RISK PROFILE AND THROMBOPROPHYLAXIS PRACTICES AMONG PATIENTS UNDERGOING LAPAROTOMY AT MOI TEACHING AND REFERRAL HOSPITAL, ELDORET.

BY

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DECLARATION

Student's declaration

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DEDICATION

This work is dedicated to my wife, sons Trevor and Treagan, and all persons or organizations that put their efforts, time and other resources in provision and improvement of surgical services and thromboprophylaxis practices.

DISCLOSURE

I did not receive any funding or grants in support for this study. Neither i nor a member of my immediate family received payments or other benefits thereof or commitment or agreement to provide such benefits from a commercial entity.

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LIST OF ABBREVIATION AND ACRONYMES

ACCP	American College of chest physician					
DVT	Deep Venous Thrombosis					
LDUH	Low Dose Unfractionated Heparin					
LMWH	Low molecular weight heparin					
MTRH	Moi teaching and referral hospital					
РЕ	Pulmonary Embolism					
RAM	Risk assessment model					
UFH	Unfractionated heparin					
VTE	venous thromboembolism					
COSESCA	College of Surgeons East, Central and Southern Africa					
ніс	High Income Countries					
LMIC	Low and Middle Income Countries					

OPERATIONAL DEFINITION OF KEY TERMS

Venous thromboembolism is a term referring to blood clots in the veins that may migrate

Deep venous thrombosis is a blood clot in the lower limbs as detected by Doppler ultrasound

Clinical deep venous thrombosis is a clot in the lower limbs veins that may cause clinical symptoms

Laparotomy is a surgical incision into the abdominal cavity to examine the abdominal organs, aid diagnosis and management of abdominal problems.

Thromboprophylaxis refers to any preventative measure or medication that reduces the likelihood of the formation of blood clots

Chemoprophylaxis/pharmacoprophylaxis is the use of pharmacological agents to reduce the risk of clot formation or migration

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RISK PROFILE AND THROMBOPROPHYLAXIS PRACTICES AMONG PATIENTS UNDERGOING LAPAROTOMY AT MOI TEACHING AND REFERRAL HOSPITAL ELDORET, KENYA.

ABSTRACT

Background: Venous thromboembolism (VTE) is a common preventable cause of hospital mortality worldwide. Abdominal surgery is a well-known risk factor of VTE. Venous thromboprophylaxis reduces this risk when used appropriately, but it has adverse effects. Various risk profile stratification scores have been developed to guide thromboprophylaxis. Most of these protocols are well practiced in high income countries where patient characteristics and operation setting are different from our local set up. VTE prophylaxis protocol by MTRH has been observed to be underutilized. Local research on risk profile, incidence of deep venous thrombosis (DVT) and thromboprophylaxis practice will provide an audit of our practice. Thus enabling individualization of thromboprophylaxis and development of local protocols.

Objective: To describe the risk profile, thromboprophylaxis practices and clinical DVT incidence in patients undergoing laparotomy at Moi Teaching Referral Hospital, Eldoret.

Methods: A prospective study was carried out in Moi Teaching and Referral Hospital on adult patients undergoing laparotomy. Consecutive sampling was used, with a minimum sample size of 325 patients. Patient's demographic features, risk factors of venous thromboembolism, diagnosis, intra operative findings, procedure done, thromboprophylaxis used and timing was recorded. Perioperative, 2 weeks and 4 weeks postoperative, Well's score was done for DVT evaluation. Doppler ultrasound of the lower limb was done on patients with a score of 2 or more to rule out DVT.

Results: The mean age of participants in the study was 38years with a male to female ratio of 1.5:1. Intra-abdominal infection was the leading indication for laparotomy. All surgeries were conducted open with 75.4% of the participants stratified at high or moderate risk of developing VTE. Most, 82.7%, of the patients were mobilized within 72 hours. Enoxaparin was the only chemoprophylaxis prescribed, mostly in the post-operative period. The duration of enoxaparin administration was not standardized and no documented use of MTRH VTE risk stratification chart was observed. Moreover, 3 % of the participants received chemoprophylaxis contrary to ACCP guidelines while 12% received enoxaparin despite having relative contraindications. Only 13% and 24% of the moderate and high risk group, respectively, received chemoprophylaxis. Utilization of mechanical prophylaxis was not observed. The incidence of symptomatic DVT was 6.8%. Advanced age, Caprini score and enoxaparin prescription was associated with higher risk of symptomatic DVT development.

Conclusion: The risk and incidence of VTE in laparotomy patients at MTRH is high despite the middle aged and intra-abdominal infection being operated more frequently. Poor VTE risk stratification and failure to utilize MTRH availed protocol, led to inadequate and inappropriate use of thromboprophylaxis.

Recommendation: Utilization of MTRH VTE protocol by prescribers, will lead to appropriate use of prophylaxis. Availing different thromboprophylaxis options for prescriber to custom make the prophylaxis prescription. Evaluation of factors influencing MTRH VTE protocol utilization.

CHAPTER ONE

1.0 INTRODUCTION

1.1Background

Venous thromboembolism (VTE) is defined by the International Society on Thrombosis and Hemostasis (ISTH), as a condition in which a blood clot forms, most often in the deep veins of the leg, groin or arm (DVT) and travels in the circulation, lodging in the lungs (pulmonary embolism/PE). It encompasses deep venous thrombosis and pulmonary embolism (PE), which are complicated by fatality, post thrombotic syndrome, chronic thromboembolic pulmonary hypertension and reduced quality of life(Cushman et al., 2020).

Venous thromboembolism (VTE) is a major public health problem as it accounts for 5-10% of hospital deaths.(Fanikos et al., 2009). Most of the diagnosed VTE occur in the hospital setting or days after discharge. Approximately, 60% of VTE occurs in hospitalized patients or post discharge from the hospital (MoH-Kenya, 2018). In Kenya, PE accounts for 14.2% of cardiovascular mortality. (*Cardiovascular Causes of Death in an East African Country: An Autopsy Study*, n.d.). Among patients admitted with PE, almost half of them develop complication, 28.1% die while 18.8% develop cor-pumonale (Ogeng'o et al., 2011) . Due to the high prevalence of VTE, its silent clinical nature, high cost of treatment and potential for rapid mortality, prevention is paramount when dealing with patients at risk of this condition.

In a hospital setup, surgical patients have a higher risk of VTE, at 64%, compared to 41.5% in patients admitted to medical wards (Cohen et al., 2008). This necessitates risk assessment and proper management of these surgical patients to reduce this risk. Multiple factors that increase the risk of VTE in surgical patients

include; indication for surgery, comorbidities, genetic factors and available support systems. These factors may contribute to the higher incidence of VTE in surgical patients. Using iodine 125 marked fibrinogen testing, the global incidence of DVT has been reported as 25% in general surgery patients without prophylaxis (Heit, 2003)

Laparotomy comes from a Greek word *lapara* meaning flank and *tomy* meaning cut. It is a surgical procedure, whereby an incision is made on the abdominal wall to gain access to the abdominal cavity. This is done for diagnosis or management of various clinical conditions. In the western world, laparoscopic laparotomy is widely practiced for various indications. In most low and middle income countries (LMIC) like Kenya, open laparotomy is most often utilized as minimally invasive surgery investment has been low.

Major abdominal surgery is a well-documented risk factor of venous thromboembolism together with its indications. Abdominal surgery leads to a hypercoagulable state, and an associated increased risk of deep vein thrombosis (Iversen & Thorlacius-Ussing, 2002). The risk of VTE in laparotomy patients has been reported to be approximately 23.7% (Sakon, Maehara, Yoshikawa, & Akaza, 2006). In Kampala, Uganda, the reported incidence of DVT post laparotomy was 5% (Muleledhu et al., 2013). Correct VTE risk assessment and thromboprophylaxis usually reduce morbidity and mortality associated with VTE in laparotomy patients. Over the years' various risk factors for VTE have been identified and graded on the odds of association to VTE development. When multiple risk factors are present there is a higher risk of venous thromboembolism. Surgery is a well-documented VTE risk factor as well as some indications for the surgery, such as cancer or trauma. Various VTE risk assessment tools and thromboprophylaxis guidelines have been developed in high income countries to enhance patient prevention of VTE occurrence through appropriate thromboprophylaxis. The tools have been validated in various clinical settings worldwide. They include: modified Caprini risk assessment model, Roger Score, American College of Chest Physician Guidelines 2012 and American Academy of Orthopedic Surgeons 2011.

Caprini risk assessment model and Roger score system have been widely applied in non-orthopedic surgical patients for stratification of patients according to VTE risk. Roger score has been validated in a single study and is considered to be 'cumbersome' (Laryea & Champagne, 2013). Caprini risk assessment model was introduced in 1991 and since then it has been validated in over 100 clinical trials worldwide, including South Africa(Obi et al., 2015). The VTE risk interpretation varies from surgical procedure or specialty groups being tested. Caprini score has been shown to provide a consistent, thorough and efficacious method for VTE risk stratification and selection of recommended VTE prophylaxis (Cronin et al., 2019)

Pharmacological agents (i.e. heparin) and mechanical devices (e.g., graduated compression stocking (GCS) and intermittent pneumatic compression (IPC)) are some of the interventions used to reduce risk of VTE. This may be used independently or as a combination depending on the VTE risk level, risk of bleeding and anticipated adverse effects of the intervention. Thromboprophylaxis, with either pharmacological or mechanical methods, has been shown to reduce incidences of venous thromboembolism by 67% in patients undergoing colorectal surgery (Geerts 2001). Despite this evidence, data from various studies, report underutilization of venous thrombus prevention methods. Only 26.7% of general surgical patients at risk of VTE received prophylaxis in Kenyatta National Hospital (KNH) and 4% received

unnecessary prophylaxis (Of et al., 2018). Pharmaco-prophylaxis of VTE is associated with increased risk of bleeding and wound dehiscence among other adverse effects (Burnett et al., 2016). Mechanical methods of thromboprophylaxis have been associated with limb ischemia and nerve injury, though none of the surgeons in COSECSA region reported these serious side effects. (Ndeleva & Lakati, 2018). It is paramount for the surgeon to weigh risk versus benefit during prophylaxis use and selection.

A survey in Nigeria, established that 66.7% of the surgeons had poor knowledge on venous thromboembolism prophylaxis despite 76.2% of them losing a patient due to suspected thromboembolism event(Kesieme et al., 2016). This highlights the need to employ strategies to help educate and remind the care givers the importance of VTE prevention measures.

American College of Chest Physicians (ACCP) developed recommendations for thromboprophylaxis in non-orthopedic surgical patients in 2012 Called-Antithrombotic Therapy and Prevention of Thrombosis, ninth edition (AT9). It describes several alternatives for stratifying the risk of VTE in general and abdominal-pelvic surgical patients. It has several grades, very low risk (caprini=0), low risk (caprini=1-2), moderate risk (caprini=3-4) and high risk (caprini=>5). Based on these grades various thromboprophylaxis types are recommended. (Gould et al., 2012)

Timing of thromboprophylaxis administration is paramount as it influences efficacy of the method used. Zaghiyan and colleagues found out that preoperative and postoperative chemical thromboprophylaxis are equally safe in protecting against VTE in major colorectal surgery (Zaghiyan et al., 2016). However, a few studies have reported pre-operative prophylaxis to be more efficacious. Patients who receive prophylaxis the evening before surgery and 2 hours before surgery had a reduction in the relative risk of DVT development (Rasmussen et al., 2006).

Initiation time, post operatively, of thromboprophylaxis is dependent on agent used and risk of bleeding post-surgery. The duration of prophylaxis may also influence degree of VTE risk reduction. Postoperative prophylaxis duration of 7–10 days or VTE prophylaxis until full mobilization of the patient is recommended most frequently in low risk surgery. (Gould et al., 2012). In moderate and high risk VTE patients the duration may extend beyond 1 week or post discharge from the hospital. A larger, double blind multicenter study with a comparable design reported a significant reduction of DVT in patients with abdominal or pelvic cancer after prolongation of prophylactic administration with LMWH from 1 week to 4 weeks (Bergqvist et al., 2002).

Venous thromboembolism (VTE) maybe a silent killer, presenting with fatal pulmonary embolism as the first sign. Surgery is a well-known risk factor of VTE. However, an appropriate thromboprophylaxis method has been proven to reduce this risk with minimal adverse effects of the method applied. (Ho et al., 1999). Most anticoagulation medications can be used for prophylaxis with recommended dose adjustment. According to meta-analyses and large clinical trials, low-dose UFH reduces the incidence of DVT from about 25% to 8%, and lowers the incidence of clinically overt and fatal PE by 50% and 90%, respectively (O'Donnell & Weitz, 2003).

Despite the evidence supporting thromboprophylaxis, it remains underused because surgeons may perceive that the risk of venous thromboembolism is not high enough to justify the potential hemorrhagic complications of anticoagulant use. The diagnosis of VTE may not be suspected before death, highlighting the fact that fatal PE can be the first manifestation of an asymptomatic DVT. Unrecognized DVT also can lead to long-term morbidity from post-thrombotic syndrome, pulmonary hypertension and may predispose patients to recurrent VTE. (Geerts et al., 2001). Post-thrombotic syndrome is characterized by swelling of the affected limb, pain, purpura, dermatitis, ulceration, pruritus and cellulitis. This may worsen over time and further necessitate amputation of the limb significantly impacting the patient's quality of life. (Nutescu, 2007). DVT and PE management is resource consuming i.e. expensive compared to prophylaxis, as it requires a hospital admission, multiple injections and at times admission to intensive care unit.(Heit, 2003).

Data from the west has established that thromboprophylaxis reduces the risk of venous thromboembolism by 67% (geerts, 2001). Conversely, inappropriate use of thromboprophylaxis might lead to life threatening conditions, i.e. bleeding, heparin induced thrombocytopenia, limb ischemia, skin damage, and increase in cost of medical care. The risk adapted primary prophylaxis of venous thromboembolism significantly lowers VTE events and implementation of proper strategies for risk assessment and prophylaxis is viewed as a key indicator of patient safety(Cohen et al., 2008)(*Health at a Glance 2015*, 2015)

Laparotomy is one of the major surgical procedures conducted at MTRH due to a wide range of conditions and by various specialists e.g. urologists, general surgeons, gynecologists among others. Approximately 7-8 laparotomies are done weekly at Moi Teaching and Referral Hospital, both emergent and elective

Moi Teaching and Referral Hospital developed a venous thromboembolism risk stratification form for all admitted patients, several years ago. However, on random perusal of patients files; few were filled and those filled out were mostly incomplete. Through observation, the prescribed prophylaxis on the treatment sheet do not follow the availed risk scoring, Caprini score system or recommended ACCP guidelines. (*APPENDIX IV*)

1.2 Problem Statement

Venous thromboembolism (VTE) is a silent killer and may present with fatal pulmonary embolism as the first sign. Abdominal surgery and some of the indication are known risk factor for VTE development. However, with appropriate VTE risk stratification and prophylaxis this risk is reduced significantly (geerts 2001).

At MTRH a national teaching and referral hospital, laparotomies are done on a daily basis. From a local study, more than 50% of surgical patients are at moderate or high risk of VTE. Perceived low incidence of VTE has led to failed or suboptimal stratification of laparotomy patients. This results in inappropriate thromboprophylaxis(Of et al., 2018).

Anecdotal evidence has revealed underutilization of availed MTRH venous thromboembolism risk forms, on patient admission files. The forms are never filled or are incomplete at the point of patient discharge from the hospital. This may lead to inappropriate or inadequate prescription of necessary venous thromboprophylaxis in laparotomy patients who are at increased risk of venous thromboembolism. VTE prevention is not only best but cheaper (Heit, 2003)

We have minimal data in our local set up describing the VTE risk profile, thromboprophylaxis practices and incidence of DVT in patients undergoing laparotomy. Our population is largely composed of young persons compared to most high income countries. Adoption of minimally invasive surgery techniques has also been slow in most low income countries. These two factors might lead to a difference in VTE risk profile and DVT incidence in the developed world and our setup.

Guideline protocols developed in other parts of the world might not be suitable for our setup due to different age groups, genetics, clinical indications of our laparotomy patients and use of different operative techniques and perioperative setup. The VTE prevention guidelines ought to take into consideration local workflow and clinical practice for ease of integration into the patients' management system. Thus, necessitating local research on venous thromboembolism risk profile, management practices and incidence of DVT among laparotomy patients.

1.3 Justification

The risk profile and incidence of DVT in our laparotomy patients may be different. This may influence response and choice of thromboprophylaxis method in our resource constrained setup. Thus data from this work will help guide in the future development of local protocols.

In addition to understanding our patients' risk profile for better service delivery, we notice that majority of our patients are young. Therefore, the pre-formed tools may not perfectly fit our patients needs in thromboprophylaxis practices.

Venous thromboprophylaxis warrants individualization and risk stratified approaches to balance safety and efficacy. An understanding of venous thromboembolism risk profile and prophylaxis options are key in developing safe and effective prophylaxis algorithm for caregivers. Research on VTE risk profile and thromboprophylaxis practices will guide in resources necessary and improve utilization of the same. Systematic review of strategies to improve VTE prophylaxis practice reported failure of passive dissemination of prophylaxis guidelines to caregivers. They recommend use of multiple strategies, including but not limited to stratification and prophylaxis reminders to caregivers, audit and feedback to refine and improve interventions (Tooher et al., 2005).

There was therefore an imminent need to conduct a local study to describe risk profile, thromboprophylaxis practices and clinical DVT incidence in patients undergoing laparotomy at MTRH which whose outcomes will guide development of context based guidelines/protocols that are compatible with our population, hence better services and outcomes.

1.4 Research Question

What is the risk profile, thromboprophylaxis practices and clinical DVT incidence among patients undergoing laparotomy at MTRH, Eldoret?

1.5 Objectives

1.5.1 Broad Objective

To describe risk profile, thromboprophylaxis practices and clinical DVT incidence among patients undergoing laparotomy at MTRH, Eldoret.

1.5.2 Specific Objectives

- To assess venous thromboembolism risk profile of patients undergoing laparotomy at MTRH
- 2. To describe thromboprophylaxis practices among patients undergoing laparotomy at MTRH
- To determine the incidence of clinical DVT among patients undergoing laparotomy at MTRH

CHAPTER TWO

2.0 LITERATURE REVIEW

Venous thromboembolism is a condition in which a blood clot forms in the deep veins of the leg, groin or arm (deep venous thrombosis) and potentially travels in the circulation lodging in the lungs (pulmonary embolism) or other parts of the body in patients with patent foramen ovale. VTE is often a life threatening but mostly preventable condition that affects many people worldwide(Cushman et al., 2020).

Globally, VTE has an annual incidence of 0.75-2.69 per 1000 individuals, as described by a systemic review (Raskob et al., 2014). About 60% of VTE occur during or within 90 days of hospitalization, making it the leading cause of preventable hospital death (Porres-Aguilar et al., 2019)(Grosse et al., 2016).

In Africa, the prevalence of post-operative DVT varies from 2.4-9.6% with diagnosis of PE having a case fatality rate of 60% (Danwang, Temgoua, Agbor, Tankeu, & Noubiap, 2017). In Kenya, PE accounts for 14.2% of cardiovascular mortality. Among those admitted with PE, 28.1% of the patients die while 18.1% develop corpulmonale (Ogeng'o, Obimbo, Olabu, Gatonga, & Ong'era, 2011)

Surgery is a well-known risk factor of venous thromboembolism. This risk is determined by a combination of individual predisposing factors and the specific surgery to be performed. In general surgery, rates of DVT and fatal PE without prophylaxis ranges from 15-30% and 0.2- 0.9% respectively (Giancarlo Agnelli, 2004). Prevalence of VTE risk in surgical patients has been reported to be 43.8% in sub Saharan Africa (Kingue et al., 2014). Different surgical disciplines have different VTE risk profile and thrombus prevention requirements. Andrew l. and colleagues, in Uganda, reported that the prevalence of DVT was 5% after performing major

abdominal surgery (Muleledhu et al., 2013).

The clinical presentation of VTE vary, ranging from symptomatic to asymptomatic DVT and PE or a combination of both. Approximately 30% of apparently isolated forms of PE are associated with silent DVT. Patients presenting with DVT symptoms have a frequency of 40-50% of silent PE. (Meignan et al., 2000)

2.1 PATHOPHYSIOLOGY

Rudolf Virchow's triad, described in 1856, (1) venous stasis, (2) hyper-coagulable states and (3) vascular endothelial injury are the pathogenic conditions leading to venous thrombus development. Different combination of these factors lead to venous thrombosis development. Each component of the triad can be caused by various body insults. These insults may work in synergy or influence two or all three components of the triad(Kushner et al., 2022).

The peripheral venous system acts as a conduit to return blood to the heart from the periphery and reservoir to hold extra blood. Calf muscles and deep vein system are a complex array of valves and pump to push blood upward to the heart against gravity. Changes in blood flow pattern, either stasis or turbulence, can be due to general condition such as congestive cardiac failure or local factors such as prolonged dependence of the limb and reduced muscle pumping activity in immobilized patient's post-surgery. Venography studies show delayed clearance of blood from the soleal sinuses and calf muscle in supine surgical patients (Lindström, Ahlman, Jonsson, & Stenqvist, 1977). Anesthesia induction leads to vasodilation, increased venous capacitance and a compromised venous return (Lindström, Ahlman, Jonsson, & Stenqvist, 1984). Half of the surgical patients, at autopsy, have shown evidence of venous thrombi.

Hypercoagulable states can occur due to genetic conditions e.g. thrombophilia disorders, medical conditions like anti-phospholipid syndrome or due to biochemical imbalance e.g. inflammatory reactors released post-surgery. In orthopedic cases it has been shown that release of tissue factor and pro-coagulant proteins leads to formation of thrombi that activates intrapulmonary coagulation (Dahl, 2000). The persistence of a hyper-coagulable state, exposes the patient to dangers of VTE for long periods post-surgery.

Vascular endothelial injury may result from mechanical or chemical trauma. Anesthesia causes loss of muscle tone and the weight of the limb in combination with a hard operating table may damage the venous endothelium. Endothelium can be damaged by exposure to endotoxin, cytokines (e.g. interleukin 1 and tumor necrosis factor), thrombin or low oxygen levels. Endothelial cell injury leads to synthesis of tissue factor and plasminogen activator inhibitor. This, together with internalization of thrombomodulin, promote thrombogenesis. (Dittman & Majerus, 1990)

These factors favor activation of the coagulation system which forms a thrombus in deep veins of the limb. The thrombus may reorganize into a solid plug of collagenous tissue or recanalize to achieve blood re flow or embolization.

Inflammation leads to release of cytokines and chemokines that may increase coagulable states. Thus inflammation has been cited as one of the triggers of thrombi formation. It leads to endothelium destruction and immune response activation that favor thrombogenesis through activation of the coagulation cascade(Branchford & Carpenter, 2018)

Post thrombotic syndrome (PTS) is one of the complications of DVT and arises from re organization of the thrombus. This results in increased venous hypertension that destroys the valves leading to impaired venous system function and presents as chronic venous insufficiency. It is characterized by varicose veins, edema, skin hyperpigmentation, chronic leg pain, induration and ulceration.

Deep venous recurrence is common with higher predisposition to more thrombus formation. Approximately 1 in 6 patients with DVT or PE will have a recurrent VTE at 2 years post initial occurrence. Follow up of patients at 8 years post VTE occurrence, 1 in 3 will have post thrombotic syndrome and nearly 30% will die (Prandoni et al., 1997).

Multiple or single embolization may occur to the pulmonary system and ranges from microscopic to macroscopic thrombi that occlude major branches of pulmonary artery. This leads to ventilation perfusion mismatch and increase in resistance to flow in the pulmonary vessels. PE may occur in isolation or as result of DVT. PE occur in 10% of patients with acute DVT though up to 75% may remain asymptomatic. (McMillian & Rogers, 2016)

2.2 RISK FACTORS

Thrombosis in venous system is a multifactorial disease, with well-established risk factors. Conventional risk factors may be acquired, e.g. immobility, or genetic e.g. factor V Leiden. Different risk factors have varied VTE attributable risk as illustrated in the table below. This forms the basis for stratification of VTE risk.

Conventional factors VT	ris Young k (%)	A Old R AR	Young (%)	Pre C v l d	P Young re (%) v	PAR Old PAR
Immobilization*	50–90	(%) 66–83	10	25	9–47	(%) 33–56
Malignancy†	86	86	3	10	15	35
CHF‡	60–71	33–60	5	22	7–11	10–25
COPD§	50-80	33	1	11	1–4	5
DM	50	0–50	6	16	6	0–14
HRT use**	50	50	4	1	4	1
Genetic _factors††	67–86	5080	7	7	12-30	7–22

Table 1: Conventional risk factors of venous thrombosis: attributable and population attributable risks in the young and older population

VT, venous thrombosis; Young, young and middle-aged population (< 65 years old); Old, older population (≥ 65 years old); AR, attributable risk; Prev, prevalence; PAR, population attributable risk; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; HRT, hormone replacement therapy (Engbers, van Hylckama Vlieg, & Rosendaal, 2010)

As the number of VTE risk factors increase in an individual patient, so does the risk of venous thrombus development. There's convincing evidence that risk of VTE increases in proportion to the number of predisposing factors. Then figure below illustrates rise in deep venous thrombosis as the number of risk factors increase.

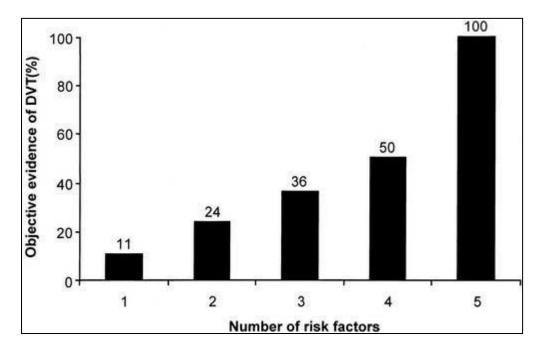


Figure 1: The proportion of patients with clinically suspected deep vein thrombosis in whom the diagnosis was confirmed by objective testing increases with the number of risk factors. (Data adapted from Wheeler et al. *ArchSurg.* 1982; 117:1206–1209.

The individual risk of VTE varies as a result of complex interaction between congenital and transient or permanent acquired risk factors. However, some risk factors have greater odds of VTE development than others. Risk factors that demonstrated increased risk of VTE include increasing age, prolonged immobility, malignancy, major surgery, multiple trauma, prior VTE and chronic heart failure. Below is a table categorizing the different risk factors with their odds of association with venous thrombus formation.

Table 2: Risk Factors for VTE

Strong risk factors (odds ratio >10)

Fracture (hip or leg)

Hip or knee replacement

Major general surgery

Major trauma

Spinal cord injury

Moderate risk factors (odds ratio 2-9)

Arthroscopic knee surgery

Central venous lines

Chemotherapy

Congestive heart or respiratory failure

Hormone replacement therapy

Malignancy

Oral contraceptive therapy

Paralytic stroke

Pregnancy/, postpartum

Previous venous thromboembolism

Thrombophilia

Weak risk factors (odds ratio <2)

Bed rest >3 days Immobility due to sitting (e.g. prolonged car or air travel) Increasing age Laparoscopic surgery (e.g. cholecystectomy) Obesity Pregnancy/, antepartum Varicose veins

(Anderson & Spencer, 2003)

2.3 Surgery

Major general surgery, i.e. abdominal or thoracic surgery lasting more than 45 minutes, is extensively documented as one of the highest risk of developing VTE. With an incidence of DVT reported to be up to 30%. Other surgeries have variable VTE risk, with major orthopedic procedures having the highest odds of venous thrombus formation. The incidence of VTE in patients operated by general surgeons has been reported to be as high as 25%, without prophylaxis visa vie 1.4-7.3% VTE incidence after surgery while utilizing thromboprophylaxis (Mukherjee et al., 2008). A weighted risk index quantifying 90-day VTE risk among surgical patients, identified an 18-fold variation in VTE risk among the overall surgical population. (Pannucci, Laird, Dimick, Campbell, & Henke, 2014)

Abdominal surgery leads to a hyper coagulable state, and an associated increased risk of deep vein thrombosis (DVT). Surgery increases thrombus formation. As the body digests the thrombus, the thrombus degradation product can be measured to assess the degree of thrombus occurrence. Measurement of fibrin monomers and fibrin D dimers in plasma during pre, peri- and post-surgical period demonstrated significant high levels on day 14 post abdominal surgery (Galster, Kolb, Kohsytorz, & Paal, 2000)

Patient factors and some surgical compilations may increase the risk of VTE associated with surgery. Inflammation, advanced age, sepsis, long duration of surgery, and coagulopathy are often present in patients undergoing major emergency abdominal surgery. These are known to increase the risk of developing VTE in surgical patients (Pannucci et al., 2012)

The hypercoagulable state may persist beyond surgery time, in hospital stay and discharge from hospital. Patients undergoing laparoscopic cholecystectomy and

hernia surgery have persistence of hypercoagulability factors post-surgery, even a month after surgery, with low prevalence of VTE at 0.46% (Ulrych et al., 2016).

The incidence of venous thromboembolism is higher in open abdominal surgery than laparoscopic surgery. The odds of developing venous thromboembolism in an open surgery was 1.8 times that of laparoscopic surgery. The incidence of VTE in open surgery was 0.59% compared to 0.28% in minimally invasive surgical cases(Nguyen et al., 2007). In a multivariate analysis, open surgery, old age, steroid use, infection, reoperation, prolonged ventilation and low albumin were associated with higher risk of venous thromboembolism. The incidence of venous thromboembolism was 1.25% in laparoscopic surgery vs 2.9% in open surgery. The difference was statistically significant(Shapiro et al., 2011).

However, some studies have found out the incidence of venous thromboembolism, in laparoscopic colorectal cancer surgery, to be 17% when using heparin prophylaxis. This is similar to the risk of VTE in open colorectal cancer surgery. This may suggest the role of other risk factors of thrombi formation in these surgical patients(Becattini et al., 2015). In this study most of the thrombi were in the lower limbs and the incidence of symptomatic deep venous thrombosis was 2%.

In colorectal surgery, diverticular disease surgery is associated with less venous thromboembolism risk when done laparoscopically. The highest incidence of venous thromboembolism was associated with rectal resection at 2.8%, and right and sigmoid colectomy done laparoscopically had lower rates of venous thromboembolism development (Buchberg et al., 2011). They concluded that open surgery had a significant higher risk of venous thromboembolism compared to laparoscopic colectomy.

Use of pharmacological thromboprophylaxis is associated with increased risk of bleeding. A study comparing the bleeding risk in open versus laparoscopic surgery, in Japanese patients, found higher risk of bleeding in laparoscopic colorectal cancer surgery than open surgery. Other factors related to the bleeding were, male gender and low platelet count(Yasui et al., 2017)

Operating time has a direct relationship with development of venous thromboembolism. Longer surgery duration is associated with blood stasis, vascular trauma and hypercoagulability, all components of Virchow's triad. This predisposes to thrombi formation in the limbs which may migrate into the venous blood stream, i.e. venous thromboembolism(Kim et al., 2015).

The duration of surgery and anesthesia has been associated with increased risk of venous thromboembolism development. Duration of surgery can be used to categories operations to major or minor. Surgeries lasting more than 45 minutes are categorized as major while those lasting less than this time as minor (Golemi et al., 2019)

2.4 Malignancy

There is a 7-fold increase in overall risk of VTE in cancer patients (Heit et al., 2002). The type of cancer, location of primary tumor, metastasis of the cancer and cancer therapy determine the relative risk of developing VTE. The frequency of VTE increases 2 to 3 fold in patients undergoing surgery for malignant disease compared to those with nonmalignant conditions. Advanced cancers of the breast, lung, brain, pelvis, rectum, pancreas and gastrointestinal tract are associated with higher incidence of VTE. (Maclellan, Richardson, & Stoodley, 2012). Patients with malignancy have a higher risk of venous thromboembolism post discharge from hospital.

The duration from cancer diagnosis and VTE development may determine the type and site of thrombus development. The patients who develop venous thromboembolism early tend to present with pulmonary embolism(Bustos Merlo et al., 2017). The incidence of venous thromboembolism is high in the first 6 months after diagnosis of cancer and this risk declines over time. Other factors related to the carcinoma may further predispose to increased risk of VTE. Associated medical comorbidities and metastatic disease had a strong correlation with venous thromboembolism development(Alcalay et al., 2006).

Cancer treatment for example chemotherapy increases the risk for VTE development. The chemotherapy regimen used might alter the coagulation factors favoring VTE occurrence. It has been shown that women with breast cancer who undergo surgery combined with chemotherapy have three times higher risk of VTE development compared with those undergoing surgery alone (Clahsen, Van De Velde, Julien, Floiras, & Mignolet, 1994)

2.5 Multiple trauma

Trauma is described as an independent risk of VTE development. Geertz et al found deep venous thrombosis in 47% of trauma patients. Approximately, 40% of patients with trauma to the face, chest or abdomen as a primary site of injury had a DVT. This compares to 56% DVT cases in those with lower limb or pelvic injury. (William H. Geerts, Code, Jay, Chen, & Szalai, 1994). Above confirms the high incidence of VTE in trauma patient despite the site of the body involved with trauma.

Due to the high anti-Xa levels and higher VTE incidence in trauma patients, standard dosing of enoxaparin 30mg twice a day has been questioned. Adjusting enoxaparin dose by anti-Xa levels led to a lower VTE incidence in trauma patient. Enoxaparin dose of 0.5mg/kg/dose twice a day was associated with achieving targeted anti-Xa

levels in trauma patients(Walker et al., 2017)

2.6 Age

There is a significant increase in risk of VTE in those above 40 years and the risk approximately doubles with each subsequent decade. VTE is rare in children and young patients with venous thrombosis have a strong predisposing factor, genetic or acquired. (Perlmutt & Fellows, 1983). Below is graph illustrating the increase in incidence of VTE with advance in age.

Incidence of VTE increases with age, (Silverstein et al., 1998)

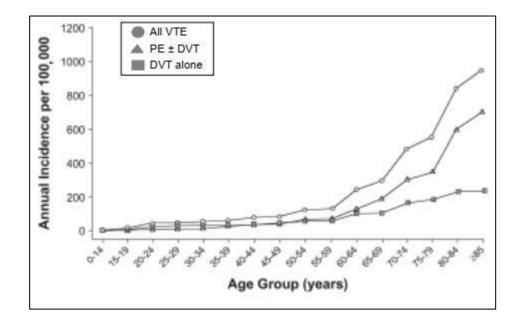


Figure 2: Incidence of VTE increases with age

Infection leads to activation of coagulation factors in the coagulation cascade resulting in thrombi formation. The inflammatory response provoked by sepsis causes an imbalance in the pro-coagulant and anti-coagulant mechanisms. This favors downregulation of natural anticoagulants, platelet activation and increased fibrin production that culminate in thrombi formation(*Venous Thromboembolism in Patients with Intra-Abdominal Infections – Global Alliance for Infections in Surgery*, n.d.)

The association between infection and VTE is time dependent. In a case control study in Denmark, the association between infection and venous thromboembolism was found to be highest in the first two weeks of infection onset. This VTE risk gradually declines thereafter as the infection resolves(Schmidt et al., 2012).

Dr. Cohoon and colleagues reported that most infections were strongly associated with venous thromboembolism development. Infections may occur as a complication of surgery or as the indication for surgery i.e. peritonitis. Intra-abdominal infections were associated with the highest odds for venous thromboembolism occurrence(Cohoon et al., 2018).

2.6 Other risk factors

Other risk factors of venous thromboembolism include congestive heart failure and respiratory failure. In the Prophylaxis in Medical Patients with Enoxaparin (MEDENOX) trial, 15% of patients with class III or IV heart failure treated with placebo had a confirmed episode of VTE (Samama et al., 1999)

Obesity or overweight may increase risk of VTE but the association is weak. Studies in this class of patients have not shown statistically significant increase in VTE incidence (Printen, Miller, Mason, & Barnes, 1978)

The influence of immobility as a risk factor is evident in hemiplegic studies where asymptomatic DVT has been reported in 60% of the paralyzed limb of stroke patient's vs. 7% in the non-paralyzed limb (Warlow, Ogston, & Douglas, 1972). Prolonged immobilization combined with other major risk factors increase the likelihood of VTE. Patients are encouraged to mobilize early post-surgery to reduce the risk of VTE.

In women, pregnancy, puerperium and use of oral estrogen contraceptives have been associated with a higher odd of VTE. Hereditary VTE risk factors contribute to overall risk of VTE in patients undergoing surgery. We have no local data on the distribution of this condition in our region but below is distribution from western world.

Inherited thrombophilic defects and estimated prevalence				
Inherited/genetic	General population	VTE population		
Antithrombin deficiency	0.3%	3%		
Protein C deficiency	0.3%	3%		
Protein S deficiency	0.3%	3%		
Factor V Leiden	4-6%	10-18%		
Prothrombin G20210A	2-3%	6-18%		
Hyperhomocysteinaemia	5%	10-18%		
Elevated factor VIIIc	6-8%	10-15%		

Table 3: Inherited thrombophilic Defects and estimated prevalence

Adapted from, (Hampton, 2001)

2.7 Clinical Manifestation and Diagnosis

2.7.1 Deep Venous Thrombosis (DVT)

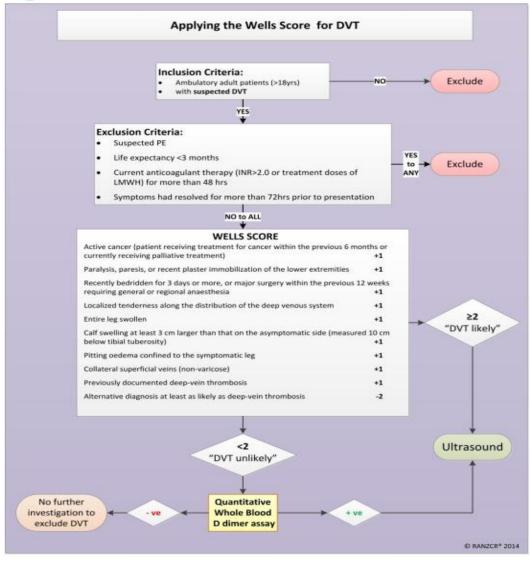
Deep venous thrombosis commonly develops in the venous system of the lower limbs. However, patients with risk factors like upper limb catheters i.e. central venous dialysis catheters may develop DVTs in the upper limb. The most common symptom is unilateral extremity pain of sudden onset with associated leg or limb swelling and warm skin to touch(Bulger et al., 2004).

Diagnosis of a venous thrombosis from a clinical assessment alone might be a challenge. This is due to the many differential diagnoses of the above common sign and symptoms. Scoring systems have been developed to assist in narrowing down the diagnosis. This score help assess which patients require as test to confirm the diagnosis. Confirmation tests are expensive and some are invasive. Well's score is widely used as it is simple and can be utilized in resource constrained settings.

Wells score of less than 2 has been shown to reliably rule out DVT(Modi et al., 2016). It's specificity has been reported to be 93% but with the sensitivity of 24% for proximal DVT (Sartori et al., 2019) . Other studies have reported a negative predictive value of 99% of Wells score in the diagnosis of both proximal and distal limb thrombosis.(Ambid-Lacombe et al., 2009)

A cross sectional study done at MTRH, to validate the Wells' score in African patient suspected to have DVT, reported a sensitivity of 97.5% and a specificity of 82.4%. DVT was confirmed in 96% of the patients who had a high probability i.e. well score more than 1. They found a strong agreement between Doppler ultrasound findings and Wells score with a kappa value of 0.817(Aliyan et al., 2015). Below is the Kenyan Ministry of Health recommended algorithm for diagnosis of DVT;

Algorithm:

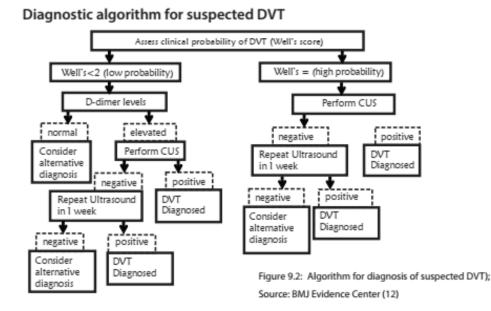


(Office et al., 2000)

The 2018 Kenya cardiovascular diseases guidelines recommend compression ultrasonography (CUS) as the gold standard for diagnosing extremity DVT. CT scan, MRI and contrast venography are reserved for evaluating vein segments not easily assessed by CUS e.g. subclavian vein and pelvic veins(MoH-Kenya, 2018).

Plasma D –dimers are elevated in VTE and is a marker of fibrin degradation. It's very useful in evaluating patients in the casualty setting. D dimers may be positive but CUS shows no evidence of DVT. It may be elevated in other conditions like myocardial infarction, heart failure, infection, pregnancy and surgery. After surgery,

the plasma D- dimers are almost always elevated as one of the markers of inflammation from the surgery or the indication of surgery. Thus the predictive value of D dimers in the diagnosis of deep venous thrombosis post-surgery is low (Bara et al., 1999). Researchers have over the years tried to determine the D dimer elevation level that predict VTE post-surgery. This requires pre-operative measurement of the D dimer levels and serial measurement thereafter, to determine the rise. However, the type of surgery, operation time and pre-operative D dimer levels all influence the magnitude of D dimer elevation and thus the interpretation(Dindo et al., 2009)



Kenya National Guidelines for Cardiovascular Diseases Management

Figure 3: Diagnostic algorithm for suspected DVT

(MoH-Kenya, 2018)

Post-operative DVT incidence varies in different parts of the world. The difference depends on the thromboprophylaxis practices undertaken and the risk profile of the patients. In Africa, the prevalence of deep venous thrombosis has been estimated to be 2.4 to 9.6% in surgical patients in a systematic review (Danwang et al., 2017). A

Nigerian study, had 2.2% incidence of DVT post-surgery (Osime et al., 1976). This contrasts a study done in Denmark where the incidence of VTE was 1.1% (Balachandran et al., 2020). All patients received pharmacological prophylaxis as recommended by ACCP. Tomas and colleagues found an incidence of DVT to be 0.2%, though their subjects were morbidly obese and prophylaxis was utilized in all patients (Escalante-Tattersfield et al., 2008). In Middle East, the incidence of venous thromboembolism has been quoted as 7.1% in critically ill patients post-surgery (Arabi et al., 2013).

2.7.2 Acute Pulmonary Embolism

Pulmonary embolism has a wide range of presentation and often nonspecific symptoms. These include; unexplained dyspnea of sudden onset, chest pain, syncope, tachycardia, distended neck veins and/or death. The symptoms results from obstruction of the large pulmonary arterial tree leading to perfusion ventilation mismatch and increased right ventricular afterload(Hepburn-Brown et al., 2019).

Diagnosis of acute pulmonary embolism calls for a combination of clinical assessment and the use predictive rules as stipulated by the 2018 cardiovascular guidelines. Imaging is used to confirm the diagnosis. Below is the Well score system for pulmonary embolism

Clinical Feature	Score		
Previous PE or DVT	1		
Pulse ≥ 100 beats/minute	1		
Surgery or immobilization within the past 4 weeks	1		
Hemoptysis	1		
Active cancer	1		
Clinical signs of DVT	1		
Alternative diagnosis less likely than PE	1		
Clinical Probability			
PE likely	≥2		
PE unlikely	0-1		

D-dimers testing is done in patients suspected of having a PE. It is not advocated in patients with a high clinical probability, post-surgery or hospitalized patients. Other markers i.e. troponin and NT-Pro BNP are done to assess prognosis. CTPA (computed tomographic angiography) is diagnostic of PE.(MoH-Kenya, 2018)

The Ministry of Health (MOH) in Kenya advocates for VTE prophylaxis in all hospitalized patients after VTE risk assessment.

2.8 Risk Assessment

Providing appropriate thromboprophylaxis to surgical patients is complex as its administration carries the risk of adverse effects such as bleeding. Thus the need for assessment of risk profile that dictates the type and amount of prophylaxis to be administered. We have no local data on incidence, risk profile, and thromboprophylaxis practices to guide in protocols for thromboprophylaxis.

American College of Chest Physician (ACCP), on Antithrombotic Therapy and Prevention of Thrombosis, ninth edition (AT9) provided recommendations, for thromboprophylaxis in non-orthopedic surgical patients. It compiles relevant medical literature as interpreted by some of the foremost authorities in the field. It endorses the use of risk assessment models to help guide the type of prophylaxis to be employed as they grade patients per the risk of VTE(Geerts et al., 2004).

Standardized VTE prevention protocol and order set implementation results in improved and sustained utilization of adequate VTE prophylaxis in the inpatient population(Maynard et al., 2010).

Multiple quantitative risk assessment models exist for clinical practice. Rogers score and Caprini Score are recognized by ACCP ninth edition as risk assessment tools for the non-orthopedic surgical population (W. H. Geerts et al., 2001). Rogers has been validated in few studies in general, thoracic and vascular surgery. Categorization by which variables are assigned point values in Rogers Scoring are cumbersome and not easy to follow (Laryea & Champagne, 2013). This makes it unfavorable for routine use in clinical practice.

The Padua score is devised for medical patients and its use in surgical patients has not been validated. The score categorizes patients based on different parameters into a score that ranges from 0 to 20 points. A patient who scores 4 or more points is considered high risk and pharmacoprophylaxis is indicated. Those who score less than 4 are considered low risk patients and pharmaco-prophylaxis is not indicated. A study comparing Padua score utilization, in surgical patients, with Caprini score reported moderate correlation with about 85 patients (40%) having high a Caprini score and a discordant Padua score. Adverse outcome, incidence, did not differ in the two groups(H.-P. Yu et al., 2022). The study concluded that the Caprini score is more sensitive in surgical patients than Padua score.

Despite existence and development of these risk categorization models, most surgeons still use 'one dose fits' all prophylaxis for postoperative venous thromboprophylaxis. Other surgeons perceive the risk of bleeding to be higher than the need for thromboprophylaxis. The risk assessment score is an objective way of determining who requires prophylaxis and to what extent as per the risk profile. Research has shown that scoring methods are valid and allow individualized assessment and proper prophylaxis(Bahl et al., 2010)

2.9 Caprini risk assessment tool for VTE

First published in 1991, the risk assessment scoring was developed by a group of physicians and nurses led by Dr. Caprini. Individual risk factors were assigned points according to their relative risk of resulting in thrombotic event. (Caprini, Arcelus, Hasty, Tamhane, & Fabrega, 1991). Thrombotic events rates increase exponentially with increase in score. Patients are categorized as low, moderate and high risk to determine type, duration and strength of prophylaxis to be used.

Caprini risk assessment model (RAM) has been validated in over 100 clinical trials worldwide (Cronin et al., 2019). The cutoff score varies depending on the surgical population being tested. ACCP 9th guidelines on thrombosis (AT9) defines 5 or more score as the high risk group in general surgery patients. Individualization of prophylaxis treatment based on calculated risk profile will avoid unnecessary prophylaxis for low risk patients and provide prophylaxis for high risk patients. Caprini is easy to use and appears to discriminate reasonably well among surgical patients at low, moderate and high risk for VTE. (W. H. Geerts et al., 2001)

The Caprini score is also applicable to other surgical fields, i.e. endocrine surgery, gynecological and neurosurgery(O'Donnell & Weitz, 2003a). It is considered acceptable by most bariatric and vascular surgeons. (Pannucci et al., 2014) . In plastic and reconstructive surgery the scoring is modified due to the different estimated VTE risk in this group(Mittal et al., 2019)

The estimated risk of VTE after caprini scoring has been estimated for the various risk category group described. This enables appropriate selection of an individualized prophylaxis method with reduced risk of bleeding or undesired side effects.

A high Caprini score is associated with a higher incidence of a post-operative deep venous thrombosis. Patients scoring higher than 11 points had 98.4-fold increase in the risk of deep venous thrombosis(Lobastov et al., 2016). This group of patients require a more effective and prolonged thrombi prophylactic regimen.

Data has shown that failure to use risk stratification result in, high risk patients receiving inadequate prophylaxis while low risk patients receiving unwarranted prophylaxis with increased risk of adverse effects. Standardized risk assessment enable proper prophylaxis administration with fewer side effects(Cassidy et al., 2014)

2.10 Thromboprophylaxis

Thromboprophylaxis is any measure that has been recognized as an effective intervention to reduce the incidence of deep venous thrombosis and PE. There are both mechanical and pharmacological methods to achieve venous thromboprophylaxis. The mechanical methods prevent stagnation of venous blood in the lower limb by enhancing venous outflow. The pharmacological methods prevent venous thrombosis formation by attenuating coagulation cascade system(O'Donnell & Weitz, 2003b)

The choice of prophylaxis to be prescribed and administered should be individualized with respect to the pre-operative, intra-operative and post-operative period. Venous thromboembolism risk stratification helps tailor the prescription. The main role of prophylaxis is to reduce the risk of developing deep vein thrombosis and pulmonary embolism but not eradicate the events or mortality associated with them. (Collins et al., 1988)(Di Nisio et al., 2015)

Due to the associated side effects of most VTE prophylaxis methods, judicious use is warranted to minimize these effects. This led to formulation of stratification scores to help choose the appropriate prophylaxis. In developed countries, use of electronic alerts and program audit have been employed to facilitate proper thromboprophylaxis and reduce preventable VTE (Smith, 2005)(Tooher et al., 2005). The incorporation of multiple strategies has been associated with improved effectiveness in risk stratification and improvement in recommended thromboprophylaxis prescription.

In most centers, worldwide there is a reported low compliance to VTE prophylaxis guidelines. This is associated with omitted prescriptions, wrong anticoagulant type and dosage, and inadequate duration of the prophylaxis(H. T. Yu et al., 2007)(Of et al., 2018)(Kingue et al., 2014a)

A study in Nigeria, assessing a prescriber's knowledge and prescription practices, revealed a low knowledge of venous thromboprophylaxis at 33.3% and no departmental guidelines on VTE prevention in the surgical units. Most of the surgeons interviewed, 76.2% had lost a patient due to thrombi embolization (Kesieme et al., 2016).

Various venous thromboembolism risk reduction methods are described below;

2.10.1 Early ambulation

Literature from orthopedic patients has proven that failure to ambulate by the second day post-surgery is associated with an increased risk of venous thromboembolism(Sadeghi et al., 2012). Most surgeons encourage their patients to mobilize as soon as it is feasible post-operatively to reduce the risk of pulmonary complication and venous thromboembolism.

Ambulation after surgery should be done early and frequently. In bariatric surgery, use of a post-operative activity tracker have been used to assess the number of inpatients steps and assess how patients characteristics affect mobilization(Reed et al.,

2021). The tracker did not affect the post-operative activity. In this study, advanced age was associated with low mobilization post-operatively.

Early mobilization is part of enhanced recovery after surgery(ERAS) protocol. The protocol improves the outcome of surgery and helps reduce cost by lowering complications and hospital stay(Hu et al., 2019). Time from surgery to initial mobilization post-surgery and incision utilized during surgery are independently associated with postoperative pulmonary complications like pulmonary embolism. Patients may have up to 3 times more risk of postoperative pulmonary complications, for each day not mobilized(Haines et al., 2013).

Early postoperative mobilization with mandatory venous thromboembolism risk stratification is associated with reduced likelihood of deep venous thrombosis and pulmonary embolism. The incidence of deep venous thrombosis and pulmonary embolism reduced by 84% and 55% respectively by following these measures(Cassidy et al., 2014).

Mobilization has been recommended by thromboprophylaxis guidelines from, ACCP. Patients at low risk of VTE development are advised to ambulate early to reduce risk of VTE post-surgery. Use of heparin in this low VTE group is associated with higher risk of bleeding than the benefit gained in VTE prophylaxis (Geahchan, Basile, Tohmeh, & DIONYS registry, 2016)

2.10.1 Mechanical Thromboprophylaxis

Mechanical methods of thromboprophylaxis include graduated compression stockings (GCS) or elastic stocking, intermittent pneumatic compression (IPC) and venous foot pump. The American College of Chest Physician propose use of intermittent pneumatic compression, though no data shows superiority in the three methods(Morris & Woodcock, 2010).

Some studies have shown similar rates of symptomatic venous thromboembolism events with or without use of additional mechanical methods of prophylaxis(Haas et al., 2016). Despite this observation mechanical methods are still used as most studies have shown their efficacy and their role in patients with higher risk of bleeding or contra indication to pharmacological prophylaxis.

Elastic stockings (ES) or Graduated compression stocking

A Cochrane review of trials comparing elastic stocking without chemoprophylaxis revealed that elastic stockings reduced the odds for DVT development by 65% but reduction in proximal DVT and PE were neither confirmed nor excluded. (Roderick et al., 2005). Graduated compression stocking are effective in reducing the risk of deep venous thrombosis and the effect is higher when combined with other methods of prophylaxis(Sachdeva et al., 2010). Research has demonstrated that, graduated compression stockings reduce the risk of deep venous thrombosis in general and orthopedic surgery patients. The reduction in proximal deep venous thrombosis and pulmonary embolism is of moderate and low risk, respectively(Sachdeva et al., 2018) Zareba et al in their systematic review of literature concluded that combined compression and chemoprophylaxis was more effective in preventing postoperative deep venous thrombosis than when either modality is used alone. Nonetheless, adding chemoprophylaxis was associated with an increased risk of bleeding and VTE risk

reduction. Adding compression devices, had low evidence of reducing VTE occurrence(Zareba et al., 2014).

Compression devices are associated with a risk of skin complication such as skin. breaks, ulcers, blisters, and necrosis. In one study, skin complications were reported in 3.9% of patients using compression stockings however, the study demonstrated the effectiveness of compression stockings. Thigh length stockings reduced the risk of symptomatic or asymptomatic proximal DVT by 31% compared to calf length with an absolute difference of 2.5% (Dennis et al., 2010)

Availability, quality and cost were stated as some of the challenges of graduated compression stocking use among COSECSA surgeons (Ndeleva & Lakati, 2018)

2.10.2 Intermittent pneumatic compression (IPC)

Intermittent pneumatic compression is thought to enhance blood flow in the deep veins of the lower limb, thus preventing venous stasis. Stasis is one of the components of Virchows triad. They also increase endogenous fibrinolytic activity by lowering plasminogen inhibitors(Roberts et al., 1972)(Comerota et al., 1997)

Intermittent pneumatic compression reduced the risk of DVT by 60% compared with no prophylaxis from analysis of trials (Jennions, Lortie, Rosenberg, & Rothstein, 2013)(Urbankova et al., 2005). Use of intermittent pneumatic compression stockings are associated with lower risk of venous thromboembolism and the association was shown to be consistent in the various heparin types(Arabi et al., 2013). IPC reduced the relative risk of deep venous thrombosis by 62% compared to placebo and 47% compared to graduated compression stockings. However, they were not protective against pulmonary embolism(Epstein, 2005) Patients who have low risk of venous thromboembolism, about 1.5%, benefit from mechanical prophylaxis with no risk of bleeding compared to heparin use. Metaanalysis suggest that the reduction of risk is similar for mechanical and heparin prophylaxis in this risk category. Thus guidelines favor mechanical prophylaxis over chemoprophylaxis due to the bleeding risk associated with chemoprophylaxis(Eppsteiner et al., 2010)

In high risk patients, combining chemoprophylaxis with intermittent pneumatic compression has been shown to be more effective than IPC alone(Ho & Tan, 2013). It is important to note that the combination had no effect on incidence of venous thromboembolism (Kakkos et al., 2016). Mechanical prophylaxis has a role in patients with high risk of bleeding or contraindication to heparin. In patients with a high bleeding risk, the intermittent pneumatic compression maybe commenced as the risk is being controlled. Mechanical compression, chemoprophylaxis and use of regional anesthesia have been associated with reduction of venous thromboembolism in high risk patients (Roderick et al., 2005) . From United Kingdom guidelines, there is no significant difference in thigh and knee length intermittent pneumatic compression devices.

Adherence is less than optimal on those prescribed for IPC, with only 19% of patients observed to have full adherence in 227 non ambulatory trauma patients though adherence across all six measurements was 53% (Edward e. cornwell, 2002). Improper fit and discomfort are other major issues that interfere with efficacy of intermittent pneumatic compression. In an observational prospective study, there was 49% error in device application and this did not differ in type or frequency between day shifts(Elpern et al., 2013). Cornwell et al, noted that half of the patients were not

compliant to sequential compression device and less than 20 percent of the patients had the devices on at any particular time of observation (edward e. cornwell, 2002) Intermittent pneumatic compression may not be appropriate in patients with extensive burns, amputees and extensive skin lesions. It is also contraindicated in patients with peripheral vascular disease due to the risk of compromising blood supply to the limbs. They are worn pre-operatively, continued in the intraoperative and post-operative period. Post-surgery, they can be removed when the patient is ambulating and refitted when the patient is lying or sitting(Clements et al., 2009)

2.10.3 Venous foot pump

These stimulate lower limb venous flow thus preventing thrombi formation. They are used in combination with other prophylaxis methods to lower the incidence of venous thromboembolism(Pour et al., 2013). The mechanism of action is not well understood but the anatomical arrangement of venous arches on the foot and their physiology might have a role(Corley et al., 2010).

2.11 Pharmacological

Guidelines recommend taking into account patient-specific and procedure specific risk of bleeding before initiation of pharmacological prophylaxis (Encke et al., 2016). The liver and kidney functions should be assessed in deciding the regimen and administering anticoagulant medications. Most of the drugs are metabolized by the liver and kidney.

2.11.1 Heparin

Heparin is an indirect thrombin inhibitor as it binds to ant thrombin III (AT) enhancing its activity against factor Xa in the coagulation cascade. It is a heterogeneous mixture of sulfated mucopolysaccharide that binds to AT, accelerating inhibition of protease clotting factors, IIa, IXa and Xa, by forming equimolar complexes. The pentasaccharide sequence has the highest affinity for ant thrombin III. Unfractionated heparin has a high molecular weight. However, the low molecular weight heparin has a shorter chain and inhibits Xa with less activity on IIa (thrombin). The low molecular weight heparin has equal efficacy, increased bioavailability and less frequent dosing requirements. Enoxaparin (clexane), dalteparin and tinzaparin are some of the available low molecular weight heparin. Fondaparinux is a synthetic pentasaccharide((UK), 2010).

Heparin is monitored using activated partial thromboplastin time(aPTT). Nevertheless, low molecular weight heparin weight based dosing results in predictable pharmacokinetics and plasm levels when the renal function is normal. Thus monitoring is not routinely done except in renal failure, obesity and pregnancy.

The major toxicity of heparin is bleeding though heparin induced thrombocytopenia may occur in about 1-4% of patients on unfractionated heparin. Thus, it is important to monitor platelet count before administration and frequently thereafter. Heparin is contra indicated in patients with hypersensitivity to the drug, active bleeding, heparin induced thrombocytopenia, intracranial hemorrhage, ulcerative lesion of the gastrointestinal tract, advanced hepatic disease and renal disease.

Protamine sulfate is a specific antagonist of heparin. Its highly basic and positively charged to combine with negatively charged heparin molecules. Neutralization of low molecular weight heparin by protamine is incomplete. Protamine dose not reverse the effects of fondaparinux.

ACCP ninth edition analysis of data revealed that low dose unfractionated heparin(LDUH) was associated with 18% reduction in odds of death from any cause, 47% reduction in odds of fatal PE and 41% reduction in odds of nonfatal PE, along with 57% increase in odds of nonfatal major bleeding (William H. Geerts et al., 2001)

Low molecular weight heparin (LMWH) was associated with 70% reduction in clinical VTE and a possible reduction in the risk of death from venous thromboembolism (risk ratio [RR], 0.54; 95% CI, 0.27-1.10). LMWH led to an approximate doubling of the risks of major bleeding (RR, 2.03; 95% CI, 1.37- 3.01) and wound hematoma (RR, 1.88; 95% CI, 1.54-2.28) (Mismetti, Laporte, Darmon, Buchmüller, & Decousus, 2001). The study concluded that low molecular weight heparin is as safe and effective as unfractionated heparin in thromboprophylaxis.

Low dose heparin is safe for thromboprophylaxis as it is associated with less bleeding complications and reduces thromboembolism risk(Leonardi et al., 2006a). Low molecular weight heparin has the same efficacy as unfractionated heparin but with a safer clinical profile(Bergqvist & Victor, 1998). Low molecular weight heparin has a higher benefit to risk ratio compared to unfractionated heparin, in preventing post-operative thrombosis (Leizorovicz et al., 1992). Low molecular weight heparin was superior to unfractionated heparin in reducing deep venous thrombosis with no difference in rates of pulmonary embolism and bleeding (Akl et al., 2008) . A randomized control trial on 115 patients concluded that enoxaparin 40mg once daily was as effective and safe as three times daily dosing of unfractionated heparin (Colwell et al., 1994)(McLeod et al., 2001)

Analysis of random control trials have not demonstrated a statistically significant difference in the initiation of heparin pre-operatively, intraoperative or post-operatively ((UK), 2010). The duration of heparin administration is dependent on the risk category of venous thromboembolism and persistence of the risk factor post-surgery. In cancer patient, extended prophylaxis to four weeks' post-surgery has been shown to be safe and effective in reducing the incidence of thrombi formation(Bergqvist et al., 2002)(Rasmussen, 2002). Four week thromboprophylaxis

with dalteparin after major abdominal surgery was associated with a reduced rate of venous thromboembolism with no rise in risk of bleeding compared to one-week prophylaxis(Rasmussen et al., 2006).

A retrospective study on twice a day enoxaparin vs once a day dosing did not show any statistical significant difference in venous thromboembolism risk reduction or clinically significant bleeding in trauma patients(Bush et al., 2011). In trauma patients, use of low molecular weight heparin was found to be superior in lowering the incidence of mortality and venous thromboembolism events(Jacobs et al., 2017)(Byrne et al., 2017).

Some studies have shown sub prophylactic peak of anti-Xa levels in cancer patients with enoxaparin 40mg once daily dosing, thus recommending studies to determine a more effective and safe dose of enoxaparin(Kramme et al., 2020).

Low molecular weight heparin can be initiated the night before surgery but the rest, i.e. fondaparinux and NOACs should be initiated post operatively(Encke et al., 2016). The risk of epidural hematomas will guide special timing intervals of prophylactic medication in spinal and epidural anesthesia.

2.11.2 Fondaparinux

Fondaparinux was associated with a possible reduction in asymptomatic or symptomatic DVT (RR, 0.75; 95% CI,0.52-1.09), but results failed to demonstrate or exclude differences in the risks of fatal PE and nonfatal symptomatic VTE. There was a possible increase in the risk of nonfatal major bleeding with fondaparinux (RR, 1.43; 95% CI, 0.93-2.21), but differences in the risks of fatal bleeding and bleeding requiring reoperation were neither confirmed nor excluded. (G. Agnelli, Bergqvist, Cohen, Callus, & Gent, 2005). Post-operative fondaparinux was as effective as low molecular weight heparin in abdominal surgery patients. The odds of developing a

venous thromboembolism were 0.49 times the odds in the low molecular weight heparin group in a polled analysis. Nonetheless, the risk of bleeding was increased by 1.48 times(Kumar et al., 2019)

2.11.3 Low dose aspirin

Aspirin, acetylsalicylic acid, is a COX inhibitor leading to decreased generation of thromboxane an important platelet activator and aggregator. It may also have a role in reducing thrombin formation and tissue factor expression. At low dose it has sufficient inhibitory effects on thromboxane synthesis while high dose have lower effects (Diep & Garcia, 2020) . In orthopedic patients, use of low dose aspirin for 4 weeks was not inferior to high dose aspirin for a longer duration (Azboy et al., 2020) There are no studies of low dose aspirin in non-orthopedic surgical patients and the Antithrombotic and Thrombotic Therapy guidelines, 9th edition, final conference voted against use of low dose aspirin as an alternative for pharmacological prophylaxis. It is to be used only in circumstances in which LDUH and LMWH are contraindicated or not available.

Vitamin k antagonist (VKA)

Warfarin and related vitamin k antagonists block vitamin k epoxide reductase complex in the liver. This leads to depletion of the reduced form of vitamin k that serves as a cofactor for gamma carboxylation of vitamin k-dependent coagulation factors(Ansell et al., 2008). The factors include; factor II(prothrombin), VII.IX and X. Without gamma carboxylation, the factors cannot adequately bind calcium and phospholipid membranes needed for their hemostatic function.

Vitamin k antagonist are to be used if heparin is not available or contraindicated for thromboprophylaxis in patients undergoing abdominal surgeries(Mastoraki et al., 2018) Warfarin requires INR monitoring and have a wide range of food and drug interactions. The vitamin k antagonists have a narrow therapeutic window, higher bleeding risk and delayed onset of action with paradoxical effects at the initiation period. These properties render them less favorable to low molecular weight heparin in thromboprophylaxis (Martin & Bekaii-Saab, 2012)

2.11.4 Novel oral anticoagulant (NOAC)

These include dabigatran, rivaroxaban, apixaban and edoxaban which have different pharmacokinetics and pharmacodynamics (Franchini, Bonfanti, & Lippi, 2015). There is limited data in non-orthopedic patients on their indication and utilization. However, they have several advantages over heparin and vitamin k antagonist. Heparin may lead to; heparin induced thrombocytopenia, bleeding, osteoporosis and requires regular monitoring. Warfarin has multiple drug and food interaction and a narrow therapeutic window.

NOACs might revolutionize VTE treatment and prophylaxis bringing many benefits for the patient and efficacy. However, there are concerns about drug interaction in GI abnormalities, hepatic and renal insufficiency and chemotherapeutic agents. Lack of reversal agents may limit their use in invasive procedures and thrombocytopenia (Mastoraki et al., 2018)

The novel oral anticoagulants include; dabigatran, rivaroxaban, apixaban and edoxaban. Apixaban showed the lowest risk of major bleeding compared to other NOACs followed by dabigatran. Apixaban and rivaroxiban demonstrated a lower risk of bleeding compared to low molecular weight heparin and vitamin k antagonists (Cohen et al., 2015).

Rivaroxiban

This is an orally administered direct factor Xa inhibitor. It has a high bioavailability, rapid onset of action and a half-life of 7-11 hours. No significant food or drug interaction has been reported. Its metabolized by the liver and kidney, thus prescription in renal and hepatic insufficiency should be cautious. No monitoring is required and no antidote is available in bleeding cases (Franchini et al., 2015b)

Rivaroxaban showed similar efficacy to heparin and VKA in treatment and prophylaxis of venous thromboembolism with a better safety profile and ease of administration than standard treatment(Cohen et al., 2014). It has been approved by the Food and Drug Administration (FDA) for VTE prevention in arthroplasty, stroke prevention and treatment of venous thromboembolism (Martin & Bekaii-Saab, 2012). The dosage is 15-30mg one daily.

Dabigatran

This an oral administered direct thrombin inhibitor. It has a low bioavailability, rapid onset of action and a half-life of 12-14 hours. Its absorption is facilitated by acids. Its excreted primarily through the kidney, thus caution in renal impairment is paramount. RE-MEDY phase 111 clinical trial showed no significant difference in VTE and VTE related deaths with the warfarin arm and superiority to placebo. There were lower rates of bleeding in dabigatran group(Goldhaber et al., 2016). It is approved by the FDA for similar indication as rivaroxaban. The dosage is 110-150mg twice daily. Major adverse effect of dabigatran is dyspepsia.

Apixaban

It is an orally administered direct factor Xa inhibitor. Its bioavailability is 50%, has a rapid onset of action and has a half-life of 12 hours. It is excreted in urine and

contraindicated in stage 5 renal failure. No drug monitoring is required.

It is FDA approved for non-valvular atrial fibrillation, venous thromboembolism treatment and prophylaxis in major orthopedic surgery(Franchini et al., 2015b). The dosage is 2.5-5mg twice daily.

Edoxaban

It is an orally administered factor Xa inhibitor. Its bioavailability is 62% and has halflife of 8-10 hours. It is mainly excreted through the hepatobiliary route. No monitoring is required and has similar indications as apixaban. The dosage is 15-30mg once daily (Franchini et al., 2015a).

Duration of prophylaxis

Timing of prophylaxis is dependent on risk of VTE development, resistance of the VTE risk factor, the type of prophylaxis used and the risk of bleeding. Low molecular weight heparin can be initiated prior to surgery, 12 hours before, intra-operatively or post operatively. The initiation time results in no difference in risk of venous thromboembolism (Amaral et al., 2022). Most of the other prophylaxis are administered, 24 to 36 hours post operatively. Mechanical prophylaxis is initiated intraoperatively and continued into the post-operative period.

Extension of prophylaxis to 4 weeks, was associated with a reduced risk of venous thromboembolism with similar rates of bleeding, in colorectal cancer patients, compared to 1-week prophylaxis (Vedovati et al., 2014). Most of the venous thromboembolism events, greater than 80%, occurred post discharge, in major surgery done in urological malignancy(Alberts et al., 2014).

Guidelines recommend the duration of prophylaxis be guided by the risk of venous thromboembolism and its persistence post-operatively(Encke et al., 2016). The

prophylaxis duration may be extended to the post discharge period.

For moderate and high risk patients the duration of prophylaxis is 7 to 10 days. This should be initiated 12-24 hour preoperatively or within 6 to 24 hours post operatively(Mastoraki et al., 2018). Extended duration of 21 to 28 days is undertaken in patients with the highest risk of venous thromboembolism (caprini score of more than 8 points). There was low incidence of venous thromboembolism with extended chemoprophylaxis. Extension of chemoprophylaxis duration did not increase the risk of bleeding events in hepatobiliary cancer surgery(Hashimoto et al., 2017).

Risk of bleeding

One the documented side effect of chemoprophylaxis is bleeding post-surgery. Most of the bleeding occurring after use of prophylaxis is minor though major bleeding may occur. Major bleeding is defined as symptomatic bleeding in critical area requiring exploration, fatal bleeding and bleeding causing more than 2g/dl fall in hemoglobin level.(Schulman & Kearon, 2005). The bleeding may occur as a complication of the surgery being performed but may also be increased by the use of blood thinners.

This calls for judicious use of chemoprophylaxis in the quest of reducing risk of venous thromboprophylaxis. The risk of bleeding attributed to chemoprophylaxis varies in different groups of patients and surgery performed. In the clinical set up minor bleeding i.e bruises, wound hematoma, drain site bleeding and hematuria are encountered more frequently(Leonardi et al., 2006b). A meta-analysis of 52 randomized studies concluded that most patients undergoing surgery can get low dose chemoprophylaxis safely. The bleeding risk occurred in less than 3% and was lower with low dosages.

It is paramount for the risk of bleeding to be assessed or estimated, as a baseline, before chemoprophylaxis is initiated. This helps reduce the incidence of bleeding and wound complications. This can be done by evaluating any active bleeding, underlying hemostatic disorders or factors that may increase risk of bleeding. The different surgical procedures have varying risk of bleeding both intra and post-operatively(Gould et al., 2012)(Spyropoulos & Douketis, 2012).

Patients with high bleeding risk are best managed with mechanical prophylaxis to reduce the risk of venous thromboembolism. This can be combined with pharmacological prophylaxis once the risk of bleeding has been reduced. Emphasis on the need of individualized prophylaxis prescriptions preoperatively, intraoperatively and post operatively is paramount.

Rare cases of huge abdominal wall hematomas have been reported with enoxaparin therapy. This is associated with an unexplained fall in hematocrit and abdominal pain(*Enoxaparin Associated with Huge Abdominal Wall Hematomas: A Report of Two Cases - ProQuest*, n.d.). Calling for prescribers to have high a index of suspicion in extended use of enoxaparin for these hematomas including spinal, epidural and psoas hematomas.

2.12 Thromboprophylaxis Guidelines

There are different existing guidelines on thromboprophylaxis in surgical patients. Most of these guidelines have been developed for major orthopedic surgeries. There may be a difference in the choice of prophylaxis recommended. The caregivers' compliance to these guidelines has been reported to be poor (Ortman & Hecht, 2007). Efficacy and safety of the thromboprophylaxis method employed is the goal of effective venous thrombus formation prevention. Some surgeons question the necessity of increasing risk of bleeding for preventing potentially asymptomatic and clinically irrelevant' VTE event. Studies have shown that most of the distal DVT remain clinically silent regardless of administration of thromboprophylaxis (Ortman & Hecht, 2007)

There is an overwhelming volume of research on venous thromboembolism postsurgery and benefits of prophylaxis as described in this thesis. This has necessitated several groups of experts to analyze consensus statement guidelines, randomized trials, meta-analyses and review articles related to venous thromboembolism prevention and coming up with guidelines. Clinical practice guidelines have been published by various professional bodies and some hospitals have established their own protocols.

The guidelines for diagnosis, management and prevention of venous thromboprophylaxis include; American Society of Hematology, the American Society of Clinical Oncology (ASCO), the European Society of Anesthesiology (ESA), the American College of Chest Physicians (ACCP). The American Academy of Orthopedic Surgeons (AAOS) and the International Initiative on Thrombosis and Cancer (ITAC).

An article aiming to review different guidelines on venous thromboprophylaxis for elective knee arthroplasty showed that, nearly all the guidelines advocated for similar methods of prophylaxis but differed in the dosage, duration and recommendation grades(Khokhar et al., 2013). The AAOS and ACCP guidelines are the most popular guidelines published in the surgical field. Both groups have similar recommendations on reducing symptomatic VTE and bleeding complication after a 2012 review. This was achieved by review of definitions, methodology and the goals of the groups(Budhiparama et al., 2014)

American Association of Orthopedic Surgeons publish guidelines related to venous thromboembolism prevention in the orthopedic field and specific subspecialities (*Preventing Venous Thromboembolic Disease in Hip and Knee Replacement Procedures - Clinical Practice Guideline | American Academy of Orthopaedic Surgeons*, n.d.).

2.13 ACCP Guidelines

First published in 1986, these guidelines are based on scoring systems to help in assessment of risk factors and to implement the use of appropriate VTE prophylaxis. They have been updated over the years, latest being the ninth edition in 2012 (Gould et al., 2012).

Before 2012, Dr. Hirsh, Dr. Dalen and colleagues had worked over 20 years building on prior editions of ACCP antithrombotic guidelines. The ninth edition took into consideration quality persisting limitation in quality evidence and relevance of weak recommendation that reflect lack of confidence in estimates and variability in patients values and preferences(Guyatt, Akl, Crowther, Schünemann, et al., 2012). The guidelines appreciate the presence of asymptomatic thrombosis and formulated strategies to estimate reduction of symptomatic thrombus with thromboprophylaxis(Guyatt, Akl, Crowther, Gutterman, et al., 2012)

The published guidelines were graded on each category depending on the degree of evidence available from literature or on expert recommendation where no supporting literature was available. The guidelines include a wide range of recommendation concerning VTE but for the purposes of this paper, only the segment discussing abdominal pelvic surgery VTE prevention is presented.

The grading of recommendations has two parts; number and the letter. For the number grade 1 implies strong recommendation and grade 2 implies weak recommendation. The letter implies the quality of evidence. Grade A is high quality, grade B is moderate quality and grade C is low quality evidence(Kearon et al., 2012)

The ACCP guidelines were revised in 2016 and 54 recommendation included but did not adjust the 2012 recommendation on thromboprophylaxis in abdominal and pelvic surgery(Kearon et al., 2016). In 2021, a second update on 9th edition of ACCP guidelines was done. The panel generated 29 guidance statements involving antithrombotic management. This entailed initial management of VTE, secondary prevention and risk reduction of post thrombotic syndrome. Four new guidance statement were added while eight statements were substantially modified(Stevens et al., n.d.)

2.14 ACCP AT9 Recommendations for Abdominal Pelvic Surgery

Very Low risk or Caprini score =0

Early ambulation with no specific pharmacological (GRADE 1B) or mechanical prophylaxis (GRADE 1C)

The estimated risk of venous thromboembolism is less than 0.5% in this group.

Low risk or Caprini score = 1-2

Intermittent pneumatic compression (IPC) is suggested over no prophylaxis (GRADE 2C).

The estimated risk of venous thromboembolism is approximately 1.5% in this category.

Moderate risk or Caprini score = 3-4 (not at high risk for major bleeding complication)

Low Molecular Weight Heparin (LMWH) (GRADE 2B), low Dose Unfractionated

Heparin (LDUH) (GRADE 2B) or mechanical prophylaxis, preferably intermittent pressure compression stocking (GRADE 2C)

The estimated risk of venous thromboembolism is 3% in this category

Moderate risk or Caprini score = 3-4 (at high risk of major bleeding)

Intermittent pneumatic compression (IPC) (GRADE 2C)

High risk or Caprini score => 5 (not at high risk of major bleeding)

Pharmacological prophylaxis, LMWH (GRADE 1B) or LDUH (GRADE 1B) and mechanical prophylaxis with elastic stocking (ES) or IPC (GRADE 2C)

Those undergoing cancer surgery, extended-duration pharmacological prophylaxis (4 weeks) with LMWH (GRADE 1B).

NOTE; patients who opt to minimize out of pocket cost might prefer limited duration over extended duration of prophylaxis and if the cost is directly borne on the patient. The risk of venous thromboembolism is at least 6% in this risk category

High risk or caprini score => 5 (at high risk of bleeding)

IPC until the risk of bleeding is diminished and pharmacological prophylaxis initiated (GRADE 2C).

Those at high risk for VTE in whom LMWH and LDUH are contraindicated or unavailable and not at risk of major bleeding low dose aspirin (GRADE 2C), fondaparinux (GRADE 2C) or mechanical prophylaxis can be used (GRADE 2C). The guidelines suggest that inferior vena cava filter should not be used for primary VTE prevention (GRADE 2C). More over the guidelines suggest that periodic surveillance of VTE with venous compression ultrasound should not be done (GRADE 2C).

Table 23—Recommendations for Thromboprophylaxis in Various Risk Groups			
	Risk and Consequences of Major Bleeding Complications		
Risk of Symptomatic VTE	Average Risk (~1%)	High Risk (\sim 2%) or Severe Consequences	
Very low (<0.5%)	No specific prophylaxis		
Low (~1.5%)	Mechanical prophylaxis, preferably with IPC		
Moderate (~3.0%)	LDUH, LMWH, or mechanical prophylaxis, preferably with IPC	Mechanical prophylaxis, preferably with IPC	
High (~6.0%)	LDUH or LMWH plus mechanical prophylaxis with ES or IPC	Mechanical prophylaxis, preferably with IPC, until risk of bleeding diminishes and pharmacologic prophylaxis can be added	
High-risk cancer surgery	LDUH or LMWH plus mechanical prophylaxis with ES or IPC and extended-duration prophylaxis with LMWH postdischarge	Mechanical prophylaxis, preferably with IPC, until risk of bleeding diminishes and pharmacologic prophylaxis can be added	
High risk, LDUH and LMWH contraindicated or not available	Fondaparinux or low-dose aspirin (160 mg); mechanical prophylaxis, preferably with IPC; or both	Mechanical prophylaxis, preferably with IPC, until risk of bleeding diminishes and pharmacologic prophylaxis can be added	

Table from, (Gould et al., 2012)

Despite availability of these guidelines on VTE prophylaxis, the adherence has been suboptimal in most of the clinical areas. With only 60.3% of eligible patients receiving appropriate prophylaxis as per VTE guidelines and up to 80.1% receive inappropriate prophylaxis in hospitalized medical patients. Employing assessment models or checklists based on clinical guidelines have been advocated for to reduce the discrepancy in clinical practice and guidelines(Abukhalil et al., 2022).

Some of the challenges, hindering VTE risk assessment and prophylaxis in clinical practice, include involvement of multiple staff in individual admission, interruptions of the prescription, lack of policy awareness among caregivers, time pressure to see many patients and the complexity of assessment tools(Basey et al., 2012)

In AVAIL ME Extension study, only 39% of surgical patients received VTE prophylaxis as per ACCP 2008 guidelines. The rate of patients who did not require or had contraindication to VTE prophylaxis received it in 78% and 66% respectively (Mokhtari et al., 2011). ENDORSE study revealed 93% of patients undergoing major surgery were at risk of VTE but only 62% received prophylaxis as per ACCP recommendation and this varied across participating countries (Kakkar et al., 2010)

The first clinical sign of VTE may be death and management of its morbidity maybe cumbersome and costly. This calls for its prevention to reduce this morbidity and mortality. All laparotomy patients at MTRH ought to be stratified using available scoring systems e.g. Caprini score as adopted by this institution for all admissions. This enables proper thromboprophylaxis administration to reduce VTE risk and avoid adverse effects of prophylaxis methods. Despite MTRH adopting and having this risk assessment forms in the inpatient files, few or none are filled.

Routine ultrasound scanning of the limbs or other methods of diagnosing VTE have not been found to be effective in detecting early incidences post-surgery, thus prophylaxis is paramount.

To improve adequate VTE thromboprophylaxis prescription, various types of passive and active system wide intervention have been advocated for. Passive interventions including; continuing medical education, dissemination of guidelines, audit and feedback have been found to be inadequate in improving rates of VTE prophylaxis in clinical practice. This led to development of active intervention like alerts, both computer or human and multifaceted interventions to improve the practice(Kahn et al., 2018). Kucher et al found that caregivers who were alerted were significantly more likely to prescribe thromboprophylaxis to their patients and this computer alert reduced the 90 day VTE risk by 41% (Kucher et al., 2005).

A service-specific and mandatory VTE decision support tool, in an online order entry, led to significant increase in guideline adherent VTE prophylaxis (66% vs 84.4%, p <0.001). Moreover, the rate of preventable harm from VTE reduced from 1% to 0.17% and the discrepancy, in sex and race, during provision of appropriate prophylaxis eliminated after the clinical decision was support system (CDSS) implementation(Haut et al., 2012). At University of Virginia, implementation of a clinical decision support system reduced the 30-day VTE (1.25% vs 0,64, p=0.033) (Turrentine et al., 2018). At Boston University, mandatory individualized VTE risk stratification and providers receiving automated suggestions based on caprini score significantly reduced DVT and PE rates by 1.9 % to 0.3% and 1.1% to 0.5%, respectively. Compliance with guideline was 100% for low to moderate VTE risk and 89% for high risk(Cassidy et al., 2014).

The American Heart Association has called for action to decrease VTE by 20% in hospitalized patients by 2030. Various policy guidelines developed include; performing VTE risk assessment and reporting the level VTE risk in all hospitals, integrating preventable VTE as a benchmark for hospital comparison and pay-forperformance programs, supporting public awareness, tracking VTE national wide with use of standardized definitions and developing centralized data stewardship (Henke et al., 2020)

CHAPTER THREE

3.0 METHODOLOGY

3.1 Study design

This was a prospective and descriptive hospital based study.

3.2 Study site

The study was carried out at Moi Teaching and Referral Hospital (MTRH) in, Eldoret which is the 2nd largest public facility in Kenya after Kenyatta National Hospital. MTRH is located in Uasin Gishu County, in the North Rift region of Kenya, about 310 kilometers northwest of the capital city of Kenya, Nairobi. It serves the greater western Kenyan region representing about 40% (approximately 16.2 million people) of the country's population. It also serves Eastern Uganda and parts of Southern Sudan.

MTRH has several surgical departments. Ward 6 for male surgical cases, except orthopedic and neurosurgery cases. Ward 8 for female surgical cases, except orthopedic, neurosurgery and gynecological cases. Approximately 30 abdominal surgeries are done every month, both elective and emergency. Recruited candidates were from surgical wards and critical care unit at MTRH, Eldoret.

3.3 Target population

All patients above 18 years who have undergone emergency or elective laparotomy at MTRH, Eldoret.

3.4 Eligibility criteria

3.4.1 Inclusion criteria

• All patients aged 18 years and above who have undergone laparotomy at MTRH

3.4.2 Exclusion criteria

- Patient on treatment for venous thromboembolism before the laparotomy
- Obstetric and Gynecological cases

3.5 Sample size

The study aims at determining the incidence proportion of DVT among patients undergoing laparotomy at MTRH. A similar study done in Uganda by Andrew et al, (2013) found incidence proportion of DVT to be 5% post abdominal surgery. Assuming the same incidence proportion in our set up, the sample size was calculated using Fisher et al., (1998) formula as follows:

$$n = \frac{Z_{1-\alpha/2}^2 P(1-P)}{d^2}$$
$$n = \left[\frac{Z_{1-\alpha/2}}{d}\right]^2 \cdot P(1-P)$$

Where,

n= minimum sample size required

 $Z_{1-\alpha/2}^2$ = Critical value for standard normal distribution at α -level of significance (α =0.05, $Z_{1-\alpha/2}$ =1.96).

p = incidence proportion of DVT (5%) from a study done by Andrew et al, (2013).

d = Margin of error (d=0.025)

Substituting the above figures a minimum sample size and adjusting for 10% lost to follow up a minimum sample size of 325 was required.

3.6 Sampling

Consecutive sampling was done until the sample size was achieved.

3.7 Study period

The study was conducted over a period of 1 year, from 1st of September 2021 to 31st of August 2022.

3.8 Execution of study

Data was collected by the principal investigator (PI) with the aid of 2 research assistants. Adult patients who had undergone laparotomy were identified in the surgical wards or Intensive Care Unit within 48 hours' post-surgery. They were informed and counseled about the study, after which informed consent was obtained. Adult relatives or next of kin were allowed to give consent for patients who were too ill to consent for the study. Data was collected from eligible candidates by the use of a predesigned questionnaire within 48 hours of laparotomy. Some data was extracted from the patient's medical records and collaborative information from patients or next of kin.

Research assistants were clinical officers. Before commencement of the study, the assistants were trained and appraised by the PI. They were ascertained to have a good grasp of the study upon audit of questionnaires filled during pretesting. Random checks were done during the study to ensure conformance. They were compensated for the time they invested in the study by the PI.

Data collected from the patients or relatives included; age, gender, past medical and surgical history, VTE risk factors and factors associated with risk of bleeding and time to ambulation post-surgery.

Data collected from the medical record included; diagnosis on admission, surgical intervention, lead surgeon, duration of surgery, prophylaxis prescribed (mechanical or pharmacological) dose, duration and administration/utilization.

Enrolled patients were assessed for risk of VTE using the Caprini Risk Assessment tool and Well's score was done to assess for a clinical DVT. If Well's score was 2 or more a Doppler ultrasound of lower limb was done and if DVT was confirmed appropriate treatment was initiated as per MTRH protocols. Evaluation of thromboprophylaxis type, time of initiation, duration, utilization and dose received was done from the anesthesia notes, postoperative notes and treatment sheet. Contraindication to various thromboprophylaxis was recorded.

Patients who did not develop a clinical VTE were scheduled for a repeat Wells score score on day 14 and 28 post operatively. Those who scored 2 or more had a Doppler ultrasound of the lower limb done to rule out DVT. When DVT was diagnosed, appropriate treatment as MTRH protocols were initiated.

Radiological DVT assessment was done according to standard MTRH protocols by a senior consultant radiologist. Patients were scanned lying down flat on the examination table, both supine and prone for thigh and calf veins respectively. The abdominal, pelvis and lower limb venous system were assessed systematically. The duplex ultrasound assessed for direction, velocity, and pattern of blood flow. Normal venous vasculature shows venous flow at baseline and augmentation of flow with calf compression and phasic respiratory ventilation with increased flow during expiration. Augmentation of flow with calf compression helps to assess for venous obstruction distal to the probe. Phasic respiratory variation helped to assess obstruction proximal to the probe.

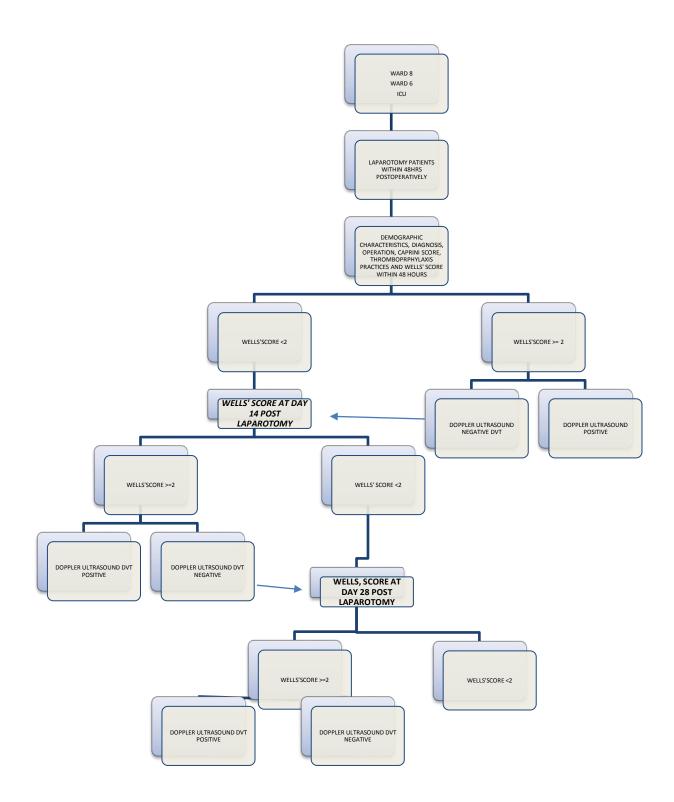


Figure 4: Study Procedure

3.9 Data analysis and presentation

All data was saved in MS Excel data sheets that were protected from access by unauthorized person through a password protected computer. Hardcopy back-up copies were securely locked in a cabinet under lock and key, only accessed by personnel involved in the project.

The analysis was done using STATA 16.1. Age was summarized as mean and corresponding standard deviation as the data assumed normal distribution. The rest of the demographic and clinical characteristics variables are categorical in nature and hence summarized as frequencies and their corresponding proportions.

To answer objective one, a total score from Caprini Risk Assessment tool was categorized as very low risk (0), low risk (1-2), moderate risk (3-4), and high risk (\geq 5). The data generated was presented as frequencies and proportions.

To answer objective two, data on thromboprophylaxis given was summarized in a frequency table. The data on when the thromboprophylaxis was given and the type of prophylaxis was summarized as proportion.

To answer objective three, the number of those who developed DVT within 28 days of follow up period less the ones with DVT within 48 hours, was divided by the number of participants in the study to determine the incidence proportion and reported as a percentage. Chi square was used to associate risk factors of venous thromboprophylaxis, thromboprophylaxis practice and the incidence of clinical DVT.

3.10 Ethical consideration

Approval was obtained from IREC, number IREC/2021/140 and permission granted from MTRH before commencement of the study.

Informed consent was obtained in writing from patient or next of kin.

Those who declined to participate and those who chose to drop out of study were not victimized. Patient's anonymity was assured by not documenting names and other characteristics that could be used to identify the participants

Confidentiality and anonymity was maintained throughout data collection, storage and analysis.

Findings and recommendations of the study will be shared with fellow doctors, the participants and the general public.

3.11 Limitations

Recall bias was one of the limitations of this study as some patients were not able remember all their past medical history or family history. This was mitigated by taking collaborative history from the relative or next of kin.

Lack of preoperative ultrasound might have led to missing DVTs occurring before surgery. This was mitigated by doing a Wells score within 48hours of laparotomy on all participants and Doppler ultrasound if the Wells score was equal to or more than 2. Doppler Ultrasound scan findings in diagnosis of DVT may be observer dependent. This may lead to over or under diagnosis of DVT. This was mitigated by identifying a senior radiologist in MTRH who did all the Doppler ultrasound during the study period.

CHAPTER FOUR

4.0 RESULTS

4.1 Introduction

The study was conducted for a year from 1st September 2021 to 31st August 2022. The participants were recruited from the surgical wards and ICU at MTRH. A total of 325 study participants were recruited after meeting eligibility criteria. Two patients died within 48 hours' post-surgery before Wells score was calculated. Thus the findings presented herein are based on 323 participants.

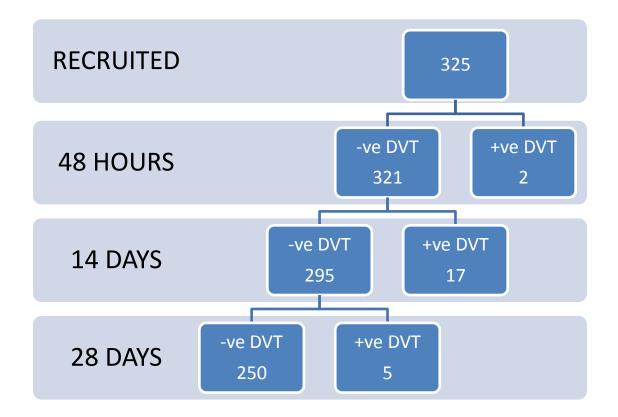


Figure 5: a flow chart of the study procedure

Above is a flow chart of the study procedure. The target population were adult patients undergoing laparotomy, diagnostic or therapeutic, at Moi Teaching and Referral Hospital. The total number of participants recruited was 325 by consecutive sampling, after meeting the inclusion criteria and taking informed consent. However, 2 participants died within 48hours postoperatively before well score was calculated. Of the remaining 323 participants, 293 had Well's score of less than 2 and 30 participants had Well's score equal to or above 2. Of those with Well's score equal or above 2 within 48 hours post-operatively, 2 participants had a positive Doppler for deep venous thrombosis.

At 14 days' post operatively, 274 participants had Well's score of less than 2 while 38, had a Well's score of 2 and above. Doppler ultrasound done0 on the 38 participants revealed 21 participants to have no DVT and 17 participants had a DVT. At 28 days' post operatively, 242 participants had a Wells score of less than 2 while 13 had a Well score of 2 or more. Doppler ultrasound done revealed 8 participants to have no deep venous thrombosis while 5 participants had deep venous thrombosis.

4.2 Social demographics and clinical characteristics of the participants

The social demographic characteristic of 323 participants is shown in the table below. The age of participants in this study ranged from 18 to 97 years. The mean age of participants was 38.76 years with a standard deviation of 16.79.

There were 128 (39.8%) female and 195(60.2%) male participants in the study. This gave a male to female ratio of 1.5:1

	Overall (N=323)
Age (yrs)	
Median (IQR)	35(25, 48)
Mean (SD)	38.762 (16.798)
Sex	
Female	128 (39.8%)
Male	195 (60.2%)

 Table 4:On age and sex distribution

4.3 Diagnosis

Intestinal obstruction, peritonitis or intra-abdominal abscess and appendicitis were the major indications for performing laparotomies. Tumors as a diagnosis was encountered in 37 (11.7%) of the patients undergoing laparotomy in MTRH.

Below is a table illustrating the diagnosis made on laparotomy and the frequency of occurrence:

Diagnosis	Frequency	%
Intestinal obstruction	93	29.3
Peritonitis/abscess	76	24.0
Appendicitis	62	19.6
Tumor	37	11.7
Blunt abdominal trauma	21	6.6
Penetrating abdominal	16	5.0
trauma		
Gall stone disease	12	3.8

Table 5: diagnosis made on laparotomy and the frequency of occurrence;

4.4 Type of surgery

At MTRH all abdominal surgeries conducted over the study period were open. The most common surgery was intestinal resection and anastomosis/repair (67.7%) followed by appendectomy (17.2%). Stoma fashioning was performed in 22 (6.9%) participants. Tumor resection was done in 6 (1.9%) participants.

Below is a table illustrating the surgery performed and the frequency of the operation;

Table 6: Surgery performed and the frequency of the operation;
Type of surgery

Appendectomy	55 (17.2%)
Biliary surgery	7 (2.2%)
By-pass surgery	9 (2.8%)
Hernia repair	3 (0.9%)
Gut resection anastomosis/repair	216 (67.7%)
Splenectomy	1 (0.3%)
Stoma	22 (6.9%)
Tumor resection	6 (1.9%)

4.5 Duration of surgery

Majority of the laparotomy lasted more than 45 minutes. This accounted for 99.3% of the cases in the study and thus were categorized as major surgeries. Only 2 surgeries lasted less than 45 minutes.

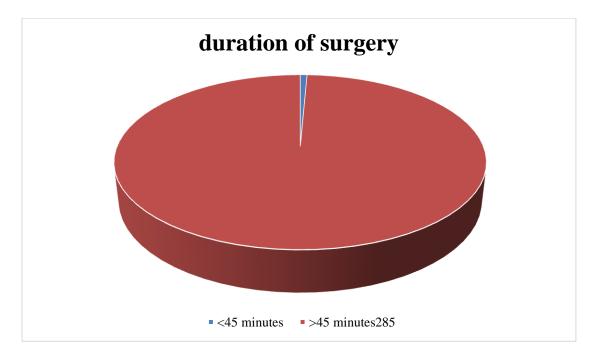


Figure 6 : Duration of surgery

4.6 Lead surgeon

Most of the laparotomy done at MTRH, 53.5%, were performed by senior residents as the lead surgeon (resident in general surgery year 3 and above for Masters of Medicine surgery or Fellows of College of Surgeons for Eastern and Southern Africa-COSESCA), while 24.5% by consultant surgeons and 22.0% by residents (general surgery residents in year 2 and membership of the college of surgeons- MCS, COSESCA).

Below is a table illustrating the proportion of surgeries done by consultants, senior resident and residents;

Lead surgeon	
Consultant	77(24.50/)
001100110110	77 (24.5%)
Senior resident	168 (53.5%)
Resident	69 (22.0%)

4.7 Mobilization

Majority of the patients, 82.7% were out of bed within 72 hours' post-surgery. Only,

Table 6 : surgeries done by consultants, senior resident and residents;

17.3 % were still confined to bed 72 hours post-surgery.



Figure 7: duration confined to bed

Objective 1; Caprini risk assessment score

Most participants were at moderate (37.7%) and high risk (37.7%) of developing VTE after stratification with the Caprini risk assessment score. The low risk and very low risk constituted 20.45% and 3.5%, respectively.

Table 7: Caprini score

 Very low risk
 12 (3.7%)

 Low risk
 67 (20.4%)

 Moderate risk
 122 (37.7%)

 Highest risk
 122 (37.7%)

Laparotomy patients were categorized by age according to the Caprini risk score. Most patients with high risk of developing VTE were between 35 and 65 years. In the moderate risk group, those below 35 years were almost equal to the 35-65 age group.

	<35	35-65	>65	
Very low risk	5	7	0	
Low risk	45	22	0	
Moderate risk	60	62	0	
High risk	37	52	33	

Objective 2; Thromboprophylaxis practices

None of the participants were put on thromboprophylaxis before surgery commenced. One participant received enoxaparin, thromboprophylaxis, intra operatively. Fifty-five participants (17.0%) were on thromboprophylaxis on post-operative day 1. No participant had thromboprophylaxis prescription or administration on and after discharge.

Enoxaparin (Clexane) was the only chemoprophylaxis agent prescribed in all the 55 participants on prophylaxis. The median duration of Clexane prescription was 3.88days (SD 1.62), with a range of 1 to 10 days in laparotomy patients. Six (10.9%) participants did not receive Clexane as prescribed by the surgeon though the reason for this was not recorded. It was observed that most of the enoxaparin prescriptions had no defined duration i.e. open ended prescription. The treatment sheets were not routinely reviewed by the ward clinician to consider stopping or adjusting chemoprophylaxis prescribed. The decision to stop clexane administration was mostly done by the nurses without much input from the prescriber.

Contraindication to pharmacological prophylaxis was rare in the study participants. Hepatic impairment (1.5%) was the most common contraindication followed by upper gastrointestinal bleeding (0.3%) and bleeding disorder (0.3%). No adverse drug reactions were documented in those receiving enoxaparin.

No mechanical method of thromboprophylaxis was utilized among the study participants. There was no prescription for mechanical thromboprophylaxis raised during the study period. Enquiry from the supply chain revealed the elastic stockings were stocked on demand. The proportion of participants with contraindication to mechanical prophylaxis was low at 0.9%. Only 3 (0.9%) participants had lower limb ulceration as contraindications to mechanical thromboprophylaxis.

No MTRH venous thromboprophylaxis risk stratification score was filled in all the laparotomy patients analyzed in this study. Neither the score sheet nor the treatment sheet was filled with a thromboprophylaxis score. By the end of the study, the records department was omitting the thromboprophylaxis risk score page, while assembling admission files, citing underutilization of the resource.

Below is a table with the distribution of thromboprophylaxis practices at MTRH among laparotomy patients;

Thromboprophylaxis preoperatively	
No	323 (100.0%)
Thromboprophylaxis intraoperatively	323 (100.070)
No	322 (99.7%)
Yes	1 (0.3%)
Thromboprophylaxis day 1 postoperatively	1 (0.370)
No	268(82.00%)
Yes	268 (83.0%)
	55 (17.0%)
Thromboprophylaxis on discharge	
No	323 (100.0%)
Pharmacological drug	N=55
Sc clexane/enoxaparin	55 (100.0%)
Duration in days	N=55
Mean (SD)	3.88 (1.62)
Range	1.00- 10.00
Whether drug was administered	N=55
No	6 (10.9%)
Yes	49 (89.1%)
Mechanical	
No	323 (100.0%)
Upper GI bleeding	
No	322 (99.7%)
Yes	1 (0.3%)
Hepatic impairment	
No	318 (98.5%)
Yes	5 (1.5%)
Bleeding disorder	
No	322 (99.7%)
Yes	1 (0.3%)
Thromboprophylaxis drug reaction	
No	323 (100.0%)
Lower limb ulceration	
No	320 (99.1%)
Yes	3 (0.9%)
Vascular disease of lower limb	
No	323 (100.0%)

Table 8: Thromboprophylaxis practices

Early mobilization which was done within 72 hours of laparotomy, was employed in most post-operative patients,76.8%. Most of the patients receiving chemoprophylaxis were at a high risk of VTE development and this was administered post-operatively. Below is a table illustrating the frequency of prophylaxis given in the different VTE risk groups;

TYPE OF PROPHYLAXIS	VARIABLE		GRADE RISK		
		VERY	LOW	MODERATE	HIGH
		LOW RISK	RISK	RISK	RISK
MOBILISATION	EARLY AMBULATION	7	52	101	88
CHEMOPROPHYLAXIS	PRE OPERATIVE	0	0	0	0
	INTRA OPERATIVE	0	0	0	1
	POST OPERATIVE DURATION	5	4	16	30
MECHANICAL		0	0	0	0

PROPORTION OF PATIENT AT RISK RECEIVING VTE CHEMOPROPHYLAXIS

RISK	NUMBER OF	NO. OF THOSE	PROPORTION OF
	PATIENT AT RISK	RECEIVING	THOSE RECEIVING
		ENOXAPARIN	PROPHYLAXIS
VERY LOW RISK	11	5	45%
LOW RISK	65	4	6%
MODERATE RISK	120	16	13%
HIGH RISK	121	30	25%

Some patients in the very low risk group of VTE received unnecessary VTE chemoprophylaxis, i.e. 5 patients received enoxaparin. The proportion of patients in the very low risk group receiving enoxaparin was higher,45%, than those in the high risk group, 25%. The 4 patients in low risk group received enoxaparin instead of mechanical prophylaxis as recommended by the ACCP guidelines. There was no recorded contraindication to mechanical prophylaxis in this group.

The patients with high risk of VTE received only chemoprophylaxis without combination with mechanical prophylaxis as recommended by ACCP 2012. Only 25% of the high risk group laparotomy patients received prophylaxis.

Objective 3; incidence of clinical DVT

The Well's score was equal to or more than 2 in 30 (9.3%) participants within 48 hours of abdominal surgery. In 38 (12.2%)participants, at 14 days post-operatively, the Well score was recorded as 2 or more. In 13(5.1%) participants, at day 28 post-operatively, the Wells' score was 2 or more on calculation.

Time	WELLS' SCORE		
	<2	>=2	
48 hours	292 (90.7%)	30 (9.3%)	
14 days	274 (87.8%)	38 (12.2%)	
28 days	242 (94.9%)	13 (5.1%)	

Doppler ultrasound was done on 81 patients. Within 48 hours' post-surgery, only 2 participants had Doppler confirmed DVT. At 14 days' post laparotomy, 17 participants had DVT on Doppler scanning of the lower limbs. At 28-day post-surgery, 5 more patients were diagnosed with DVT via Doppler ultrasound.

DVT among those with Wells' score >2					
Time	DVT				
	Yes	No	Cumulative percentage of 323		
48 hours	2 (6.7%)	28 (93.3%)	0.62%		
14 days	17 (44.7%)	21 (55.3%)	5.88%		
28 days	5 (38.5%)	8 (61.5%)	7.43%		

Clinical DVT incidence proportion in patients undergoing laparotomy at MTRH was calculated as follows;

incidence proportion of clinical DVT

= number of new DVT cases over study period

 \div total number of patients undergoing laparotomy over the study period

Number of new DVT cases was calculated by identifying the total number of laparotomy patients with positive DVT (24patients) over the follow up period (28 days), subtract the number of patients with positive DVT (2patients) at 48hours (assumed to be the DVT cases before the laparotomy). This number was divided by the total number of patients undergoing laparotomy in the study group (323).

The total number of patients with DVT was 24 patients; calculated by summing up the DVT cases at 48hours, 2 patients, at 14days, 17 patients and at 28 days, 5 patients.

$\frac{number of new DVT cases(24-2)}{total number of participants (323)}$

= 0.068

As a	percentage;	= 0.068	$\times 10$)()
			-	-

The incidence proportion of clinical DVT in patients undergoing laparotomy at MTRH is = 6.8%

4.8 Association between variables

Variable	DVT at 14 days		
	No (N=295)	Yes (N=17)	p value
Age (yrs)	· · · · · ·	, , , , , , , , , , , , , , , , ,	0.137 ¹
N	294	17	
Median	34.50	40.00	
Q1,Q3	25.00,	30.00,	
	47.00	71.00	
Sex			0.485^{3}
Female	113	8 (6.6%)	
	(93.4%)	× ,	
Male	180	9 (4.8%)	
	(95.2%)		
Diagnosis	× /		0.022^{2}
Appendicitis	60	0 (0.0%)	
	(100.0%)	× /	
Blunt abdominal injury	20 (95.2%)	1 (4.8%)	
Gall stone disease	12	0 (0.0%)	
	(100.0%)	× /	
Intestinal obstruction	83 (94.3%)	5 (5.7%)	
Penetrating abdominal	16	0 (0.0%)	
injury	(100.0%)	× /	
Peritonitis/abscess	69 (93.2%)	5 (6.8%)	
Tumour	28 (82.4%)	6 (17.6%)	
Caprini			<
			0.001 ²
Highest risk	98 (86.7%)	15 (13.3%)	
Moderate risk	119	1 (0.8%)	
	(99.2%)		
Low risk	62	0 (0.0%)	
	(100.0%)		
Very low risk	10 (90.9%)	1 (9.1%)	
Clexane			< 0.001 ²
No	253	6 (2.3%)	
	(97.7%)	- ()	
Yes	41 (78.8%)	11 (21.2%)	
Key	()	()	

 Table 9: Association between DVT vs Caprini, Age, Gender, Diagnosis,

 Chemoprophylaxis use

1. Mann-Whitney U Test, 2. Fishers exact Test, 3. X^2 Test

The clinical diagnosis leading to laparotomy being done was associated with a higher chance of developing DVT. There was statistically significant association of a higher caprine score and DVT development post operatively. Prescribing enoxaparin was associated with a higher chance of developing DVT post operatively. Age and sex did not have an association with DVT development

	Clexane		
		Yes	
Variable	No (N=268)	(N=55)	p value
Diagnosis			<
			0.001 ²
Appendicitis	58 (95.1%)	3 (4.9%)	
Blunt abdominal injury	19 (90.5%)	2 (9.5%)	
Gall stone disease	11 (91.7%)	1 (8.3%)	
Intestinal obstruction	84 (90.3%)	9 (9.7%)	
Penetrating abdominal	13 (81.2%)	3 (18.8%)	
injury			
Peritonitis/abscess	53 (69.7%)	23 (30.3%)	
Tumour	26 (70.3%)	11 (29.7%)	
Lead surgeon			0.002^{3}
Consultant	57 (74.0%)	20 (26.0%)	
Resident	52 (75.4%)	17 (24.6%)	
Senior resident	150	17 (10.2%)	
	(89.8%)		

Table 10: Association between Enoxaparin prescription, diagnosis and lead surgeon

Key

1. Mann-Whitney U Test, 2. Fishers exact Test, 3. X² Test

The indication for laparotomy was associated with enoxaparin prescription by the care givers at MTRH. This association was statistically significant with a p value of <0.001. The senior most surgeon on the operating table for laparotomy determined whether enoxaparin was to be prescribed or not. Procedures performed by consultant surgeons had a higher probability of enoxaparin being prescribed than when the procedure were done by residents.

CHAPTER FIVE

5.0 DISCUSSION

5.1 SOCIAL DEMOGRAPHIC CHARACTERISTIC

5.1.1 Age

Majority of patients who underwent laparotomy at MTRH were middle aged with a mean age of 38years and a standard deviation of 16.7 years. This correlates with the age group of patients undergoing major abdominal surgery in the low and middle income countries. In Uganda, the mean age of patients undergoing laparotomy was 45years (Muleledhu et al., 2013a). The median age of surgical patients in the ENDORSE study Senegal was 49years (Bâ et al., 2011) and in South Africa mean age was 45 years (Van Der Merwe et al., 2020). Most of the patients undergoing laparotomy in middle income countries are young and middle aged. These patients have different physiology and body response to injury compared to the elderly. The venous thromboembolism risk in this age group is considered low compared to the elderly.

In contrast, the age group of most patients undergoing laparotomy in the high income countries (HIC) are elderly. This may be attributed to the high number of elderly adults in their population and higher life expectancy. The median age of patients in a Denmark study, on incidence of VTE post emergency laparotomy, was 64 years(Balachandran et al., 2020). The mean age of patients in Rodriguez's study was 70 years in patients undergoing laparotomy due to wound dehiscence (Rodríguez-Hermosa et al., 2005). Average age after major abdominal surgery was 59 years in an analysis of postoperative VTE risk evaluation by Debraj et al (Mukherjee et al., 2008).

The age distribution in the studies is a representation of the population distribution in the different parts of the world. The life expectancy is higher in the developed countries than low and middle income countries. Age is an important and independent risk factor of venous thromboembolism(Silverstein et al., 1998). The higher the age, the higher the chance of getting venous thromboembolism post-surgery. Elderly patients usually have limited mobility and other comorbidities that may predispose them to the increased risk of venous thrombosis.

5.1.2 Sex

There were more males than females patients undergoing laparotomy in our study, with a ratio of 1.5:1. The Kenya demographic and health survey in 2021, had estimated the Kenyan male to female ratio to be 1:1(*Kenya Male to Female Ratio, 1950-2021 - Knoema.Com*, n.d.). Though our study was a hospital based study, males visiting MTRH are more likely to have abdominal conditions, requiring abdominal surgery, than females.

Similar findings were observed in Uganda, where the male to female ratio was 1.6:1 in patients undergoing major abdominal surgery(Muleledhu et al., 2013b).

This contrasts a study in Pakistan where the majority of patients were females (Theochari et al., 2022). This study though included gynecological conditions.

The difference in gender ratio may be explained by exclusion of gynecological and obstetric cases in our study. This population was categorized separately due to the different physiology and hormonal influences to venous thromboembolism occurrence ("ACOG Practice Bulletin No. 84: Prevention of Deep Vein Thrombosis and Pulmonary Embolism," 2007).

5.2 Clinical Characteristic

5.2.1 Diagnosis

Intra-abdominal infection was the leading cause of abdominal surgery in this study at 43.6%, followed by intestinal obstruction and tumors at 29.3% and 11.7%, respectively. Among the intra-abdominal infections, appendicitis and its related complication, was the most prevalent indication for laparotomy at MTRH. Worldwide, appendicitis is the most common cause of intra-abdominal sepsis managed by emergency general surgery (Sartelli et al., 2017). In India, the most common indication for laparotomy was acute cholecystitis followed by tumors and intestinal obstruction(Lebowa et al., 2021). The commonest cause of community acquired intra-abdominal infection in Tazo et al study was appendicitis(Inui et al., 2009). The common indication for emergency laparotomy in Rwanda and South Africa was appendicitis while in USA it was small bowel obstruction and peptic ulcer disease (Rickard et al., 2020). Appendicitis was the most frequent indication of abdominal surgery in Nigeria, followed by intestinal obstruction cause of acute abdomen in adults managed in Ethiopia(Kotiso & Abdurahman, 2016)

In contrast, mechanical small bowel obstruction accounted for the majority of emergency laparotomy done in a study by Jonathan and colleagues, in India (Somasundram et al., 2020) . In Slovenia, the proportion of patients undergoing abdominal surgery due to malignancy was 45% in 223 patients recruited(H.-P. Yu et al., 2022)

Sepsis increases the risk of venous thromboembolism. The high number of patients with intra-abdominal infection, in this study, may have contributed to the higher risk

of thrombosis in the young and middle aged population.

The proportion of patient with abdominal tumors as the indication for laparotomy was low. These were both benign and malignant tumors. Active cancer has been shown to increase the odds of venous thromboembolism. Most cancer patient in our set up present at advanced stage of the disease which is not, usually, amenable to surgery. Thus majority of the surgeries done in colorectal carcinoma are diversion stomas. This may explain the low number of laparotomies done in tumor patients at MTRH(Tenge et al., 2009)(Korir et al., 2015).

In high income countries, tumor surgery is common as the health promotion programs, disease surveillance, adequate population data collection, screening programs and advanced perioperative care enable early detection and management of the conditions. (Koo et al., 2020)(*United States Cancer Statistics / Cancer / CDC*, n.d.)(Jörgren et al., 2013).

5.2.2 Type of surgery

Open abdominal surgery was performed in all laparotomy cases in this study. This correlate with a study in Uganda where all major abdominal surgeries were done using an open method(Muleledhu et al., 2013a). at Lubumbashi, Congo, only 1.5% of minimally invasive abdominal surgeries were done (Arung et al., 2016). In South Africa 15% of the appendectomies were done laparoscopically (Naidoo et al., 2022) .This contrast most studies in the high income countries where several cases are done or attempted using minimally invasive surgery (Balachandran et al., 2020), (Geahchan, Basile, Tohmeh, & on behalf of the DIONYS registry, 2016).

Data analyzed by Shapiro and colleagues, had 71% open vs 29% laparoscopic colorectal cancer surgery. Open surgery, older age, sepsis and prolonged ventilation were associated with higher risk of venous thrombosis (Shapiro et al., 2011). The study advocates for use of minimally invasive approach when feasible.

Open surgery has higher odds, 1.8, of developing venous thromboembolism, than laparoscopic surgery(Nguyen et al., 2007). Patients undergoing open abdominal surgery had a double chance of developing venous thromboembolism than laparoscopic surgery patients(Buchberg et al., 2011).

The three of the scheduled laparoscopic surgeries, during the study period, were converted to open due to machine malfunction. The faulty machine may have led to few scheduled laparoscopic abdominal surgeries. Due to lack of laparoscopic surgery done, there was no data for comparison with open abdominal surgery in this study.

5.2.3 Duration of surgery

Almost all abdominal surgeries conducted lasted more than 45 minutes. Surgery lasting more than 45 minutes is considered a major surgery according to Caprini score. The time is calculated as the total time the patient was under anesthesia(Golemi et al., 2019). This is associated with higher risk of venous thromboembolism and thus scoring high in the VTE risk stratification(Kim et al., 2015). Duration of surgery was an independent predictor of postoperative venous thromboembolism in bariatric surgery. Thus most patients undergoing laparotomy at MTRH are at increased risk of VTE development post-operatively. After multiple logistic regression, in major abdominal surgery, operation time was found to be an independent risk factor for venous thromboembolism together with age, sex and body part to be operated(Sakon et al., 2006).

A study in all general surgical patients at Kenyatta National Hospital(KNH), found that 63.8% of the surgeries lasted more than 45 minutes(Of et al., 2018). The study included all general surgical cases done by the general surgeon in the facility.

Objective 1

Caprini Score

Majority, 75.4% of patient undergoing laparotomy were at moderate (37.7%) and high (37.7%) risk of developing VTE as per the Caprini risk stratification. This correlates with a Caprini study which had 65% in the moderate and high risk group.(Caprini et al., 1991). At Kenyatta National Hospital, the proportion of surgical patients at moderate and high risk were 60%(Of et al., 2018). The number of patient at risk of venous thromboembolism has been described to be between 35.6 to 60.3% (Danwang et al., 2017). In the USA the risk of VTE in surgical patients has been estimated to be 56% in moderate and high risk groups (Anderson et al., 2007). Approximately 75% of the patient undergoing surgery were at moderate to high risk of venous thromboembolism in Barcelona, Spain(Vallano et al., 2004).

In a study published in Slovenia, the proportion of patients with high risk, (a score of more than 5), of venous thromboembolism in abdominal surgery was 71%(H.-P. Yu et al., 2022)

This illustrates similar rate of VTE risk across the world despite different age groups, indication for surgery, perioperative environment and operations performed. The high risk score calls for individualized risk assessment of venous thromboembolism and appropriate prophylaxis measures among laparotomy patients. Adequate thromboprophylaxis helps reduce preventable VTE development.

Objective 2

THROMBOPROPHYLAXIS PRACTICES

Early mobilization

Early mobilization is one of the strategies employed to reduce risk of VTE development. Majority, 82.7%, of the participants in this study were mobilized within 72hours post-laparotomy. This compares to Patrick study in KNH where 96% of the surgical patient were out of bed within 72 hours post-surgery (Of et al., 2018) and Chile (Lara-Madrid et al., 2023).

Emphasis on early ambulation, risk stratification and prophylaxis have been associated with lower risk of venous thromboembolism development (Cassidy et al., 2014). Experts recommend early mobilization, self exercises and physiotherapy postsurgery in all patients, despite their risk of venous thromboembolism (Encke et al., 2016). Early mobilization is also associated with less postoperative pulmonary complications, early return of bowel function and reduced hospital stay (Terzioglu et al., 2013).

In our study, all patients with very low risk of venous thromboembolism were mobile by the 3rd day post-surgery, as recommended by ACCP guidelines.

Early mobilization and use of non-pharmacological means of prophylaxis are encouraged on all post-operative patients because they are associated with low adverse effects, e.g. bleeding, and the other benefits of ambulation (Kozek-Langenecker et al., 2018)

Pharmaco-prophylaxis

Enoxaparin was the only chemoprophylaxis prescribed in the current study. This was prescribed in a common dose of 40mg subcutaneously once a day. The duration of administration was an average of 3.88 days with a range of one to ten days. This compares with a study in Kenyatta National Hospital where enoxaparin was the main pharmacological prophylaxis used (Of et al., 2018). Enoxaparin was the most prescribed chemoprophylaxis in a multinational observation study in sub-Sahara Africa (Kingue et al., 2014b). Most surgeons prescribe a 'blanket' prophylaxis type and dose of chemoprophylaxis without considering patient characteristics, the individual venous thromboembolism risk profile, drug interaction and side effects. Our study did not evaluate the availability and reasons for not prescribing other chemoprophylaxis drugs. Studies have shown similar efficacy of thromboprophylaxis et al., 2012). Thus, the choice of medication should be based on patient preference, ease of administration and cost implication. Dalteparin maybe more expensive than enoxaparin.

Most of the prescription and administration of prophylaxis was done on day one post abdominal surgery, 83%, with only 0.3% getting prophylaxis intraoperatively. This compares with a Lebanon study where majority of prophylaxis was done in period A, (post-operative period) (Geahchan, Basile, Tohmeh, & on behalf of the DIONYS registry, 2016). However, none of the patients was discharged on prophylaxis in our study as practiced in the period B (at discharge from hospital) of the Lebanon study. Patients with highest risk of VTE development are recommended to get extended duration thromboprophylaxis, i.e. 14 to 28 days' post-surgery. Enoxaparin can be administered 8-12 hours before surgery, intraoperatively or within 24- 36 hours postoperatively.

The duration of prophylaxis administration was not standardized in the study group despite guidelines recommending a minimum of 7 to 10 days or until full mobilization. Use of full mobilization criteria to assess when to stop prophylaxis is considered subjective(Lyman et al., 2013). In our study, enoxaparin was prescribed without specifying the duration of administration to the laparotomy patients. The treatment sheet, with the chemoprophylaxis enoxaparin, were infrequently reviewed by the attending ward doctor. Our observation revealed that, enoxaparin was stopped by the administering nurse without much input from the prescriber.

An extended prophylaxis duration of 3-4 weeks for those at highest risk of VTE with malignancy is recommended (Bergqvist et al., 2002). For abdominal malignancy operations, extension of prophylaxis to 3 to 4 weeks is associated with reduced incidence of VTE and no significant increase in bleeding or other complications related to enoxaparin (Avid et al., 2002). Masoto and colleagues, reported favorable safety and efficacy with prolonged prophylaxis after abdominal and pelvic cancer surgery (Sakon et al., 2010) . None of the laparotomy patients in MTRH received extended duration of thromboprophylaxis. This might be due to failure to use VTE risk stratification score provided for by the institution.

In the low risk group, 4 patients (6%) received chemoprophylaxis instead of mechanical prophylaxis as recommended by ACCP guidelines in this risk category (Geahchan, Basile, Tohmeh, & on behalf of the DIONYS registry, 2016). The findings were similar to Patrick et al in KNH, where 4% received enoxaparin despite being in the low risk group (Of et al., 2018). None of the participants in this group received mechanical prophylaxis despite the risk of bleeding being high while using

There was underutilization of chemoprophylaxis as only 13% and 24% of the patient in the moderate risk group and high risk group, respectively, received prophylaxis which compares to the study in KNH at 11.3%. This also correlates with the Senegal ENDORSE study on surgical patients (Bâ et al., 2011). Rocher et al in South Africa found that 26% of the study participants received correct thromboprophylaxis in a Tertiary hospital. A systematic review of literature in Africa, revealed wide range of prescriptions, were 37.5 to 96.5 %, of surgical patients received thromboprophylaxis depending on the specialty (Danwang et al., 2017). This contrasts the Lebanon study where almost 90% of the study participants got prophylaxis (Geahchan, Basile, Tohmeh, & on behalf of the DIONYS registry, 2016) and in USA with prophylaxis given to 76% of patients in high risk group (Tapson et al., 2007). In a study assessing venous thromboembolism prophylaxis and adherence to guidelines, 81% of surgical patients received prophylaxis (Vallano et al., 2004). Reasons reported for underutilization of thromboprophylaxis include; lack of familiarity and utilization of guidelines, lack of resources, underestimation of VTE risk, concern over risk of bleeding and perception of guidelines being difficult and resource intensive to implement (Kakkar et al., 2004).

Five participants in the very low risk group received unnecessary chemoprophylaxis despite the risk of bleeding associated with this practice. This compares to 4% of the low risk group who received chemoprophylaxis in the KNH study. This may be attributed to the lack of utilization of MTRH risk stratification forms, which were attached to the patient's files but were not filled in all the participants of the study. The risk stratification forms help guides the choice of thromboprophylaxis method to

be utilized in an individualized manner. A study in Brazil revealed that high risk patients are under treated while the low risk patients are over treated thus recommending appropriate risk stratification and prophylaxis(Deheiznelin et al., 2006)

Chemoprophylaxis, enoxaparin, was administered to 7 patients with relative contraindication to heparin use (Mismetti et al., 2001). This may illustrate the lack of tailoring of prophylaxis to individual needs by the prescribers of VTE prophylaxis at MTRH.

Mechanical prophylaxis

Mechanical prophylaxis was never prescribed nor utilized in our study on laparotomy patients. Most surgeons in the COSESCA region reported availability, cost and adherence as some of the hindrances to utilization of mechanical methods of VTE prophylaxis (Ndeleva & Lakati, 2018). This contrasts the practice in other centers and ACCP 2012 guideline recommendation, where mechanical prophylaxis by either GEC,IPC or bandage is utilized for VTE prophylaxis (Geahchan, Basile, Tohmeh, & on behalf of the DIONYS registry, 2016), (Of et al., 2018).

Mechanical prophylaxis is recommended for patients with high bleeding risk or other contraindication to chemoprophylaxis. This is continued till the bleeding risk is low to safely use chemoprophylaxis. They are also utilized in patients with low risk of venous thromboembolism as the only method of prophylaxis. Combination of mechanical and pharmacological agents is recommended in very high risk group as it is associated with lower risk of thrombi formation (Lobastov et al., 2021).

Objective 3

Incidence of symptomatic DVT

The incidence of symptomatic deep venous thrombosis was found to be 6.8%. This correlates with the findings in Uganda, where the incidence of DVT was 5% in laparotomy patients. In Africa, the prevalence of deep venous thrombosis was estimated to be 2.4 to 9.6% in surgical patients in a systematic review (Danwang et al., 2017) The findings are similar to a Nigerian study that had 2.2% incidence of DVT (Osime et al., 1976). This contrasts a study done in Denmark where the risk of VTE was 1.1% (Balachandran et al., 2020). Of note, all patients received pharmacological prophylaxis in this group. Tomas and colleagues found an incidence of DVT to be 0.2%, though their subjects were morbidly obese and prophylaxis was utilized in all patients (Escalante-Tattersfield et al., 2008). In Middle East, the incidence of venous thromboembolism has been quoted as 7.1% in critically ill patients (Arabi et al., 2013). After open and laparoscopic gastric bypass surgery the incidence of deep venous thrombosis was quoted to be 0.79%, though all the participants received recommended prophylaxis. Four cases developed bleeding post-surgery(Brasileiro et al., 2008)

The high risk profile of VTE and the incidence of DVT, in laparotomy patients at MTRH, illustrates the importance of proper risk stratification of patient and prophylaxis as VTE is considered one of the preventable conditions in the clinical set up.

DVT was more common in patient with high Caprini score. These patients have multiple risk factors of developing VTE. This concurs with other studies on VTE incidence(Rocher et al., 2019)(Mokhtari et al., 2011)

Enoxaparin prescription was associated with higher risk of DVT development. This might be due prescription of enoxaparin to patients with multiple risk factors or partly due to suboptimal prescription of both mechanical and chemical thromboprophylaxis. The prescribers might have an idea of VTE risk in this group of patients. All patients in high risk group receiving prophylaxis, had chemoprophylaxis prescribed as a sole agent, contrary to ACCP guidelines which advocates for combination with mechanical method. Furthermore, the duration of prophylaxis was not standardized and did not follow guidelines (Bergqvist et al., 2002).

Participants with intra-abdominal infection and tumors had a higher chance of enoxaparin being administered as these diagnoses were associated with higher risk of VTE. This may demonstrate prescribers' knowledge of some of the VTE risk even without the use of availed VTE risk profile forms or scores by MTRH. Procedures conducted by consultant surgeons had a higher rate of chemoprophylaxis being prescribed. Senior practitioners may have managed or lost a patient with VTE leading to emphasis of prophylaxis when they operate (Kesieme et al., 2016). A study in South Africa attributed low thromboprophylaxis uptake to junior doctor writing prescription post-surgery (Rocher et al., 2019). Consultant are engaged in complex laparotomies and operating sicker patients than the residents at MTRH.

CHAPTER SIX

CONCLUSION AND RECOMMENDATION

6.1 Conclusion

In conclusion, most of the laparotomy patients at MTRH are at moderate and high risk of VTE development, calling for proper VTE risk assessment and prophylaxis. There is limited use of stratification scores by prescribers despite MTRH providing Caprini score charts in patients' files. Risk stratification helps individualize prophylaxis and minimize adverse effects of thromboprophylaxis.

MTRH passive dissemination of protocol on venous thromboprophylaxis is underutilized leading to inappropriate risk assessment and poor selection of thromboprophylaxis method in laparotomy patients.

Although ACCP 2012 recommend dual prophylaxis, for high risk group, only chemoprophylaxis is utilized at MTRH. This calls for increased awareness among prescriber on the role of mechanical prophylaxis in VTE prophylaxis as this may help reduce the incidence of VTE. To the MTRH management, it is paramount to avail several option of prophylaxis for tailor made management of post-operative patients in respect to VTE prophylaxis. Patients with a low risk are recommended to get mechanical prophylaxis due to the higher risk of bleeding.

Most laparotomy patients with high risk of developing VTE do not receive thromboprophylaxis. This may lead to occurrence of preventable VTE at MTRH. Several patients with a very low risk of VTE development received enoxaparin thus predisposing them to adverse effects of the drug (bleeding and wound complication). Enoxaparin prescribed to laparotomy patients, at MTRH, had no specified duration of administration. Most prophylaxis treatment sheet are not reviewed in the wards post operatively. The chemoprophylaxis on treatment sheet of laparotomy patients is stopped by the ward nurse with minimal input from the ward doctor. No laparotomy patients were on extended duration prophylaxis i.e. discharged on chemoprophylaxis or mechanical prophylaxis.

The incidence of clinical DVT in laparotomy patients at MTRH is high despite most patients being young and middle aged. Infectious conditions were more prevalent in patients undergoing laparotomy at MTRH. Thus, VTE risk stratification approach may guide in the use of prophylaxis to reduce the morbidity and mortality associated with venous thromboembolism.

6.2 Recommendation

VTE risk stratification is paramount to help identify patients who require prophylaxis in laparotomy patients. Risk stratification will assist in improving the number of laparotomy patients at risk of VTE get appropriate prophylaxis. Using MTRH availed risk stratification guide will reduce the number of laparotomy patients with very low risk receiving unnecessary chemoprophylaxis.

Prescribers to specify the number of days the chemoprophylaxis is administered to laparotomy patients. Frequent review of the treatment sheets on VTE prophylaxis in the ward is important in detecting adverse effects of method employed and when to stop it. There is need to employ multifaceted passive strategies to improve on utilization of MTRH availed venous thromboprophylaxis tools. This can be done by creating interventional programs to enhance awareness and improve adherence to guidelines. This can be done through seminars, workshops and continuous medical education targeting prescribers on the issues of VTE risk stratification and proper prophylaxis utilization.

These interventions can be followed by post-interventional survey to assess impact and identify areas of improvement. A committee can be formed to oversee program implementation, monitoring and evaluation. Single passive dissemination of guidelines is less likely to improve venous thromboprophylaxis practices. Thus active strategies and reminding prescribers to assess patient risk and choose appropriate prophylaxis are likely to improve the practice.

Clinical decision support system (CDSS) with integrated computer or human alert are active strategies that will help care givers in proper risk stratification of VTE and prescribe necessary prophylaxis in laparotomy patients.

Multifaceted interventions and alert interventions included in clinician's workflow may help health workers improve use of appropriate thromboprophylaxis thus reducing the morbidity and mortality of VTE in hospitalized patients. Adoption of a MTRH specific system wide measure will be key in improving thromboprophylaxis for laparotomy patients and the hospital at large.

There is need to mobilize and avail mechanical methods of prophylaxis to enable prescribers to have more options during thromboprophylaxis in laparotomy patients. This calls for the hospital management to allocate resources to this noble course. Local guideline development with engagement of prescribers, nurses and the hospital administration will enhance adherence to evidence based practices and allow for utilization of locally available resources to prevent VTE. This can be started by optimizing the MTRH Caprini score forms utilization and improving it as the users give feedback.

Local research on effectiveness and cost implication of prophylaxis and management of VTE can be organized by the Ministry of Health in collaboration with county government to inform policies on prophylaxis in our local setup. This is important as most guidelines adopted are developed in high income countries where clinical practices and resources availability are different.

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Serial no.
Date of admission
Age
Sex
Diagnosis
Type of surgery
Duration of surgery a) <45minutesb) >45minutesb
Lead surgeon a) consultantb) senior residentc) resident
Confined to bed for a) < 72hoursb) >72hourspost-surgery.
Any thromboprophylaxis given a) preoperatively
b) intraoperatively
c)day 1 postoperatively
d) at discharge
if yes, which one and duration of prescription
i. Pharmacological drug,dosefrequency
duration(days), was it administered yes or no
ii. Mechanicalif yes, is it utilized yes, no
Contraindication to pharmacological prophylaxis
a) Risk of bleeding-upper GI bleeding
-hepatic impairment
-known bleeding disorder
b) known thromboprophylaxis drug reaction or allergiesif any specify the
drug and reaction

APPENDICES APPENDIX I:DATA COLLECTION TOOL

contraindication to mechanical prophylaxis	
lower limb ulceration	
known vascular disease of lower limb	
Filling of MTRH/patients file caprini score chart;	
complete, incomplete or not done	
Modified Caprini score chart	
1 point for each risk factor	points
Age 40-60 years	
Acute myocardial infarction(<1 month)	
BMI >25kg/m2	
CHF exacerbation(1 month)	
History of inflammatory bowel disease(IBD)	
Procedure with local anaesthesia	
Swollen legs/varicose veins(current)	
Sepsis(1 month)	
Severe lung disease eg pneumonia, COPD(< 1 month)	
Medical patient currently at bed rest	
1 point for women only(for each risk factor)	
	1
Oral contraceptives or HRT	
Pregnancy or postpartum(< 1 month)	
History of unexplained stillborn infant, spontaneous abortion(>3), premature	
birth with toxemia or growth restricted infant	

2 points for each risk factor	
61-74 years	
Central venous access insitu	
Immobile >72hours	
Leg plaster cast or brace	
malignancy	
Surgery >45 minutes	
points for each risk factor	
Age> 75	
Established thrombophylia	
Heparin induced thrombocytopenia	
History of venous thrombosis/thromboembolism	
Family history of VTE (first degree relative)	
points for each factor	
Acute spinal cord injury(< 1month)	
Stroke(<1 month)	
Multiple trauma(<1 month)	
Major surgery lasting over 6 hours	
Total points	

WELL'S SCORE

Clinical features	points	Score within	Score at 2	Score at 4
	•	48hrs	weeks post	weeks post
		postoperatively	operatively	operatively
active	1 point			
cancer(treated				
within last 6				
months				
Paralysis, paresis	1 point			
or recent cast				
immobilization of				
limb				
Recently bed	1 point			
ridden for>3days				
or major surgery				
in last 12 weeks				
Local tenderness	1 point			
along distribution				
of deep vein				
system				
Entire leg swollen	1 point			
Calf swelling	1 point			
>3cm compared				
with				
asymptomatic				
leg(measured				
10cm from tibial				
tuberosity)				
Pitting edema(1 point			
greater in the				
symptomatic leg)				
Collateral	1 point			
superficial				
veins(non-				
varicose)				
Previous	1 point			
documented DVT				
Alternative	- 2 points			
diagnosis at least				
as likely as DVT				
TOTAL SCORE	-			

NB; Alternative diagnosis may be; superficial phlebitis, post-thrombotic syndrome, cellulitis, muscle strain, leg swelling in paralyzed limb, venous insufficiency, edema due to ccf or cirrhosis, external venous obstruction(e.g. due to tumor), lymphagitis or lymphedema, popliteal cyst, hematoma, pseudo aneurysm or knee abnormality

2or more points DVT likely

<2 points DVT unlikely

Doppler ultrasound findings

1. Within 48hrs post operatively(if WELL SCORE IS 2 OR MORE)

DVT PRESENT; YES----- NO-----

VEIN SITE; CALF------, THIGH-----OR ABDOMINAL PELVIS ----

2. Day 14 post operative Doppler ultrasound(if WELL SCORE IS 2 OR MORE)

DVT PRESENT; YES----- NO-----

VEIN SITE; CALF-----, THIGH-----OR ABDOMINAL PELVIS ----

3. Day 28 post operative Doppler ultrasound: (if WELL SCORE IS 2 OR MORE)

DVT PRESENT; YES----- NO-----

VEIN SITE; CALF-----, THIGH-----OR ABDOMINAL PELVIS ----

APPENDIX II: CONSENT FORM Study Title

THROMBOPROPHYLAXIS PRACTICES IN PATIENTS UNDERGOING LAPAROTOMY AT MOI TEACHING AND REFERRAL HOSPITAL, ELDORET. Investigator

Dr. Njeri Dennis (postgraduate student, Moi University).

Supervisors

Dr. Andrew Wandera (Supervisor, Department of General Surgery, Moi University) Dr. Simiyu Taabu (Supervisor, Department of General Surgery, Moi University)

PART I: Information Sheet

Introduction

We are carrying out a study on thromboprophylaxis practices in patients undergoing laparotomy at MTRH. This has become a common problem in our facility. I am going to give you information on this study and then request you to participate in the study. You are free to ask any questions that you may have concerning the study and make a free will to participate.

Purpose

Venous thromboembolism is deadly disease and may occur post abdominal surgery. Thromboprophylaxis have been developed to reduce its occurrence. The study seeks to determine the risk of venous thromboembolism in laparotomy patients and the prophylaxis they are given at MTRH.

Benefits of the study

By carrying out this study, we will be able to establish the risk profile of laparotomy patients and the current measures in prophylaxis. As a result, we will be able to advice on measures that will improve prescription of VTE prophylaxis.

Discomforts of the study

We do not anticipate that this study will be uncomfortable to you or harm you in any way.

Confidentiality

The information that we collect from this study will be confidential. Information about you that will be collected from the research will be put away and no-one but the researchers will be able to see it. Any information about you will have a number on it instead of your name. Only the researchers will know what your number is and we will lock that information up with a lock and key. It will not be shared with or given to anyone without your consent.

Right to refuse or withdraw

You have the right to refuse to participate in the study or even to withdraw from the study at any point. This will not lead to any penalties or denial of quality of care.

PART II: Certificate of Consent

RESEARCH TOPIC: THROMBOPROPHYLAXIS PRACTICES IN PATIENTS UNDERGOING LAPAROTOMY AT MOI TEACHING AND REFERRAL HOSPITAL, ELDORET

INVESTIGATOR: Dr Njeri Dennis

MOBILE NO: 0727267918/0773612987

I.....of P.O Box.....

Tel.....hereby give informed consent to participate in this study at MTRH, Uasin Gishu County. The study has been explained to me clearly by Dr. Njeri Dennis (or his appointed assistant).

I have understood that by participating in this study, I shall volunteer information regarding my illness and other co-morbidities. I am aware that I can withdraw from this study at any time. I have also been assured that all information shall be treated and managed in confidence. I have not been induced or coerced by the investigator (or his appointed assistant) to cause my signature to be appended in this form and by extension participate in this study.

Kiswahili: Fomu Ya Kibali

MADA YA UTAFITI: THROMBOPROPHYLAXIS PRACTICES IN PATIENTS UNDERGOING LAPAROTOMY AT MOI TEACHING AND REFERRAL HOSPITAL, ELDORET

MTAFITI - Dr Njeri Dennis

RUNUNU: 0727267918/0773612987

Mimi	 			_ wa	Sanduku	la	Posta
	 Nambari	ya	Simu				

najitolea kwa hiari yangu mwenyewe kutoa kibali cha kujihusisha katika utafiti uliotajwa hapo juu unaendelezwa katika kaunti ya Uasin Gishu. Nimepokea maelezo ya tafsili kuhusu utafiti huu kutoka kwa Daktari Njeri Dennis (au mtafiti msaidizi wake) katika lugha, kanuni na masharti ninayoelewa vyema. Nimehakikishiwa kuwa, sitaadhirika kamwe kutokana na kujihusisha kwangu katika utafiti huu. Ilibainishwa kuwa kujihusisha katika utafiti huu ni kwa hiari na nina uhuru wa kujiondoa wakati wowote ule bila ya kuhujumiwa. Zaidi ya hayo, nilihakikishiwa kuwa, kanununi zote za maadili ya utabibu,uhuru, haki, na manufaa zitazingatiwa katika utafiti huu.

Jina la Mhojiwa	
Sahihi	
Tarehe	
Jina la shahidi	-
Sahihi	_
Tarehe	

Statement by the researcher/person taking consent

I have accurately read out the information sheet to the parent of the potential participant, and to the best of my ability made sure that the person understands that the following will be done:

1. He or she will be included in the study as a study participant.

2. Results of the study will be communicated to all the involved stakeholders.

I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

A copy of this ICF has been provided to the participant.

Print Name of Researcher/person taking the consent_____

Signature of Researcher /person taking the consent_____

Date _____

Day/month/year

APPENDIX III: BUDGET

Item	Quantity	Unit price (KSh)	Total (KSh)
Laptop	1	50,000	50,000
Stationery	-	-	20,000
Printer	1	20,000	20,000
Internet bundles	3000/month	3 months	9000
Data management and analysis	-	-	30,000
Grand total	I		179,000

APPENDIX IV: VENOUS THROMBOEMBOLISM RISK STRATIFICATION SCORE



An ISO 9001:2015 Certified Hospital



MOI TEACHING AND REFFERAL HOSPITAL VENOUS THROMBOEMBOLISM RISK STRATIFICATION SCORE

Patient Name: Age: .	t Name: Hospital Number: Age:			Sex:
Wgt:kg Ward:	0	DOA:	DOD:	Service
Race:	•••••	Diagnosis:		

	SECTION A	A: Risk factor	s(Caprini Score model))
Each Risk Factor Repre	esents 1 Point		Each Risk Factor Rep	presents 2 Point
Swollen legs (current) Varicose veins Obesity (BMI >25) Minor Surgery planned Sepsis (<1 month) Serious lung disease inclue Oral contraceptives or hor Pregnancy or postpartum (History of unexplained still	Acute myocardial infarction Congestive heart failure (<1 Medical patient currently at History of inflammatory bo History of prior major surge Abnormal pulmonary funct uding pneumonia (<1 month) rmone replacement therapy (<1 month) illborn infant, recurrent spont birth with toxemia or growth	at month) at bed rest owel disease gery(<1month) tion (COPD)	Malignancy (present or Laparascopic surgery (> Patient confined to bed Immobilizing plaster cas Each Risk Factor Rep Age 75 years or older History of DVT/PE Positive factor V Leiden Elevated serum homocy Heparin-induced thromb	 Major surgery (>45min previous) >45minutes) (>72hours) st (<1month) resents 3 Point Family history of throm positive prothrombin 20 positive Lupus anticoage steine
Each Risk Factor Rep			Elevated anticardiolipin Other congenital or acqu	antibodies
 Stroke (<1month) Elective major lower extree Hip, pelvis or leg fracture Acute spinal cord injury (presented) 	e (<1month)	Subtotal:	If yes: Type HIV	

Duration of prophylaxis

1. Acutely ill medical patient = until full ambulation

- 2. Surgical patients = 10 14 days 3. After TKR/THR = 28 35 days

Total Risk	Risk level	Incidence		PROPHY	LAXIS REGIMEN	
Factor Score		of DVT				•
0-1	Low risk	2%	Early ambulati	on		
2	Moderate Risk	10-20%	Sequential con	lowing medication npression device (S units SQ BID/Enox		ces:
3-4	Higher Risk	20-40%	Choose ONE of	of the following me npression Device (units SQ TID ovenox: 40mg S 30mg S	dications +/- compress	;, CrCI > 30mL/min) rCI = 10-29mL/min)
5 or more	Highest Risk	40-80%	Sequential Con	of the following me mpression Device (units SQ TID (Pref ovenox 40mg 2 30mg 2	edications PLUS comp	ression devices s, CrCI > 30mL/min) rCI = 10-29mL/min)
i) Anticoagula H – Hypertensi			N C: Prophyla		deration (risk of ble mittent pneumatic :	eeding)
\mathbf{A} – Abnormal	function - Re	enal [1]		Does pa	tient have severe perip	heral arterial disease?
S – Stroke [1]	- L	iver [1]		-	tient have congestive h	
B - Bleeding [L - Labile INR E - Elderly > 6:	R [1]			Does pa	itient have an acute sup	perficial/deep vein thror
D – Drugs: - A - A Total Score:	•		high risk (cons			
				CTION D: Outo	comes	
i) Risk stratific ii) Pro	cation done: Yo ophylaxis given] No 🗔		iv) Complications:	 Yes No Major bleeding Minor bleeding
	ophylaxis regi V – heparin	men:	Dose	Duration		DVT VTE
					• • •	nen:
\square FXaI \square Antip	platelet		·····			
☐ IVC f ☐ Warfa		_				

Scored by:

	Are You at Risk for DVT?
	are at risk for Deep Vein Thrombosis (DVT), a blood clot that forms in one of the deep veins of your leg
그는 것 같은 전 것 같이 한 것이 많은 것 것 같아요. 것 같아요. 것 같아요. 같이 많이	urrent health may determine if you are at risk for developing this condition. Please take a moment to
The second s	plete it for a loved one). Then be sure to talk with your doctor about your risk for DVT and what you
n do to help protect against it.	
Please select your AGE :	
0 - 40 years old (0 points)	
41 - 60 years old (1 point)	
61 - 74 years old (2 points)	
Age 75 or older (3 points)	Score:
Add 1 POINT for each statemen	
요즘 눈물 모양이 안 물리에 다가 들었다. 것이 가지 않는 것이 많아 있는 것이 많아 있는 것이 없다. 않다. 것이 없다. 것이 없다. 것이 없다. 않다. 않다. 않다. 것이 없다. 않다. 않다. 것이 없다. 것이 없다. 것이 없다. 것이 없다. 것이 없다. 것이 없다. 않다. 것이 없다. 것이 없다. 것이 없다. 것이 없다. 것이 없다. 않다. 않다. 않다. 않다. 않다. 것이 없다. 않다. 것이 없다. 않다. 것이 없다. 것이 없다. 것이 없다. 않다. 것이 없다. 것이 없다. 것이 없다. 않다. 않다. 않다. 않다. 않다. 않다. 않다. 않다. 않다. 않	rgery under general or regional anesthesia that lasted for MORE THAN 45 minutes.
이번에 가장 방법에서 전쟁을 받았다. 한국민들은 것 같아.	currently have varicose veins. (NOT spider veins)
Within the last month, I have had or	
Within the last month, I have had a	
	currently have a serious infection and was hospitalized, for example pneumonia, cellulitis, etc.
	vel disease (includes Crohn's or ulcerative colitis).
I have or have had congestive heart	
I have a chronic lung disease (for ex	ample COPD, emphysema) NOT including asthma.
	Score:
For WOMEN ONLY, add 1 POIL	for each statement that applies to you:
	traceptive pills, skin implantable devices, hormonal patches, IUD with hormones, depo shot) or
	including condoms or barrier devices.
I am pregnant or had a baby within	
I have a history of an unexplained st born smaller than appropriate (low v	illborn infant, THREE (3) or more spontaneous abortions, premature birth with preeclampsia, or baby
com analier chan appropriate (iou i	Score:
Add 2 POINTS for each stateme	
My doctor told me I have cancer, leu	
	emovable plaster cast or mold that has kept me from bending and/or walking normally on this leg.
In the second s second second se second second s	ently have a PICC line, Port, or central venous access catheter in my neck or chest that delivers blood o
* medicine directly into my heart.	Score:
Add <u>3 POINTS</u> for each stateme	
I have had a blood clot in my legs, a	
	randparents, aunts, uncles, siblings, cousins) suffered from a blood clot?
Have you or any blood relative ever	been told that you have an abnormal blood test indicating an increased risk of blood clotting?
	Score:
Please select points for each sta	atement that applies to you
	REE (3) DAYS associated with sustained walking of fewer than 30 feet. (1 point)
	MORE DAYS associated with sustained walking of fewer than 30 feet. (2 points)
	Score:
Add 5 POINTS for each stateme	
a statute and the second s	hip or knee joint replacement surgery. (include if scheduled surgery)
Within the past month, I have had a	
Within the past month, I have had a	serious trauma (for example multiple broken bones due to fall or car accident).
같은 가지 않는 것을 알았다. 정말은 일이라 집에서 가지 않는 것을 가 없다.	stroke (clot or hemorrhage in the brain, transient ischemic attack).
Within the past month, I have had a	spinal cord injury with paralysis
	Score:
If you have a SCHEDULED SUI	RGERY coming up, please select an option.
	neral or regional anesthesia for LESS THAN 45 minutes. (1 point)
	neral or regional anesthesia for MORE THAN 45 minutes, including laparoscopic or arthroscopic. (2
	cement – already included in the score of 5)
points) (concentration form replan	Soorer
points) (concentration total joint repla	Score:

Overweight (BMI > 25)	ement that applies based on patient's BMI:
overweight (bini > 25)	Score:
Add 1 POINT for each add	ditional risk factor:
hese risk factors have not been	n tested in validation studies but have been shown in the literature to be associated with thrombosis)
Morbid obesity (BMI > 40)	
Smoking	
Diabetes requiring insulin	
Chemotherapy	
Blood transfusion	
Human immunodeficiency viru	is (HIV)
Length of surgery greater than	2 hours (EXCLUDING total joint arthroplasty - already included in the score of 5)
•	Score:
	he patient and adjust score as necessary:
	. Includes pitting edema of any kind.
	female patient. (see #3 "For women only", statement 3)
	bosis. Includes first, second and third degree relatives. Includes both superficial and deep vein thrombosis. nbosis. Includes first, second and third degree relatives.
	Adjusted Score:
	Total Score:

Below are Categories of individual risks, adapted from (These, 2003)

Low Risk	Moderate Risk	High Risk	Highest Risk		
Calf vein: <5% Proximal DVT: <1% Fatal PE: <0.1%	Calf vein: 10% to 20% Proximal DVT: 2% to 4% Fatal PE: 0.1% to 0.4% • Minor surgery: aged 40 to 60 years or 1 risk factor	Calf vein: 20% to 40% Proximal DVT: 4% to 8% Fatal PE: 0.4% to 1.0% • Major general surgery: aged 40 to 60 years with 1 risk factor • Major surgery or illness: aged >60 years with no risk factors • Major medical illness, trauma, burns • Minor surgery or illness with prior VTE • Lower limb	Calf vein: 40% to 80% Proximal DVT: 10% to 20% Fatal PE: 1% to 5% • Fracture/surgery involving pelvis, hip, leg • Major surgery or illness with prior VTE • Major surgery for metastatic cancer • Major surgery or trauma with risk factors		

APPENDIX V: IREC APPROVAL



P.O. BOX 3

ELDORET Tel: 33471//2/3

INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE (IREC)



MOI UNIVERSITY COLLEGE OF HEALTH SCIENCES P.O. BOX 4606 ELDORET Tel: 33471/2/3 2nd September, 2021

Reference: IREC/2021/114 *Approval Number: 0003965* Dr. Njeri Dennis Ng'ang'a, Moi University, School of Medicine, P.O. Box 4606-30100, <u>ELDORET-KENYA.</u>

Dear Dr. Njeri,

THROMBOPROPHYLAXIS PRACTICES IN PATIENTS UNDERGOING LAPAROTOMY AT MOI TEACHING AND REFERRAL HOSPITAL, ELDORET

This is to inform you that *MTRH/MU-IREC* has reviewed and approved your above research proposal. Your application approval number is *FAN: 0003965.* The approval period is 2nd September, 2021- 1st September, 2022.

This approval is subject to compliance with the following requirements;

- i. Only approved documents including (informed consents, study instruments, Material Transfer Agreements (MTA) will be used.
- ii. All changes including (amendments, deviations, and violations) are submitted for review and approval by *MTRH/MU-IREC*.
- iii. Death and life threatening problems and serious adverse events or unexpected adverse events whether related or unrelated to the study must be reported to *MTRH/MU-IREC* within 72 hours of notification.
- iv. Any changes, anticipated or otherwise that may increase the risks or affected safety or welfare of study participants and others or affect the integrity of the research must be reported to *MTRH/MU-IREC* within 72 hours.
- v. Clearance for export of biological specimens must be obtained from *MOH at the recommendation* of *NACOSTI* for each batch of shipment.
- vi. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. Attach a comprehensive progress report to support the renewal.
- vii. Submission of an executive summary report within 90 days upon completion of the study to MTRH/ MU-IREC.

Prior to commencing your study; you will be required to obtain a research license from the National Commission for Science, Technology and Innovation (NACOSTI) https://oris.nacosti.go.ke and other relevant clearances from study sites including a written approval from the CEO-MTRH which is mandatory for studies to be undertaken within the jurisdiction of Moi Teaching & Referral Hospital (MTRH) and its satellites sites.

Since	rely,		ETH	TIONAL RESEA	ARCH	34			
CHAI	F. E. WERE RMAN		AF	2 SEP 202	ED MMT	TEE			
cc	CEO Principal	:	MTRH CHS	Dean Dean	-	SOP SON	Dean Dean	-	SOM SOD

APPENDIX VI: HOSPITAL APPROVAL (MTRH)



MOI TEACHING AND REFERRAL HOSPITAL

Telephone :(+254)053-2033471/2/3/4 Mobile: 722-201277/0722-209795/0734-600461/0734-683361 Fax: 053-2061749 Email: ceo@mtrh.go.ke/directorsofficemtrh@gmail.com

Nandi Road P.O. Box 3 - 30100 **ELDORET**, KENYA

Ref: ELD/MTRH/R&P/10/2/V.2/2010

Dr. Njeri Dennis Ng'ang'a Moi University School of Medicine P.O. Box 4606-30100 ELDORET-KENYA

3rd September, 2021

THROMBOPROPHYLAXIS PRACTICES IN PATIENTS UNDERGOING LAPAROTOMY AT MOI TEACHING AND **REFERRAL HOSPITAL, ELDORET**

You have been authorised to conduct research within the jurisdiction of Moi Teaching and Referral Hospital (MTRH) and its satellites sites. You are required to strictly adhere to the regulations stated below in order to safeguard the safety and well-being of staff, patients and study participants seen at MTRH.

- The study shall be under Moi Teaching and Referral Hospital regulation. 1
- 2 A copy of MTRH/MU-IREC approval shall be a prerequisite to conducting the study.
- Studies intending to export human bio-specimens must provide a permit from MOH at 3 the recommendation of NACOSTI for each shipment.
- No data collection will be allowed without an approved consent form(s) to participants 4 unless waiver of written consent has been granted by MTRH/MU-IREC.
- 5 Take note that data collected must be treated with due confidentiality and anonymity.

The continued permission to conduct research shall only be sustained subject to fulfilling all the requirements stated above.

MOI TEACHING AND REFERRAL HOSPITAL PPROVED 03 SFP 2021 003/00/202 The DR. WILSON K. ARUASA, MBS, EBS MOI TEACHING AND REFERRAL HOSPITALBOX 3-30100, ELDORE Senior Director, Clinical Services C.C.

- **Director of Nursing Services** -
- HOD, HRISM _

All correspondence should be addressed to the Chief Executive Officer Visit our Website: www.mtrh.go.ke TO BE THE LEADING MULTI-SPECIALTY HOSPITAL FOR HEALTHCARE, TRAINING AND RESEARCH IN AFRICA