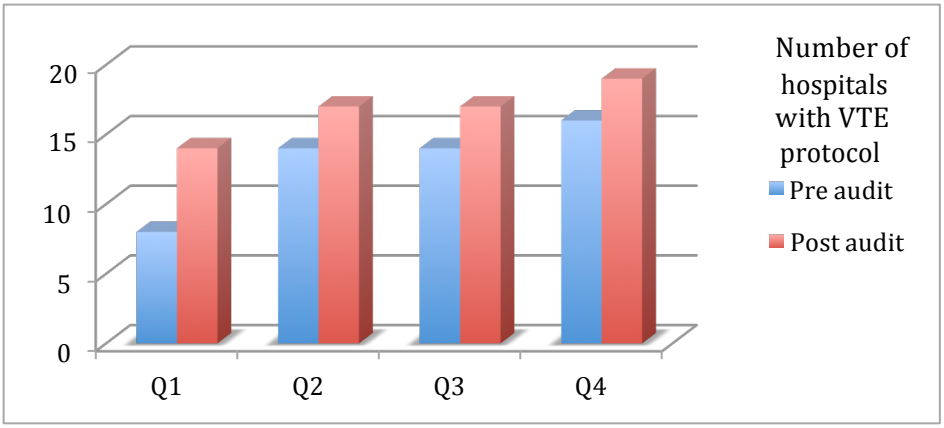

Figure 1.1 (26)

Kucher et al (31) studied the use of electronic alerts to improve prescribing practices. They found a significant improvement in prophylaxis prescriptions from 15% to 34%. The ACCP views the use of an electronic alert as highly recommended (grade 1A) (5). However, this intervention strategy is impractical in the South African setting due to the unavailability and limited use of computers in hospital wards.

The study by Mirkazemi et al (13) referred to earlier aimed to describe the degree to which thromboprophylaxis prescribing practices were consistent with guidelines. The reference guideline was primarily the 2004 ACCP guideline (9). The provision of thromboprophylaxis was documented retrospectively, taking into account that some patients may have been on these agents pre operatively. Most patients (99%) received some form of pharmacological thromboprophylaxis post operatively. However, when the agent, dose and duration of therapy was compared to the guideline, only 9% and 1% of knee and hip arthroplasty patients respectively received appropriate, guideline compliant thromboprophylaxis. The increased length of in---hospital stay following knee arthroplasty may account for the improved duration of treatment reported in this group. Most of these patients (63.3%, n=292) received general anaesthesia, and 16.4% (n=292) received some form of neuraxial anaesthesia (13).

Galante et al (28) studied adherence to thromboprophylaxis guidelines during 2008 and 2009, at an Argentinian institution that has a set prophylaxis policy.

During the first stage of the intervention a total of 100 prescriptions were audited and it was found that 31% were in line with the institutional VTE prophylaxis. The intervention consisted of: simplified guidelines, distribution to both doctors and nurses, reminders placed in strategic areas and audit and feedback (28). This multi---pronged intervention is in line with other recommendations that merely developing a guideline is not enough (5, 22, 26, 29, 32).

After the intervention, compliance to guidelines rose to 71.1%. The intervention was carried out over a three---week period commencing immediately after the first stage. A further three weeks passed (intervention free period) before the second stage (follow up) was carried out. No further follow up was performed, so it is not known if these improvements have been sustained over time (28). The longevity of improvements after an intervention was also questioned by Anderson et al (26).

A 2016 study by Watt et al (33) compared the prescribing practices of junior doctors to the NICE guidelines (4). The study was conducted in three surgical units (vascular surgery, general surgery and urology) at a general hospital. The study also aimed to assess the impact of educational interventions on prescribing practices. Data collection was in the form of retrospective audits of prescription charts. Data were collected at four points: 1. Baseline 2. Following pro forma introduction and feedback 3. A second baseline data collection. 4. Following VTE prophylaxis teaching (33).

The results of this study showed variable compliance to all aspects of the VTE guidelines. Compliance to all aspects of the guidelines was only achieved in 25% of cases. Emergency cases and urology had the lowest compliance rates. Verbal feedback to senior urology doctors was shown to have a significant impact on practice. However, educational interventions (in this case pro forma feedback and verbal education sessions) were not associated with statistically significant improvements in compliance to the prescribed guidelines, in contrast to studies stated above.

A 2012 study by Mirkazemi (29) attempted to define the attitudes towards thromboprophylaxis and clinical practice amongst orthopaedic surgeons and also to determine their familiarity with international and national guidelines (29). Despite the survey being distributed to all Australian Society Arthroplasty members, only 24% (n=25) completed the survey. The poor response rate makes it difficult to extrapolate these findings. The risk of non--- response bias is high. This shortcoming has been acknowledged in the article (29).

Consistent with previous literature discussed, (13, 27) all surgeons prescribed some form of thromboprophylaxis. These studies were all done in the Australia so a bias may exist. Some surgeons chose aspirin as their agent of choice even though guidelines advise against such practice (4---6, 27). One---third of surgeons were familiar with the recommended national guidelines, but 80% believed the guidelines were inappropriate. 76% of surgeons in this study indicated that their institutions(s) did have a thromboprophylaxis protocol. This finding is in line with other studies that indicate that while it is imperative to develop institution specific protocols, just having a protocol is not enough (5, 26---28, 31). Of the surgeons who said their institution did have a thromboprophylaxis protocol, most indicated there were no measures in place to ensure implementation (29).

Another Australian study by Pow (34) in 2014 showed a promising improvement in thromboprophylaxis use. A retrospective chart review of 402 consecutive patients undergoing either THR or TKR was performed. This study showed 99% of patients received mechanical prophylaxis, and 100% of patients received some form of chemoprophylaxis. However, the duration of chemoprophylaxis remains a potential area for improvement. The incidence of in---hospital VTE was 4.7%. Limitations of this study include the retrospective nature of the study design. The study was also conducted at a private hospital specialising in arthroplasty, thus results may not be reproducible or as favourable in other clinical settings (34).

Insufficient knowledge of guidelines has been identified as a barrier to implementation (35). Knowledge studies will be discussed below, relating to venous thromboembolism and also to other clinical guidelines.

Mirkazemi et al (29) also evaluated the knowledge of orthopaedic surgeons with respect to two thromboprophylaxis guidelines: the Australian society of arthroplasty and National Health and medical Research Council guidelines. Knowledge was tested using four vignettes and a direct question related to the guidelines and factors that influence prescribing. The survey was web based and open for six weeks (29). From this article it is hard to draw any conclusions re knowledge as: the sample size is very small, and the statistics were reported as ranges with considerable variability. For example "between 44% and 84% prescribed an appropriate dose."

A Nigerian study by Kesieme et al (36) evaluated the knowledge of surgeons in various tertiary hospitals. In this study, 66.7% of surgeons were found to have poor knowledge of VTE prophylaxis, and 33.3% were found to have good knowledge. Less than 70% was considered poor knowledge. No significant difference was found between the differing rank of surgeons (senior registrar and consultant) in this study (36).

In Saudi Arabia, Dorzi et al (37) designed a self---administered knowledge questionnaire relating to VTE, and obtained a mean score of 7.8 (maximum 15) amongst healthcare professionals. The scores did not change significantly following didactic lectures.

There are studies in the literature testing physicians' familiarity and knowledge of other guidelines. Sabido et al (38) evaluated the knowledge and attitudes of low back pain based on clinical guidelines. The study included 56 doctors and found an average percentage of correct answers of 41%.

Jahansefat et al (39) explored knowledge, attitude and adherence of healthcare professionals to evidence based guidelines for the prevention of Ventilator

associated pneumonia. The study included physicians (paediatricians, anaesthesiologists, cardiac surgeons) and nurses. Knowledge was tested using a validated multiple---choice questionnaire, consisting of 10 questions. Knowledge of the guidelines was poor; physicians achieved a mean score of 5.54 (39).

A Swiss study evaluating the knowledge of guidelines in COPD included 455 doctors (40). It was concluded that knowledge of core elements of the available COPD guidelines was poor. The authors underscored the gap between guideline development and dissemination and implementation.

From the above discussion, a recurring theme is that clinicians are not adhering to and do not have knowledge about clinical guidelines, despite the availability of numerous guidelines. Cabana et al (35) reviewed this topic. The authors aimed to describe barriers to the translation of various clinical guidelines to practice. Articles appearing in two searches describing guidelines and published between January 1996 and January 1998 were reviewed for inclusion. After various exclusion criteria were applied, 76 articles were included in the study. For the purpose of this study a barrier was defined as "any factor that limits or restricts complete physician adherence to a guideline." Study validity was improved by: using multiple investigators, a standardised search strategy, standardised categorisation and obtaining consensus amongst multiple investigators (35).

The authors concluded that before a guideline influences patient outcomes, it must first change physician knowledge and attitudes before translating into physician behavior changes (35). The barriers were classified according to the following headings. Barriers effecting physician knowledge include lack of awareness and lack of familiarity. Those related to attitude include lack of agreement, lack of outcome expectancy and inertia of previous practice. External barriers are said to effect physician behaviour. The results of this study should be borne in mind when exploring the response to various thromboprophylaxis guidelines (35).

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Section 2: Authors guidelines

The formatting of this Research Report complies with the University of the Witwatersrand's Style Guide for Theses, Dissertations and Research Reports. The formatting of the draft article may differ from the rest of the Research Report in order to comply with the author guidelines for the journal to which it is intended to be submitted.

In this section the author guidelines that the researcher followed with regard to formatting the article are included and followed by the draft article. The journal to which this article is intended to be submitted is the South African Journal of Anaesthesia and Analgesia.

FULL AUTHOR GUIDELINES

Title page

All articles must have a title page with the following information and in this particular order: Title of the article; surname, initials, qualifications and affiliation of each author; The name, postal address, e---mail address and telephonic contact details of the corresponding author and at least 5 keywords.

Abstract

All articles should include an abstract. The structured abstract for an Original Research article should be between 200 and 230 words and should consist of four paragraphs labeled Background, Methods, Results, and Conclusions. It should briefly describe the problem or issue being addressed in the study, how the study was performed, the major results, and what the authors conclude from these results. The abstracts for other types of articles should be no longer than 230 words and need not follow the structured abstract format.

Keywords

All articles should include keywords. Up to five words or short phrases should be used. Use terms from the Medical Subject Headings (MeSH) of Index Medicus when available and appropriate. Key words are used to index the article and may be published with the abstract.

Acknowledgements

In a separate section, acknowledge any financial support received or possible conflict of interest. This section may also be used to acknowledge substantial contributions to the research or preparation of the manuscript made by persons other than the authors.

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Cite references in numerical order in the text, in superscript format (Format> Font> Click superscript). Please do not use brackets or do not use the foot note function of MS Word.

In the References section, references must be typed double---spaced and numbered consecutively in the order in which they are cited, not alphabetically.

The style for references should follow the format set forth in the Uniform Requirements for Manuscripts Submitted to Biomedical Journals (http://www.icmje.org) prepared by the International Committee of Medical Journal Editors. Abbreviations for journal titles should follow Index *Medicus* format. Authors are responsible for the accuracy of all references. Personal communications and unpublished data should not be referenced. If essential, such material should be incorporated in the appropriate place in the text.

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The following are sample references:

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Tables should be self---explanatory, clearly organised, and supplemental to the text of the manuscript. Each table should include a clear descriptive title on top and numbered in Roman numerals (I, II, etc) in order of its appearance as called out in text. Tables must me inserted in the correct position in the text. Authors should place explanatory matter in footnotes, not in the heading. Explain in footnotes all non---standard abbreviations.

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All figures must be inserted in the appropriate position of the electronic document. Symbols, lettering, and numbering (in Arabic numerals e.g. 1, 2, etc. in order of appearance in the text) should be placed below the figure, clear and large enough to remain legible after the figure has been reduced. Figures must have clear descriptive titles.

Photographs and images

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Ethical considerations
Papers based on original research must adhere to the Declaration of Helsinki on ";Ethical Principles for Medical Research Involving Human Subjects"; and must specify from which recognised ethics committee approval for the research was obtained.

Conflict of interest
Authors must declare all financial contributions to their work or other forms of conflict of interest, which may prevent them from executing and publishing unbiased research. [Conflict of interest exists when an author (or the author's institution), has financial or personal relationships with other persons or organizations that inappropriately influence (bias) his or her opinions or actions.]* *Modified from: Davidoff F, et al. Sponsorship, Authorship, and Accountability. (Editorial) JAMA 2001: 286(10) The following declaration may be used if appropriate: ";I declare that I have no financial or personal relationship(s) which may have inappropriately influenced me in writing this paper."

Section 3: Draft article

The knowledge of South African Venous thromboembolism: Prophylactic and therapeutic practice guidelines of registrars in anaesthesiology and orthopaedic surgery at the University of the Witwatersrand

Zeenat Dadabhay, MBBCh(Wits), DA(SA), FCA(SA)
Helen Perrie, MSc
Juan Scribante, MCur
Palesa Motshabi-Chakane, BSc, MBChB, DA(SA), FCA(SA)

Department of Anaesthesiology, School of Clinical Medicine, Faculty of Health Sciences, University of the Witwatersrand

Corresponding author:
Zeenat Dadabhay
PO Box 42876, Fordsburg, 2034
drzdadabhay@gmail.com
0823322100

Keywords: thromboprophylaxis, knowledge, anaesthesiology, orthopaedic surgery, venous thromboembolism

Abstract

Background: The South African Venous thromboembolism: Prophylactic and therapeutic practice guideline has been developed to aid clinicians with the correct administration of thromboprophylaxis. This can reduce the incidence of venous thromboembolism (VTE) and thus the associated morbidity, mortality and socio economic implications. However, studies have shown that without other interventions, adherence to clinical guidelines is poor.

Method: A prospective, contextual, descriptive study was undertaken to determine the knowledge of registrars in anaesthesiology and orthopaedic surgery of the Venous thromboembolism: Prophylactic and therapeutic practice guideline (2013). A self-administered questionnaire was developed in consultation with experts. Convenience sampling was used and all registrars present at departmental academic meetings were invited to participate.

Results: Of the participants only 12 (12%) obtained the specified pass mark of greater than or equal to 80%. Of the participants 10 (14%) of the anaesthetic registrars and 2 (7%) of the orthopaedic registrars achieved the required pass mark. Anaesthetic registrars achieved a mean score of 56%Orthopaedic registrars achieved a mean score of 44%. Two junior registrars (4%) and 10 senior registrars (18%) achieved the required pass mark. Senior registrars scored significantly ($p=0.002$) higher than their junior colleagues (56% vs 48%)

Conclusion: Knowledge of The Guideline amongst registrars was poor and room for improvement and intervention in order to improve practices relating to VTE at teaching hospitals associated to Wits exist.

Introduction

Venous Thromboembolism (VTE) is an important preventable cause of in-hospital deaths[1] and constitutes a challenge worldwide. Estimates of VTE related deaths and events vary: in the United States of America (USA) up to 117 cases per 100 000 population are estimated to occur annually.[2] Cohen et al[3] in a large epidemiological study report figures of over one million deaths or events annually in six participating European Union countries. In 2015, Heit[4] quoted an incidence of 104 – 183 per 100 000 person years in a Caucasian population. No information regarding the incidence of VTE in South Africa could be identified. In addition to the morbidity and mortality associated with VTE, the economic burden should not be underestimated. In 2007, Yu et al[5] estimated the costs of VTE in the USA as between $3.2 to $15.5 billion.

Orthopaedic surgery patients are at particularly high risk for deep vein thrombosis (DVT): the incidence may be up to 80% in polytrauma patients and 60% for hip and knee replacement.[6,7] The degree of tissue damage in orthopaedic surgery, the nature of surgery as well as the fact that many of these patients may be immobile following surgery are additional risk factors.[6] In the South African context, the high prevalence of human immunodeficiency virus (HIV) further confounds the VTE risk.[6] Patients with HIV have a 2 to 10 fold increase in VTE events.[8]

At the hospitals associated with Wits, orthopaedic surgeons are usually the primary prescribers of thromboprophylaxis, however there are wide reaching implications for the anaesthetist and knowledge of these agents is therefore required. These implications include the possibility of pulmonary emboli (PE)[9], the considerations regarding neuraxial anaesthesia[10] and patients who may be on anticoagulant agents preoperatively.[11]

Despite consensus that prophylaxis reduces morbidity and mortality[12], evidence exists that VTE prophylaxis is under prescribed.[13-16] In an attempt to rectify this, numerous guidelines have been developed worldwide. In South Africa the Venous thromboembolism: Prophylactic and therapeutic practice guidelines first became available in 2004[17] and were revised in 2009[18] and 2013.[6]

It has been shown that the publication of a guideline is not sufficient to ensure its translation into clinical practice[19] and various barriers to implementation including lack of knowledge exists.[21] Galante et al[16] studied adherence to thromboprophylaxis guidelines during 2008 and 2009, at an Argentinian institution that has a set prophylaxis policy. It was found that only 31% of prescriptions were in line with the institutional VTE prophylaxis. A 2012 study by Mirkazemi et al[20] attempted to define the attitudes, Clinical practice and guideline familiarity towards VTE amongst orthopaedic surgeons. One-third of surgeons were familiar with the recommended national guidelines, however 80% believed the guidelines were inappropriate. In this study 76% of surgeons indicated that their institution(s) did have a thromboprophylaxis protocol.[20] A Nigerian study by Kesieme et al[22]

evaluated the knowledge of surgeons in various tertiary hospitals and in this study, 66.7% of surgeons were found to have poor knowledge of VTE prophylaxis.

The knowledge of the 2013 South African Venous thromboembolism: Prophylactic and therapeutic practice guidelines [6] (hereafter referred to as The Guideline) by anaesthesiology and orthopaedic surgery registrars affiliated to the University of the Witwatersrand (Wits) is unknown. Therefore a study was undertaken to describe this knowledge.

Methodology

Approval to conduct the study was obtained from the Human Research Ethics Committee (Medical) at Wits and other relevant authorities. A prospective, contextual, descriptive research design was used.

The study included registrars who were affiliated to the Departments of Anaesthesiology and Orthopaedic Surgery during the study period. At the time of data collection, the departments had 108 and 49 registrars respectively. In consultation with a biostatistician it was agreed to invite all registrars in the aforementioned departments to participate and to target a minimum response rate of approximately 60% for both departments. [23] A convenience sampling method was used.

A questionnaire based on The Guideline was developed to assess knowledge. Five experts from anaesthesiology, orthopaedic surgery and medical education reviewed the questionnaire to ensure face and content validity. After consideration of the experts' suggestions, a questionnaire consisting of 10 multiple-choice questions was finalised. The answer to each question consisted of one correct answer, two distractors and "I am not sure" to discourage guessing. No marks were deducted for an incorrect answer. Adequate knowledge (pass mark) for this study was a minimum of 80%, as knowledge of VTE prophylaxis was considered core knowledge.

Both departments have regular academic meetings during which one author (ZD) gave a brief overview of the study and invited registrars to participate. An information letter and questionnaire were distributed to participants agreeing to participate. The questionnaire was anonymous; apart from basic demographic details no personal information was required. After approximately 15 minutes, all questionnaires (complete or incomplete) were returned into sealed boxes. ZD was present during the completion of questionnaires to prevent data contamination and answer any questions.

Raw data were entered into a Microsoft Excel spreadsheet and analysed using descriptive and inferential statistics. The data were analysed using Stata 13.1 (StataCore, USA) in consultation with a biostatistician. As data were normally distributed means and standard deviations and independent t-tests were used and 95% confidence intervals were reported. A p value of <0.05 was considered statistically significant.

Results

Data were collected at academic meetings. One hundred and twenty-five questionnaires were distributed. A total of 102 questionnaires were returned of which two were not completed. Therefore 100 questionnaires were included in the study: 71 from the Department of Anaesthesiology, and 29 from the Department of Orthopaedic Surgery, resulting in a sample realisation of 80%. This sample represents 66% of anaesthetic registrars and 59% of orthopaedic registrars.

Of the registrars, 12 (12%) obtained the specified pass mark. Of those who passed, 10 (83%) were anaesthetic registrars and 2 (17%) were orthopaedic registrars. Table I shows a breakdown of the percentage of correct answers for each question.

Table 3.1: Percentage of correct answers by question

	Question description	**Correct %**
1	In the absence of bleeding, pharmacological thromboprophylaxis should be prescribed	82
2	Classify rivoroxaban	82
3	When an epidural catheter may be removed	28
4	The correct use of fondaparinux	40
5	Drug not registered for use in total knee and hip replacement	32
6	Correct dose of enoxaparin for prophylaxis after a high risk procedure	64
7	Not a patient-related risk factor for development of VTE	46
8	Regarding aspirin	90
9	Neurological monitoring after centroneuraxial blockade associated with anticoagulation	50
10	True statements with regards to duration of prophylaxis	10

The overall mean mark achieved was 52%. Anaesthetic registrars achieved a mean score of 56% [SD 1.84, 95% CI 51 – 60]. Orthopaedic surgeons achieved a mean score of 44% [SD 1.9, 95% CI 37 – 51]. A statistically significant difference in the knowledge of anaesthetic registrars and orthopaedic registrars ($p=0.005$) was demonstrated. Figure 1 illustrates the percentage of correct answers of anaesthetic and orthopaedic registrars.

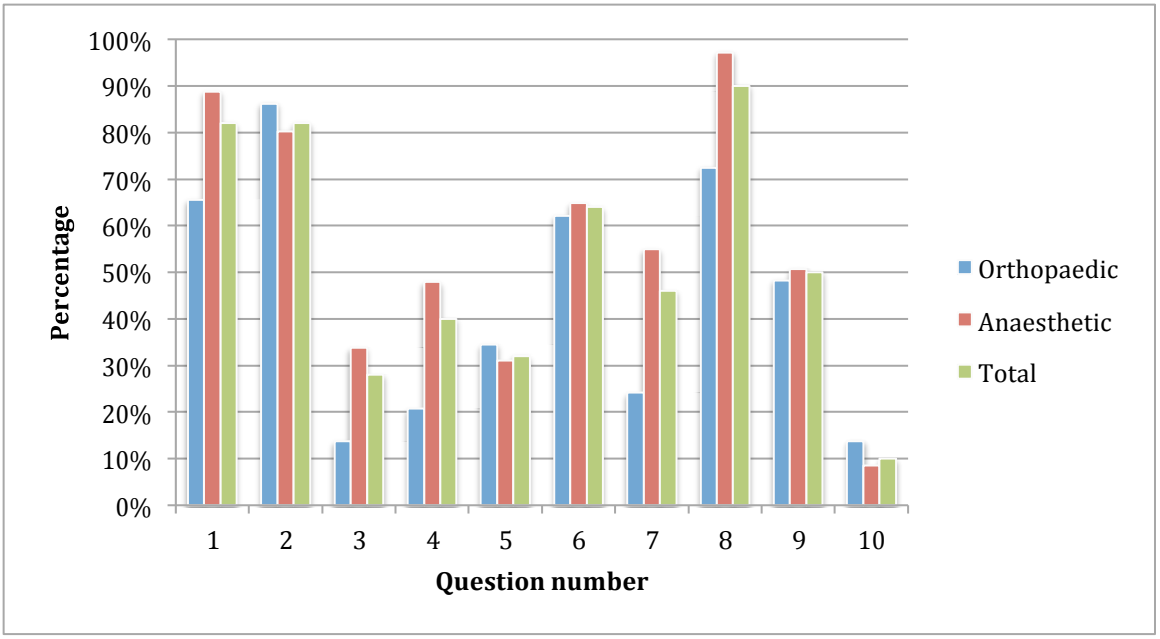

Figure 3.1: Percentage of correct answers by speciality

A total of 45 junior registrars and 55 senior registrars participated in the study. Respondents with 0 to 2 years experience as registrars are considered juniors, and those with more than two years are considered seniors. Of the junior registrars 2 (5%) passed, and of the seniors 10 (12%) passed. Senior registrars achieved a mean score of 58% [SD 1.8, 95% CI 53 – 63]. Junior registrars achieved a mean score of 46% [SD 1.9, 95% CI 40 – 51]. A statistically significant difference in the knowledge of junior and senior registrars was demonstrated (p=0.002)

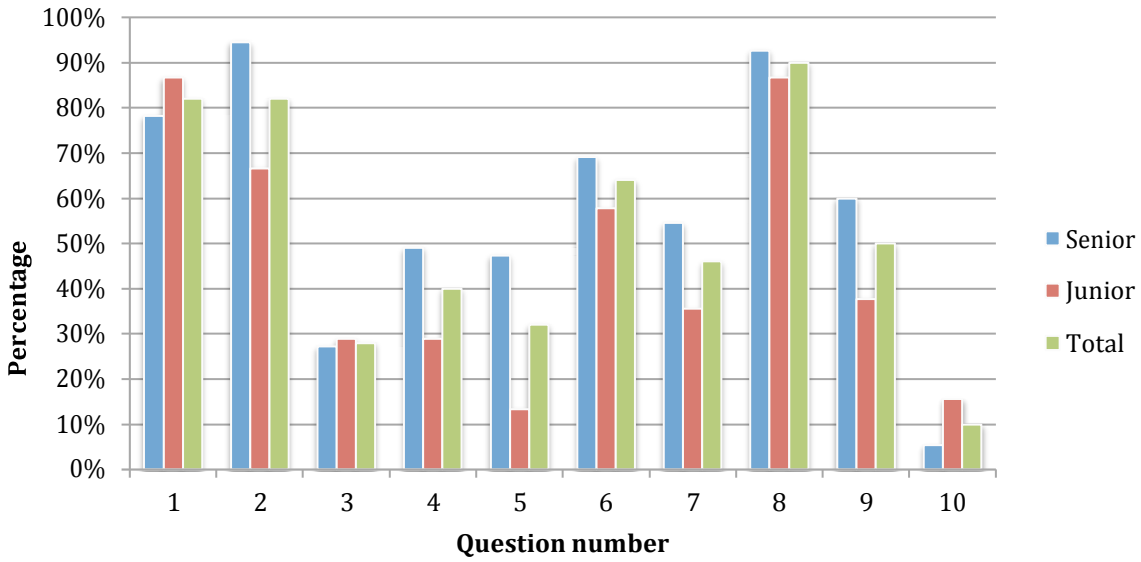

Figure 3.2: Percentage of correct answer by experience

Discussion

Cabana et al [21] have pointed out that the translation of clinical practice guidelines to every day practice is poor. Barriers to guideline implementation include knowledge.[21] International studies have shown that even in academic institutions thromboprophylaxis guideline adherence is low.[5,13-16,20]

In this study, 12% of respondents achieved the required pass mark. Kesieme et al[22] found that only 33,3% of surgeons in tertiary hospitals in Nigeria had adequate knowledge of VTE. Kesieme et al's[22] study is similar to this study as it is also in a tertiary setting in an African country. However, the pass mark was set at 70% and all respondents were senior registrars or consultants, this may explain the higher rate of adequate knowledge found in the Kesieme et al.[22] In Saudi Arabia Dorzi et al[24] investigated VTE knowledge amongst clinicians and reported a mean mark of 52%. This is consistent with the mean score in this study. Studies exploring knowledge of other clinical guidelines have achieved similar mean scores. [25,26] Sabido et al[25] tested knowledge of chronic back pain clinical guidelines and reported a mean of 41%,[25] and Jahansefat et al[26] reported mean knowledge of ventilator associated pneumonia amongst critical care health-workers of 55%.

In this study a statistically significant difference was reported between junior and senior registrars. The study by Kesieme et al[22] found no difference in scores amongst physician seniority. However, as stated earlier the groups compared were not the same as this study. Kesieme et al's[22] study comprised of senior registrars and consultants, while this study compared junior and senior registrars. Junior registrars may be inexperienced in prescribing VTE, and may be more unfamiliar with other aspects relating to VTE. Watt et al[27] audited prescriptions by junior doctors and found NICE guideline compliance[28] in 25% of cases. This is much higher than the knowledge score reported in this study, but prescribing practices may not reflect theoretical knowledge.

Mirkazemi et al identified literature in which orthopaedic surgeons felt aspirin alone was sufficient as a sole prophylactic agent.[29] However, in this study over 60% of orthopaedic registrars recognised that aspirin alone does not provide adequate thromboprophylaxis.

Duration and continuation of thromboprophylaxis has consistently been identified as an area needing improvement. [5,14,27] This is consistent with the findings in this study. Only 10% of registrars correctly answered the question relating to duration and timing of thromboprophylaxis.

Although this study is contextual and thus it may not be able to be generalised to other settings, it does address a significant patient safety issue at hospitals affiliated to Wits.

The knowledge tested in this study referred particularly to The Guideline. It is possible that general knowledge of thromboprophylaxis is better than the results of this study indicate. Additionally, The

Guideline is not officially prescribed in Wits's teaching institutions and therefore variability in prescribing practices may lead to different answers been given as compared to The Guideline tested.

A multi-pronged intervention strategy is needed to address guideline compliance. Simple strategies such as verbal feedback to prescribing doctors, feedback to relevant departments, hospital administration, flow charts, simplified guidelines, reminders and constant audit and feedback have all been shown to improve guideline adherence.[2,5,13,16,20,30-32] It has been demonstrated that simple interventions such as pocket cards, algorithms, audits and educational talks can improve compliance with VTE guidelines thus improving the quality of patient care.[13,16] As noted in one study: "the adoption of hospital-wide thromboprophylaxis protocols, coupled with periodic local audits of practice, could substantially improve current prophylaxis practices".[13] Familiarity with The Guideline should also be encouraged and taught in both departments. Further studies could broaden the inclusion criteria (e.g. other disciplines, include medical officers, consultants and specialists in private practice), or provide feedback/comparisons after an intervention.

Conclusion

Knowledge of The Guideline amongst registrars was poor and room for improvement and intervention in order to improve practices relating to VTE at teaching hospitals associated to Wits exist. Emphasis should be on establishing and maintaining the five rights of medication administration:[33] "The right patient, the right drug, the right dose, the right time and the right route."

Conflict of interest

We declare that we have no financial or personal relationships which may have inappropriately influenced us in writing this paper.

Acknowledgments
This research was done in partial fulfilment of a Master of Medicine degree.

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Section 4: Appendices

Appendix A: Letter to Head of Orthopaedic Surgery

Dr Zeenat Dadabhay
MBBCh (WITS) DA (SA)
082 3322 100
zsaloojee@gmail.com

Dear Prof Ramokgopa
Re: Request for permission to conduct research

My name is Zeenat Dadabhay, I am a registrar in anaesthesiology currently doing my MMed. The purpose of my study will be to describe the knowledge of thromboprophylaxis registrars have, and compare this to the current South African guidelines. I would like the participation of registrars in your department as orthopaedic surgery patients are at particular risk for DVT/VTE.

The study may not be directly beneficial to your department immediately, but may contribute to identifying areas of knowledge in which improvements can be made. This knowledge is important for anaesthesiology and orthopaedic surgery registrars both clinically and for exams.

Anonymity will be maintained as no identifying information will be required on the questionnaire. Confidentiality will be ensured as only my supervisors and I will have access to the completed questionnaires, and the results of my study will be reported in general terms with no identifying information noted.

If you have any questions or concerns concerning the study, you are free to contact me on 082 3322 100.

Thanking you in advance for you participation,

Dr Zeenat Dadabhay

Appendix B: Information Letter

Dear Colleague,

My name is Zeenat Dadabhay; I am a registrar in anaesthesiology currently doing my MMed. The purpose of my study will be to describe the knowledge of thromboprophylaxis registrars have, and compare this to the current South African guidelines.

Should you agree to participate in my study, I will ask you to complete a multiple---choice questionnaire. The questionnaire should take 10---15 minutes to complete. You will remain anonymous as the questionnaires will not ask for identifying information from you and will not be marked for identification in any way. Completed questionnaires will be placed in sealed, unmarked envelopes.

Confidentiality will be ensured as only my supervisors and I will have access to the completed questionnaires, and the results of my study will be reported in general terms with no identifying information noted. Your participation in the study is entirely voluntary. You may choose not to participate, or to withdraw from the study at any time with no repercussions. Results of the study will be made available to you, if you so wish.

I realize that you will not benefit directly from participation in the study. However, I hope the results of the study will help identify gaps in knowledge of registrars that we may improve.

Should you have any questions, or require a copy of the guidelines please do not hesitate to contact me. I will make copies of the guideline available to your department after completion of data collection The study has been approved by the Human Research Ethics and Postgraduate committees of the University of the Witwatersrand. You may also contact the chairman of the Human Research Ethics Committee, Professor Cleaton---Jones on (011) 717 1234

Thanking you for taking the time to consider this study,

Dr Zeenat Dadabhay
082 3322 100
zsaloojee@gmail.com

APPENDIX C: QUESTIONNAIRE

<u>Knowledge of South African Venous thromboembolism: Prophylactic and therapeutic guideline</u>
There is only one correct answer per question.
Please cross the answer you think is correct.
If more than one option is chosen it will be marked as incorrect.
All questions are based on the 2013 Venous thromboembolism: Prophylactic and Therapeutic Practice Guideline.
Please refer to info sheet for more details and contact numbers
VTE: Venous---thromboembolism

Please indicate which department you are part of:

	Anaesthesiology
	Orthopaedic surgery

Please indicate how many years of registrar training you have had:

	0---1
	1---2
	2---3
	3---4

In the absence of bleeding, pharmacological thromboprophylaxis should be prescribed:

	Immediately postoperatively
	Between 6---12 hours postoperatively
	Between 12---24 hours postoperatively
	Between 24---36 hours postoperatively
	I am not sure

Classify Rivaroxaban:

	Direct Xa (10a) inhibitor
	Direct 11a (2a) inhibitor
	Anti platelet agent
	Vitamin K antagonist
	I am not sure

An epidural catheter may be removed:

	2 hours after the last dose of Rivaroxaban
	6 hours after the last dose of Rivaroxaban
	22---26 hours after the last dose of Rivaroxaban
	36 hours after the last dose of Rivaroxaban
	I am not sure

The correct use of Fondaparinux according to the guideline is:

	2.5 mg sc daily postoperatively
	2.5 mg sc BD postoperatively
	2.5 mg sc daily 6 hours preoperatively and postoperatively
	2.5 mg sc BD preoperatively and postoperatively
	I am not sure

Which of the following drugs IS NOT registered for use in total knee and hip replacement:

	Rivaroxaban
	Nadoroparin
	Dabigatran
	Fondaparinux
	I am not sure

The correct dose of Enoxaparin for prophylaxis after a high risk procedure according to the guideline is:

	40 mg (4000 anti---Xa units) BD
	80 mg (8000 anti---Xa units) BD
	80 mg (8000 anti---Xa units) daily
	40 mg (4000 anti---Xa units) daily
	I am not sure

According to the guideline, which of the following IS NOT a patient---related risk factor for development of VTE:

	HIV/AIDS
	Age > 50 years
	Inflammatory bowel disease
	Obesity
	I am not sure

With regards to aspirin:

	It offers adequate VTE prophylaxis
	It may be prescribed as the sole agent
	Offers weak VTE prophylaxis compared to Low molecular weight heparin
	It is recommended for prophylaxis in orthopaedic procedures
	I am not sure

After centroneuraxial blockade associated with anticoagulation:

	Neurological monitoring is mandatory for a minimum of 12 hours
	Neurological monitoring is mandatory for a minimum of 2 hours
	Neurological monitoring is mandatory for a minimum of 72 hours
	Neurological monitoring is not mandatory with bloodless insertion
	I am not sure

With regards to the duration of prophylaxis according to the guideline, all the following are true, EXCEPT:

	After hip replacement surgery, prophylaxis should be continued for 5 weeks.
	After knee replacement surgery, prophylaxis should be continued for 4 weeks.
	For major orthopaedic surgery, at least 7---10 days prophylaxis is indicated
	LMWH prophylaxis should be continued until the patient is fully mobile.
	I am not sure

Thank you for completing this questionnaire

APPENDIX D: ETHICS CLEARANCE

R14/49 Dr Zeenat Dadabhay

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M140124

NAME: (Principal Investigator)	Dr Zeenat Dadabhay
DEPARTMENT:	Anaesthesiology Helen Joseph Hospital
PROJECT TITLE:	Knowledge of South African Venous Thromboembolism Guidelines of Anaesthesiology and Orthopaedic Surgery Registrars at the University of the Witwatersrand
DATE CONSIDERED:	31/01/2014
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Mrs Helen Perrie

APPROVED BY: _____
Professor P Cleaton-Jones, Chairperson, HREC (Medical)

DATE OF APPROVAL: 07/10/2015

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Secretary in Room 10004, 10th floor, Senate House, University.
I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report**.

_____ _____
Principal Investigator Signature Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

APPENDIX E: TITLE

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG | FACULTY OF HEALTH SCIENCES

7 March 2017
Person Number: 0303850W

TAA Letter

Dr Zeenat Dadabhay
13 Westwoods
2 Craighall Road
Victory Park
2193

Dear Dr Dadabhay

Master in Medicine (Anaesthesiology): Approval of title change

We have pleasure in advising you that your change of title has been approved;

Old: The knowledge of thromboprophylaxis of registrars in Anaesthesiology and Orthopaedic Surgery

New: The knowledge of South African venous thromboembolism: prophylactic and therapeutic practice guidelines of registrars in anaesthesiology and orthopaedic surgery at the University of the Witwatersrand

UNIVERSITY OF THE WITWATERSRAND
07 MAR 2017
FACULTY OF HEALTH SCIENCE
YORK ROAD, PARKTOWN
2193
JOHANNESBURG

Yours sincerely

Miss Thando Mbolekwa
On behalf of Mrs Sandra Benn
Faculty Registrar

Section 5: Proposal

The knowledge of South African Venous thromboembolism: Prophylactic and therapeutic practice guidelines of registrars in anaesthesiology and orthopaedic surgery at the University of the Witwatersrand

Zeenat Dadabhay

Student no: 0303850W

Supervisor:

Helen Perrie

Department of Anaesthesiology

Co---supervisor:

Dr Palesa Motshabi

Department of Anaesthesiology

5.1 Introduction

Venous Thromboembolism (VTE) is an important preventable cause of in-hospital deaths (1) and constitutes a challenge worldwide. Estimates of VTE related deaths and events vary: in the United States of America (USA) up to 117 cases per 100 000 population are estimated to occur annually (2). Cohen et al (3) in a large epidemiological study report figures of over one million deaths or events annually in six participating European Union countries. In 2015, Heit (4) quoted an incidence of 104 – 183 per 100 000 person years in a Caucasian population. No information regarding the incidence of VTE in South Africa could be identified. In addition to the morbidity and mortality associated with VTE, the economic burden should not be underestimated. In 2007, Yu et al (5) estimated the costs of VTE in the USA as between $3.2 - $15.5 billion.

Orthopaedic surgery patients are at particularly high risk for deep vein thrombosis (DVT): the incidence may be up to 80% in polytrauma patients and 60% for hip and knee replacements (6, 7). The degree of tissue damage in orthopaedic surgery, the nature of surgery as well as the fact that many of these patients may be immobile following surgery are additional risk factors (6). In the South African context, the high prevalence of human immunodeficiency virus (HIV) further confounds the VTE risk (6). Patients with HIV have a 2 to 10 fold increase in VTE events (8).

At the hospitals associated with Wits, orthopaedic surgeons are usually the primary prescribers of thromboprophylaxis, however there are wide reaching implications for the anaesthetist and knowledge of these agents is therefore required. These implications include the possibility of pulmonary emboli (PE) (9), the considerations regarding neuraxial anaesthesia (10) and patients who may be on anticoagulant agents preoperatively (11).

Despite consensus that prophylaxis reduces morbidity and mortality (12), evidence exists that VTE prophylaxis is under prescribed (13---16). In an attempt to rectify this, numerous guidelines have been developed worldwide. In South

Africa the Venous thromboembolism: Prophylactic and therapeutic practice guidelines first became available in 2004 (17) and were revised in 2009 (18) and 2013 (6).

The publication of a guideline is not sufficient to ensure its translation into clinical practice (19). Galante et al (16) studied adherence to thromboprophylaxis guidelines during 2008 and 2009, at an Argentinian institution that has a set prophylaxis policy. During the first stage of the intervention it was found that 31% of audited prescriptions were in line with the institutional VTE prophylaxis. A 2012 study by Mirkazemi et al (20) attempted to define the attitudes towards thromboprophylaxis and clinical practice amongst orthopaedic surgeons and also to determine their familiarity with international and national guidelines. One---third of surgeons were familiar with the recommended national guidelines, however 80% believed the guidelines were inappropriate. In this study 76% of surgeons indicated that their institutions(s) did have a thromboprophylaxis protocol (20). Lack of knowledge of guidelines has been identified as a barrier to implementation (21). A Nigerian study by Kesieme et al (22) evaluated the knowledge of surgeons in various tertiary hospitals and in this study, 66.7% of surgeons were found to have poor knowledge of VTE prophylaxis.

The knowledge of the 2013 South African Venous Thromboembolism: Prophylactic and therapeutic practice guideline (6) (hereafter referred to as The Guideline) by anaesthesiology and orthopaedic surgery registrars affiliated to the University of the Witwatersrand (Wits) is unknown. Therefore a study was undertaken to describe the current knowledge of these registrars at Wits with regards to The Guideline.

5.2 Problem Statement

VTE remains a common, yet often preventable clinical complication. Thromboprophylaxis may significantly impact on patient morbidity and mortality and as such remains an important aspect of care.

The updated South African Venous Thromboembolism: Prophylactic and Therapeutic Practice Guideline (6) which include the use of new oral anticoagulants (NOACs) was released in 2013. However there are no institutional or departmental protocols at WITS compelling adherence to these guidelines.

Orthopaedic surgery patients are known to be at particularly high risk for VTE (6, 7)The knowledge of these updated guidelines by anaesthesiology and orthopaedic surgery registrars affiliated to the University of Witwatersrand (WITS) is unknown.

5.3 Aims

The aim of this study is to describe the current knowledge of anaesthsiology and orthopaedic surgery registrars at the WITS with regards to the 2013 South African Venous Thromboembolism: Prophylactic and Therapeutic Practice Guideline.

5.4 Objectives

The objectives of this study are to:

- describe the registrars level of knowledge of the guideline
- describe the difference in knowledge between anaesthesiology and orthopaedic surgery registrars.
- describe the difference in knowledge between junior and senior registrars

5.5 Research assumptions

The following definitions will be used in this study:

Registrar: a medical doctor registered with the Health Professionals Council of South Africa to train as a specialist.

The guideline: in this study this will refer to the 2013 South African Venous Thromboembolism: Prophylactic and Therapeutic Practice Guideline.

Adequate knowledge: in this study will refer to a mark of 80% or above.

5.6 Demarcation of the study field

The study will take place amongst registrars in the Departments of Anaesthesiology and Orthopaedic Surgery at WITS. The hospitals affiliated to WITS are: Chris Hani Baragwanath Academic Hospital (CHBAH), Charlotte Maxeke Johannesburg Academic Hospital (CMJAH), Donald Gordon Medical Centre and Helen Joseph Hospital/Rahima Moosa Mother & Child Hospital.

5.7 Ethical considerations

Approval to conduct this study will be obtained from the Postgraduate Committee and the Human Research Ethics Committee (Medical) of WITS. Verbal approval will also be obtained from the Head of the Department of Orthopaedic Surgery.

Registrars will be invited to participate in the study. An information sheet (Appendix B) and self---administered questionnaire (Appendix C) will be distributed. Questionnaires will be returned into a sealed box in a sealed envelope. Return of a completed questionnaire will be considered granting of informed consent. Anonymity will be maintained as no personal identification will be required on the questionnaire and confidentiality will be maintained, as only the researcher and supervisor will have access to the raw data. Raw data will be kept for six years.

The study will be conducted in accordance with the South African Good Clinical Practice Guidelines (23) and with ethical standards determined by The Helsinki Declaration (24).

5.8 Research methodology

5.8.1 Study design

This study will be a prospective, contextual, descriptive study.

A prospective study design is one in which variables are measured as the study is taking place. (25) This study is prospective as the variables: knowledge and prescribing practices will be tested at specified time periods (academic meetings).

A contextual study takes place in a specific location or area described as a "small scale world" such as gangs, hospital wards or clinics (26) This will be a contextual study as it will only take place within a specified group and area: registrars in anaesthesiology and orthopaedic surgery at WITS.

Descriptive designs describe a phenomena and the researcher does not manipulate any variables (25). This study is descriptive as it describes the knowledge of registrars.

5.8.2 Study population

The study population will be registrars working in the Departments Anaesthesiology and Orthopaedic Surgery at WITS.

5.8.3 Study sample

Sample size

The department of Anaesthesiology has approximately 100 registrars and the Department of Orthopaedic Surgery approximately 50. In consultation with a biostatistician it was agreed to invite all registrars in the aforementioned departments to participate.

Sampling method

A convenience sample involves the selection of readily available participants and may also be referred to as “accidental” or “available” sampling (25). This is a convenience sample as registrars at the academic meetings will be enrolled in the study.

Inclusion and exclusion criteria

Registrars in the departments of anaesthesiology and orthopaedic surgery will be invited to participate in the study.

Excluded from the study are:

- registrars not present at the meeting(s)
- registrars who choose not to participate.

5.8.4 Data collection

Questionnaire development:

Before data collection can begin, a questionnaire had to be developed to assess knowledge. The questionnaire (Appendix C) consists of multiple---choice questions relating to the guideline. Four experts (anaesthsiology and

orthopaedic surgery) reviewed the questionnaire to ensure face and content validity.

The questionnaire consists of nine multiple---choice questions. Options consist of one correct answer, two distractors and 'I am not sure' to discourage guessing. No marks will be deducted for an incorrect answer.

Data collection process:

Both departments have regular academic meetings. Registrars at these meetings will be invited to participate in the study and the researcher will give a brief overview of the study. An information letter (Appendix B) and questionnaire (Appendix C) will be distributed.

The questionnaire will be anonymous and each one will be given a study number. Apart from basic demographic details no personal information will be required. After approximately 15 minutes, questionnaires will be returned in sealed envelopes. The researcher will be present during the filling out of questionnaires and will collect returned questionnaires immediately. This will prevent data contamination.

Raw data will be entered into a Microsoft Excel spreadsheet.

Copies of the guideline will be provided to the departments after the completion of the study.

5.8.5 Data Analysis

The data will be analysed using Microsoft excel and the software program Statistica 11.0 in consultation with a biostatistician.

Data will be analysed using means and standard deviations if the data is normally distributed and medians and inter quartile ranges for skewed data. A chi---squared test will be used to determine if there is any association between having adequate knowledge and discipline (anaesthesiology and orthopaedic surgery.) A p value of ≤0.05 will be considered statistically significant, 95% confidence intervals will be calculated.

5.9 Significance of study

The South African thromboprophylaxis guidelines have been developed to aid clinicians with the correct administration of thromboprophylaxis. The correct administration of prophylaxis can reduce the incidence of VTE and thus the associated morbidity, mortality and socio---economic implications. However, studies have shown that without other interventions, adherence to clinical guidelines is poor.

Orthopaedic patients are at high risk for VTE and specific guidelines are applicable to this subgroup. Anaesthesiology and orthopaedic registrars deal with issues relating to VTE on a daily basis and require an intimate knowledge of these guidelines. However, there are no measures in place to determine the level of knowledge of these guidelines.

If knowledge of the guideline is found to be inadequate, interventions may be introduced to improve practice and patient safety.

5.10 Validity and reliability

Validity indicates that the conclusions of the study are justified based on the study design. Reliability is a representation of the consistency of the measure. (27)

The validity and reliability of this study will be ensured by the following:

- The performance of a thorough literature review
- An adequate, representative sample size.
- The questionnaire will be validated by experts
- Appropriate data gathering techniques will be used and data will be accurately recorded on a well---developed data collection sheet.
- A suitable study design has been chosen.
- The researcher will be the only data collector.
- Data analysis will be conducted in conjunction with a biostatistician.

5.11 Potential limitations

The study is contextual and may not be able to be generalized to other settings. However, it does address a significant patient safety issue at hospitals affiliated to WITS.

Convenience sampling was used and this may introduce a bias as over or underrepresentation may occur. As all the registrars in the two departments will be invited to participate, this will decrease bias.

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