

Prevalence and Risk Factors of Preoperative Deep Vein Thrombosis in Elderly Patients with Hip Fractures

DR MOHD KHAZRAN BIN HAMID

**Dissertation Submitted in Partial Fulfillment of the
Requirement for the Degree of Master of Medicine
(ORTHOPAEDICS)**



UNIVERSITI SAINS MALAYSIA

2020

Prevalence and Risk Factors of Preoperative Deep Vein Thrombosis in Elderly Patients with Hip Fractures

FROM THE YEAR 2014 TO 2020

STUDY VENUE: HOSPITAL UNIVERSITI SAINS MALAYSIA

ACKNOWLEDGEMENT

The author would like to express his deepest gratitude and thanks to the following individuals for their advice, guidance, comments and support in completing this dissertation.

- Dr Al Hafiz bin Ibrahim, Main supervisor, lecturer of Orthopedics Department, HUSM, for his guidance throughout this study and in completing this paper.
- Professor Dr Amran Ahmed Shokri, Co-supervisor, lecturer of Orthopedics Department, HUSM, for his guidance and support in this study.
- My colleague, Dr Tan Chin Lok, who gave the idea to continue this study.
- My beloved wife, Dr Faziana binti Wahab, who sacrificed her time and effort in helping me to finish this dissertation.
- Martina Irwan Khoo, PhD candidate from the Chemical Pathology Department, HUSM, for her help in data reviewing and statistical analysis.
- Colleagues and all staff in the Orthopedics Department, HUSM.

TABLE OF CONTENTS

CONTENTS	PAGE
TITLE	ii
ACKNOWLEDGEMENT	iii
TABLE OF CONTENTS	iv-v
ABSTRAK (BAHASA MALAYSIA)	vi - vii
ABSTRACT (ENGLISH)	viii - ix
CHAPTER 1: INTRODUCTION	
1.1 Introduction	1-3
1.2 Objective	4
CHAPTER 2: STUDY PROTOCOL	
2.1 Study protocol	5 - 29
2.2 Ethical approval letter	30 - 32
CHAPTER 3: MANUSCRIPT	
3.1 Abstract	34 - 35
3.2 Introduction	36 - 37
3.3 Methodology	38 - 39
3.4 Results	40 - 41

3.5	Discussion	42 - 44
3.6	Conclusion	45
3.7	References	46 - 49
3.8	Tables and Figures	50 – 52

CHAPTER 4: APPENDICES

4.1	Data collection sheet	54
4.2	Raw Data	55 - 62
4.3	Guidelines/Instruction to Authors of selected Journal	63 - 66

ABSTRAK

Pengenalan

Patah tulang pinggul biasa berlaku dalam kalangan warga tua selepas terjatuh. Mereka berisiko tinggi mengalami komplikasi seperti tromboemboli vena; trombosis urat dalam (DVT) dan embolisme paru (PE) yang boleh menyebabkan morbiditi dan kematian. Sehingga kini, tiada data tempatan berkenaan kelaziman DVT sebelum pembedahan dalam kalangan warga tua yang mengalami patah tulang pinggul serta faktor risiko yang berkaitan. Oleh itu, kajian ini bertujuan untuk mengetahui kelaziman DVT dalam kalangan warga tua yang mengalami patah tulang pinggul dan untuk menilai faktor risiko berlakunya DVT pra-pembedahan pada populasi ini.

Kaedah Kajian

Kajian ini merupakan keratan rentas retrospektif yang melibatkan 91 pesakit yang mengalami patah tulang pinggul dan menerima rawatan di HUSM dari Januari 2014 hingga November 2019. Kajian ini menggunakan data dari PACS (Sistem Pengarkiban dan Komunikasi Gambar) dan juga rekod perubatan pesakit. Maklumat ini kemudian direkodkan dalam profoma pengajian. Data dimasukkan dan dianalisis menggunakan SPSS versi 26.0.

Keputusan

Keseluruhan prevalensi trombosis urat dalam pra-pembedahn pada pesakit tua dengan patah tulang pinggul adalah 5.4 %. Faktor-faktor risiko yang penting adalah seperti tempoh imobilisasi, jenis pencegah DVT yang diberi merupakan aspek penting dalam pembentukan DVT seperti dalam jadual demografik.

Kesimpulan

Kelaziman Trombosis Vena Dalam (DVT) adalah rendah (5.4 %) dalam kalangan warga tua yang patah tulang pinggul mungkin disebabkan langkah pencegahan yang diambil terhadap DVT pada populasi ini. Selain itu, faktor-faktor risiko seperti tempoh imobilisasi, jenis pencegah DVT yang diberi dan kanser adalah faktor yang penting dalam pembentukan DVT dalam kajian ini.

Kata Kunci:

Trombosis Vena Dalam, Patah Tulang Pinggul, Faktor Risiko

ABSTRACT

Introduction

Hip fractures are common in the elderly population after a fall. Consequently, they are at a high risk of developing complications such as venous thromboembolism, deep vein thrombosis (DVT) and pulmonary embolism (PE), which may cause significant morbidity and mortality. To date, there are no local data regarding the prevalence of DVT before surgery in elderly patients with hip fractures and risk factors associated with it. This study aimed to establish the prevalence of DVT in elderly patients following a hip fracture in the local population and evaluate the risk factors for the occurrence of preoperative DVT in this population.

Materials and methods

This research is a retrospective cross-sectional study involving 91 patients with a history of hip fracture and received treatment in HUSM from January 2014 to November 2019. Patient screening was conducted via the PACS (Picture Archiving and Communication Systems) system and the patients' medical records. Patients with hip fractures and had ultrasound Doppler of lower limb one day before surgery were selected. All selected risk factors, including demographic data information was then recorded in a study proforma. Data were entered in Microsoft Excel and analysed using SPSS version 26.0.

Results

The overall prevalence of preoperative deep vein thrombosis in elderly patients with hip fracture was 5.4 %. The mean duration of immobilisation in DVT patient is 18.4 days. None of them received Enoxaparin as prophylaxis. Two out of five DVT patients had underlying malignancy.

Conclusion

Preoperative DVT prevalence is relatively low (5.4 %) in elderly patients with hip fracture in this study, which may be contributed by precautions taken to prevent DVT in this population. The critical risk factors for DVT development were the duration of immobilisation, types of DVT, prescribed prophylaxis and malignancy.

Key Words:

Deep Vein Thrombosis, Hip fracture, Risk factor

CHAPTER 1: INTRODUCTION

1.1 INTRODUCTION

Hip fractures are common in the elderly population after a fall. The two most common hip fractures in the elderly are femoral neck fracture and intertrochanteric femur fracture(1). Elderly patients with hip fractures are prone to get complications such as urinary tract infection, orthostatic pneumonia, pressure sores and venous thromboembolism(2). Venous thromboembolism, such as deep vein thrombosis (DVT) and pulmonary embolism (PE), are the major causes of morbidity and mortality, particularly in the elderly population(3). The high prevalence of VTE is associated with prolonged confinement to bed and delay in surgical treatment(4). Several literatures have described the prevalence of DVT and PE after hip fracture surgery. However, only a few reported preoperative VTE prevalence in this group of patients after a hip fracture that ranged from 9 % to 18.9 % (5–7).

In elderly patients, the high prevalence of preoperative VTE is related to extended bed rest and delay surgical treatment, which may occur due to various reasons. Hefley et al. and Zahn et al. showed that VTE's prevalence increases to as high as 54 % to 62 % in patients with delay in admission after a fracture or delayed operation for more than 48 hours (8,9). Other factors associated with a high risk of VTE include female gender, pulmonary disease and history of VTE. Interestingly, Xia et al. mentioned that patients on oral antiplatelet therapy have protective factors for VTE development after fractures.

The initial prophylaxis, early detection and treatment of DVT before surgery can reduce progression to thromboembolism and fatal PE. To date, there are no local data regarding the prevalence of DVT before surgery in elderly patients with hip fractures and their associated risk factors.

The purpose of this study is to determine the prevalence of DVT in elderly patients following hip fractures in the local population. Besides, risk factors for the occurrence of

preoperative DVT in this population were also evaluated. Confirming and identifying risk factors associated with DVT is likely to reduce the prevalence and mortality of VTE, especially when these risk factors are modifiable.

1.2 OBJECTIVE

General Objective:

To determine the prevalence of deep vein thrombosis in elderly patients following a hip fracture

Specific Objective:

To identify and determine risk factors associated with the occurrence of deep vein thrombosis in elderly patients following a hip fracture in the local population.

CHAPTER 2: STUDY PROTOCOL

DISSERTATION PROPOSAL

**TITLE: Prevalence and Risk Factors of
Preoperative Deep Vein Thrombosis in Elderly
Patients with Hip Fractures**

NAME: DR MOHD KHAZRAN HAMID

MATRIK NO: P-UM00267/17

MMC No: 48488

SUPERVISOR:

DR AL HAFIZ BIN IBRAHIM

CO-SUPERVISOR:

PROFESSOR DR AMRAN AHMED SHOKRI

Introduction

Hip fractures are common in the elderly population after a fall. The two most common hip fractures in the elderly are femoral neck fracture and intertrochanteric femur fracture(1). Elderly patients with hip fractures are at high risk of developing complications such as urinary tract infection, orthostatic pneumonia, pressure sores and venous thromboembolism. Venous thromboembolism, such as deep vein thrombosis (DVT) and pulmonary embolism (PE), is a major cause of morbidity and mortality, particularly in the elderly population(3). The high prevalence of VTE is associated with prolonged confinement to bed and delay in surgical treatment. Several literatures described the prevalence of DVT and PE after hip fracture surgery. However, only a few had explained the prevalence of preoperative VTE in this group of patients after a hip fracture. The reported prevalence of preoperative VTE range from 9 % to 18.9 % [1, 2, 3].

In elderly patients, the high prevalence of preoperative VTE is related to extended bed rest and delay surgical treatment, which can occur due to various reasons. Hefley et al. and Zahn et al. showed that the prevalence of VTE has increased to as high as 54 % to 62 % in patients where there is a delay in admission after fracture or operation was postponed for more than 48 hours [4, 5]. Other factors associated with a high risk of VTE include female gender, pulmonary disease and history of VTE. Interestingly, Xia et al. noted that patients on oral antiplatelet therapy have protective factors against VTE development after fractures.

The initial prophylaxis, detection and treatment of DVT before surgery can reduce thromboembolism progression and fatal PE. To date, there are no local data regarding the prevalence of DVT prior to surgery in elderly patients with hip fractures and any risk factors associated with it.

The purpose of this study is to establish the prevalence of DVT in elderly patients following a hip fracture in the local population. Risk factors for the occurrence of preoperative DVT in this population were also evaluated. Identifying and confirming the risk factors associated with DVT is likely to reduce the prevalence and mortality of VTE, especially when these risk factors are modifiable.

Problem statement & study rationale

Deep vein thrombosis is a major complication of hip fractures in the elderly with high morbidity and mortality. Understanding the prevalence and the risk factors contributing to DVT development can provide insight and knowledge for better prevention.

A cross-sectional retrospective study will be conducted involving elderly patients with hip fracture who underwent compression and Doppler ultrasonography (USG) before surgery in HUSM. These tests were carried out one day before or on the morning of the surgery. These imaging modalities were chosen due to their non-invasive and high sensitivity in diagnosing DVT. Then, the results can be easily accessed through PACS (Picture Archiving and Communication Systems). Other risk factors were noted based on the patients' medical records.

Literature review

Hip fracture in elderly patients results in immobilisation and prolonged bed rest due to delayed presentation to the hospital or delayed surgery, contributing to increased risk of developing deep vein thrombosis. Previous literature described preoperative DVT prevalence from 9 % to 18.9 % [1, 2, 3]. It was reported that most patients who underwent bilateral lower limb venography after admission to identify any deep vein thrombosis and were started with prophylactic anticoagulation, with indirect multidetector computed tomography (MDCT) venography for detection of PE conducted in one of the studies.

In a different study, a high incidence of preoperative DVT was recorded at 29.4 % (35 out of 119 patients) [6], where patients had prolonged bedridden time and preoperative prophylactic anticoagulation was not routinely used. This finding raised the question of whether the high incidence could be due to insufficient prophylactic anticoagulation or prolonged immobilisation. Meanwhile, two other studies showed a DVT prevalence of 54 % to 62% in patients with hip fractures with delayed admission or operation of more than 48 hours [4, 5]. Hefley et al. described the prevalence of preoperative DVT as 10 % and the prevalence of DVT in patients whose surgery was performed in less than 48 hours was 6 %. In the present study, a tremendous increase in prevalence was observed at 54 % for patients with delayed admission or delayed surgery more than 48 hours [4]. Furthermore, prophylactic anticoagulation was not used in these patients. Zahn et al. described a prevalence of 62 % preoperative DVT in patients when surgery was delayed for more than 48 hours, although all their patients received 5000 units of unfractionated subcutaneous heparin on admission and every 12 hours after that [5].

Recent Clinical Practice Guidelines suggested the prescription of low molecular weight heparin for preoperative prevention of VTE. However, the use of unfractionated heparin

to prevent VTE in hip fracture patients was not recommended [7, 8]. Therefore, the type of anticoagulation might influence the risk of developing DVT.

Traditionally, venography was used to diagnose DVT, which was utilised in most studies [9]. Venography is performed using an intravenous contrast medium and radiograph. Ultrasonography is non-invasive, convenient and free of intravenous contrast. A systematic review and meta-analysis of diagnostic accuracy of ultrasonography showed a sensitivity of 94.2 % and specificity of 93.8 % for proximal DVT, while Duplex ultrasonography (combined compression and Doppler ultrasonography) has a sensitivity of 96.5 % and specificity of 94.0 % [10].

Conceptual framework

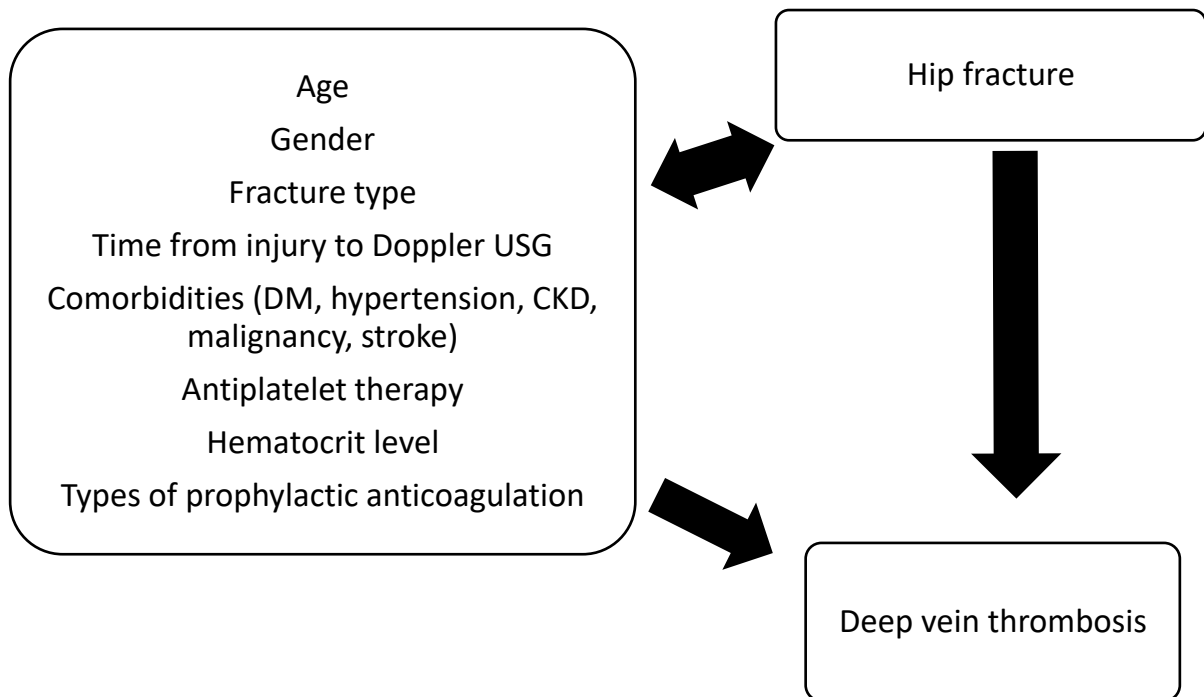


Figure 1. Conceptual framework of interaction between hip fracture with deep vein thrombosis and the interactions of risk factors with deep vein thrombosis

Target research question(s)

1. What is the prevalence of deep vein thrombosis in elderly patients following a hip fracture?
2. What are the risk factors that may contribute to the occurrence of deep vein thrombosis in elderly patients following a hip fracture?

Objective

General Objective:

To determine the prevalence of deep vein thrombosis in elderly patients following a hip fracture

Specific Objective:

To identify and determine risk factors associated with the occurrence of deep vein thrombosis in elderly patients following a hip fracture

Research design

A retrospective cross-sectional study will be conducted in Hospital Universiti Sains Malaysia from January 2014 to November 2020. The main objective is to determine the prevalence, which can be measured through a cross-sectional study. The prevalence of DVT and exposures (underlying comorbidities, medication, etc.) will be identified. Then, the Odds Ratio will be determined as a measure of association, rather than opting for a single exposure as the cause for developing DVT.

Study area

The study will be conducted in Hospital Universiti Sains Malaysia (HUSM) since it is a tertiary centre in Kelantan to manage hip fracture.

Study population

The reference population are elderly patients presented with hip fracture in HUSM.

Subject criteria

A. Inclusion criteria

1. Age $\geq$ 60 years old

2. Hip fracture:

Neck of femur fracture

Intertrochanteric femur fracture

3. Underwent bilateral lower limb compression and Doppler ultrasonography after admission and before surgery

4. Any elderly with hip fracture prescribed with antiplatelet due to other conditions such as cardiac illness.

B. Exclusion criteria

1. Underlying established deep vein thrombosis of the lower limb before hip fracture
[Underlying established DVT will be obtained from patients' history and through HUSM's PACS archive (ultrasounds done previously would be saved into the system)].
2. Bilateral hip fractures - This factor will be excluded due to its rare occurrence and is usually associated with high energy trauma with increased risks of DVT.
3. Hip fracture associated with pelvic or other lower extremities fractures.
4. Lower limb compression and Doppler ultrasonography performed after surgical treatment.

Sample size estimation

The estimated sample size was calculated based on Roberts et al., showing a 9 % prevalence of preoperative thromboembolism in patients with hip fracture. A single proportion formula was used to calculate the sample size.

Based on the study, the prevalence of preoperative DVT was 9 % (0.09). If the Type 1 error probability and precision are 0.05 and 0.05, the calculated sample size will be 126 samples.

$$\begin{aligned}n &= \frac{\left(Z_{1-\frac{\alpha}{2}}\right)^2 p(1-p)}{d^2} \\&= \frac{\left(Z_{1-\frac{0.05}{2}}\right)^2 0.090 (1-0.090)}{(0.05)^2} \\&= \frac{(1.96)^2 (0.0819)}{0.002500} \\&\approx 126 \text{ samples}\end{aligned}$$

where

- n = sample size,
- Z = level of confidence,
- α = alpha,
- p = expected prevalence or proportion
- d = precision.

Sampling method and subject recruitment

The non-probability sampling method will be applied in this study. Patients who fulfil the inclusion and exclusion criteria will be recruited from January 2014 to November 2020. The initial screening will be done via the HUSM PACS system, which will narrow the search by focusing on lower limb Doppler ultrasound and the target age. Those who meet the criteria will be examined whether they have a hip fracture by searching for pelvic or hip radiographs.

Research tool

This study will utilise data from the database in PACS and patients' records. The patients' records will provide information such as age, gender, associated disease, time from injury to ultrasonography, antiplatelet therapy, type of anticoagulation and blood results. Meanwhile, the type of fracture and confirmation of DVT status will be identified through PACS.

Operational definition

1. Elderly:

Chronological age will be used in line with the United Nations definition for people aged 60 years or older [UN WPA 2017].

2. Deep vein thrombosis:

The presence of thrombus or thrombi (blood clot) that cause partial or total occlusion of the deep veins of the lower limb. The diagnosis of deep vein thrombosis will be by compression and Doppler ultrasonography.

3. Hip fracture:

In this study, hip fracture is determined by the fracture of the neck of the femur or intertrochanteric femur diagnosed on plain radiographs.

4. Compression and Doppler Ultrasonography:

A non-invasive diagnostic imaging technique that utilises the application of ultrasound. Combined compression and colour Doppler ultrasonography are used in the diagnosis of deep vein thrombosis. A systemic review and meta-analysis of diagnostic accuracy of ultrasonography showed a sensitivity of 94.2 % and specificity of 93.8 % for proximal DVT, while Duplex ultrasonography (combined compression and Doppler ultrasonography) has a sensitivity of 96.5 % and specificity of 94.0 %. [9]

Data collection method

All relevant data will be collected in a data collection sheet proforma. The patients' registration numbers will be recorded with their names omitted to ensure confidentiality, and each patient will be assigned a case number.

Data analysis

The collected data will be analysed using SPSS version 26.0 and descriptive statistics will be used to summarise the socio-demographic characteristics of the subjects. Categorical data will be presented as frequency (percentage), while the numerical data will be presented as mean (SD) $\pm$ standard error. Comparisons between 2 groups (subjects with DVT and subjects with no DVT) will be analysed using the Chi-square test and Fisher's exact test to compare categorical variables, whereas the Student t-test will be used to compare continuous variables.

The association between preoperative DVT and possible risk factors will be analysed using multiple logistic regression. For univariable analysis, simple logistic regression (SLogR) will be applied to select the preliminary variables associated with preoperative DVT. Variables with a p-value of less than 0.25 from univariable analyses and clinically significant will be chosen for multiple logistic regression (MLogR). MLogR will be performed to evaluate factors associated with preoperative DVT.

Expected results

Table 1: The percentage of subjects with and without DVT

Total number of patients	N (100 %)
DVT	n ₁ (%)
No DVT	n ₂ (%)

General objective: Prevalence of preoperative DVT in elderly patients with hip fracture = n₁

Table 2: The baseline demographic characteristics, risk factors and laboratory parameter of subjects (DVT and no DVT)

Variable	DVT [n ₁ (%)] Mean(SD) / n(%)	No DVT [n ₂ (%)] Mean(SD) / n(%)	p-value
Age (years)			
Female gender			
Neck of femur fracture			

Intertrochanteric fracture			
Time from injury to Doppler USG (Duration of immobilisation)			
Smoking			
Comorbidity Diabetes mellitus Hypertension Chronic kidney disease Malignancy Stroke			
Concomitant medication Antiplatelet			
Hematocrit (%)			
Type of prophylactic anticoagulation None			

Unfractionated heparin			
Enoxaparin			
Fondaparinux			

Table 3: Multiple logistic regression analysis of identified risk factors in association of occurrence preoperative DVT in elderly patients with hip fracture, with adjusted confounders, showing the adjusted odds ratio (OR), 95 % confidence interval (CI), and corresponding p-value.

Risk factors	Adjusted OR	95 % CI	p-value
Risk factor a (e.g. gender)			
Risk factor b (e.g. smoking)			
Risk factor c (e.g. malignancy)			
Risk factor d (e.g. hematocrit)			
Risk factor e (e.g. duration of immobilisation)			

Specific objective: To identify and determine risk factors associated with the occurrence of deep vein thrombosis in elderly patients following a hip fracture.