A Prospective Study Comparing the Effect of Rivaroxaban vs. Enoxaparin Given as a Prophylaxis for Deep Venous Thrombosis in Patients Undergoing Bariatric Surgery

Thesis

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List of Abbreviations

Abb.	Full term
ACCP	*American College of Chest Physicians*
ASBS	*American Society of Bariatric Surgery*
BMI	*Body Mass Index*
COPD	*Chronic Obstructive Pulmonary Disease*
CVI	*Chronic Venous Insufficiency*
DM	*Diabetes Mellitus*
DVT	*Deep Vein Thrombosis*
Fig.	*Figure*
HTN	*Hypertension*
IPC	*Intermittent Pneumatic Compression*
IQR	*Interquart Range*
IVC	*Inferior Vena Cava*
LMWH	*Low Molecular Weight Heparin*
No	*Number*
NOACs	*New Oral Anticoagulants*
OA	*Osteoarthritis*
PO	*Oral intake*
RCT	*Randomised controlled Trials*
S.D	*Standard Deviation*
Sig.	*Significance*
UFH	*Unfractionated Heparin*
USA	*United States of America*
VKA	*Vitamin K antagonists*
VTE	*Venous Thromboembolism*
VV	*Varicose Veins*

ABSTRACT

Background: Obesity is a risk factor for deep vein thrombosis (DVT) and venous thromboembolism (VTE). VTE is the most common cause of mortality in patients undergoing bariatric surgery. There is a remarkable variation in practice regarding methods, dosages and duration of prophylaxis in this patient population. Most of the literature is based on European & American patients and specific guidelines for Egyptians do not exist.

Aim of the Work: to compare between obese patients undergoing bariatric surgery who receive Enoxaparin prophylactic dose perioperative and others who receive Rivaroxaban prophylactic dose perioperative, concerning the incidence of development of VTE postoperatively.

Patients and Methods: This study was conducted on 40 patients From December 2017 till February 2019. Patients included in the study were essentially attending the Vascular Out-patient Clinic at Ain Shams University Hospitals and Nasser Institute for research & Treatment at Cairo and received postoperative prophylactic doses of Enoxaparin and Rivaroxaban after undergoing bariatric surgeries.

Results: This study showed less incidence of DVT in Patients who received Rivaroxaban (5%) than those who received Enoxaparin (10%) but the difference in between the 2 of the was statistically insignificant. In terms of bleeding tendency, both drugs showed no incidence of bleeding tendency.

Conclusion: From the previous results, further Randomized Controlled studies should be done on a larger cohort of patients undergoing bariatric surgery to determine the efficacy and to set new guidelines for DVT prophylaxis in bariatric patients bearing in mind terms of efficacy, safety and compliance on therapeutic regimens.

Keywords: *Rivaroxaban – Enoxaparin - Deep Venous Thrombosis - Pulmonary Embolism*

INTRODUCTION

Obesity is a risk factor for deep vein thrombosis (DVT) and venous thromboembolism (VTE). VTE is the most common cause of mortality in patients undergoing bariatric surgery. There is a remarkable variation in practice regarding methods, dosages and duration of prophylaxis in this patient population. Most of the literature is based on European & American patients and specific guidelines for Egyptians do not exist.

Surgical approaches to weight loss, bariatric surgeries, are commonly performed procedures for morbidly obese individuals; the estimated number of bariatric procedures in the USA alone was close to 180,000 in 2013. Bariatric surgery is effective in achieving weight loss and improving obesity-related complications ***(Buchwald et al., 2004; Maggard et al., 2005; Colquitt et al., 2014).***

Thus, in patients with morbid obesity, i.e., a body mass index of ≥ 40 or ≥ 35 kg/m2 with co-morbidities, bariatric surgery is presently considered to be the only effective therapy for obesity. Extensive data demonstrate that surgery can improve or even reverse many comorbidities such as type 2 diabetes, hypertension, obstructive sleep apnoea and steatohepatitis ***(Adams et al., 2012; Caiazzo et al., 2014; Ashrafian et al., 2015).***

There are also potential risks or complications, among them venous thromboembolism (VTE). Reported rates of VTE, including deep vein thrombosis (DVT) and pulmonary embolism (PE), following bariatric surgery are 0.3%–2.2%, with rates of PE being approximately 1%, despite application of methods to prevent these complications ***(Stein et al., 2013; Froehling et al., 2013; Lancaster et al., 2008; Winegar et al., 2011; Jamal et al., 2015; Finks et al., 2012).***

VTE is a challenging problem after bariatric surgery but there are few randomized controlled trials studying thrombo-prophylaxis in this population. Most bariatric surgery patients carry multiple risk factors for VTE and therefore are at least at moderate risk for VTE postoperatively. Despite the elevated VTE risk, the incidence of postoperative VTE is low. A meta-analysis of 19 studies with 3991 patients demonstrated a weighted mean incidence of PE of 0.5% with fixed-dose chemoprophylaxis and an incidence of symptomatic VTE of 0.6% with weight-based chemoprophylaxis ***(Becattini et al., 2012).*** PE is a frequent cause of postoperative mortality in the bariatric surgery population and is a common finding at autopsy ***(Sapala et al., 2003; Morino et al., 2007; Melinek et al., 2002).*** The risk of VTE is lower for laparoscopic compared with open bariatric surgery patients (0.34% versus 1.54%) ***(Winegar et al., 2011).***

Various strategies have been used to prevent VTE in patients undergoing bariatric surgery, including pharmacologic and mechanical approaches. However, the optimal approach remains unclear. Based on the ACCP guidelines, LMWH, unfractionated heparin, or mechanical prophylaxes with Intermittent Pneumatic Compression (IPC) are recommended. There is no consensus on the standard of care for chemo-prophylactic agent, dosing, timing, or duration. Dosing of pharmacologic prophylaxis is challenging in postsurgical bariatric surgery patients because dosing by body weight may lead to excessive anticoagulation and bleeding. Some studies utilize anti-factor Xa levels to determine adequacy of anticoagulation, but therapeutic levels do not necessarily predict a reduction in VTE. The ACCP guidelines recommend consulting with a pharmacist to determine dosing in obese patients ***(Gould et al., 2012).*** Prophylactic removable inferior vena cava (IVC) filter use had previously been recommended in high risk bariatric patients such as those with BMI >60, severe pulmonary hypertension, or previous VTE ***(Sapala et al., 2003).*** More recent data argues against the use of prophylactic IVC filter placement. In 322 of 97,218 patients who received IVC filters and had either gastric bypass or gastric band, there was an increased risk of DVT, length of hospital stay and mortality compared to the non-IVC group ***(Li et al., 2012).*** In this study, there was no benefit for prophylactic insertion of IVC filters. A meta-analysis of prophylactic IVC filters in

bariatric surgery demonstrated an increase in the risk of DVT by 3-fold while the increase in mortality was not statistically significant ***(Kaw et al., 2014).*** Long-term complications associated with IVC filters are concerning ***(Nicholson et al., 2010)*** and most filters are never retrieved ***(Karmy-Jones et al., 2007).*** There is insufficient data from randomized studies to support the use of prophylactic IVC filters.

AIM OF THE WORK

The main aim of this study is to compare between obese patients undergoing bariatric surgery who receive Enoxaparin prophylactic dose perioperative and others who receive Rivaroxaban prophylactic dose perioperative, concerning the incidence of development of VTE postoperatively.

Chapter 1
SURGICAL ANATOMY OF THE VENOUS SYSTEM OF THE LOWER LIMBS

The lower limb is drained by 3 venous systems:

1. Superficial system.
2. Deep system.
3. Perforating "communicating" veins.

The superficial venous system

The superficial veins are located superficial to the muscular fascia. In the legs, a subcomponent, the saphenous system, is present. The saphenous compartment ***(Caggiati et al., 1999)*** is surrounded superficially by a hyperechoic saphenous fascia which is called the "Egyptian eye" seen on duplex imaging as shown in Figure 1. It contains the great saphenous trunk, accompanied by small arteries, and the saphenous nerve below the knee.

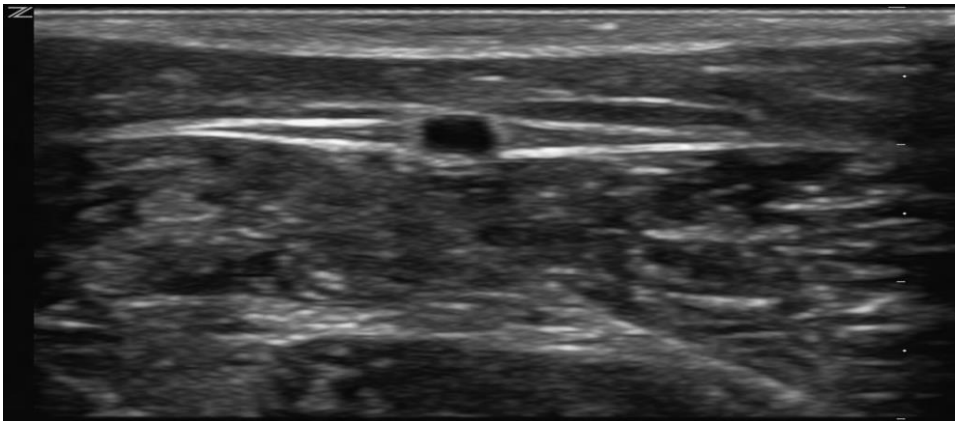

Figure (1): Transverse B-mode ultrasound image of the "Egyptian eye." The pupil is the great saphenous vein; the eyelids are the superficial and deep layers of fascia surrounding the saphenous sub-compartment.

The saphenous fascia has been referred to in the past as the superficial fascia, the Colles or Scarpa fascia, or the subcutaneous pseudo-fascia. These terms are no longer recommended. The remaining superficial compartment below the dermis contains the accessory saphenous tributaries (anterior and posterior), which ascend parallel to the great saphenous vein. Also, it contains a complex and variable system that connect with other veins in the same superficial compartment. For example, the inter-saphenous vein (previously known as the vein of Giacomini as shown in Fig. 3) connects the great and small saphenous veins. The reticular venous plexus and sub-papillary venous plexus are also included in this area.