

Role of Thrombolytic Therapy in the Management of Acute Iliofemoral Deep Venous Thrombosis

Essay

Submitted for the partial fulfillment of Master Degree in General Surgery

By

Ali Abdallah El Saadany

*M.B, B. Ch
Faculty of Medicine*

Under Supervision of:

Prof. Dr. Wagih Fawzy Abd El-Malek

*Prof. of General and Vascular Surgery
Faculty of Medicine - Ain Shams University*

Dr. Atef Abd Al-Hameed Desoky

*Assistant Prof. of General and Vascular Surgery
Faculty of Medicine - Ain Shams University*

Dr. Mohamed Ismail Mohamed

*Lecturer of General and Vascular Surgery
Faculty of Medicine - Ain Shams University*

*Faculty of Medicine
Ain shams university*

2015

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

وَأَنْزَلَ اللَّهُ عَلَيْكَ
الْكِتَابَ وَالْحِكْمَةَ
وَعَلَّمَكَ مَا لَمْ تَكُنْ تَعْلَمُ
وَكَانَ فَضْلُ اللَّهِ
عَلَيْكَ عَظِيمًا

صدق الله العظيم

سورة النساء آية (١١٣)





*First of all, gratitude and thanks to **ALLAH** who enabled me to overcome all problems which faced me throughout this work. Sincere thanks and appreciation to those persons who were assigned to give me a precious hand to be able to complete this essay.*

*I would like to express my deepest thanks and extreme sincere gratitude to my kind **Prof. Dr. Wagih Fawzy Abd El-Malek**, Professor of General and Vascular Surgery, Ain Shams University, for his masterly teaching, kind supervision, and continuous help during the course of the work. Also for his kind encouragement and valuable advice.*

*I would like to express my deepest appreciation to **Dr. Atef Abd El-Hamid Desoky**, Assistant Prof. of General and Vascular surgery, Ain Shams University, for his kind guidance, valuable advices, great efforts.*

*I am very grateful and deeply indebted to dear **Dr. Mohamed Ismail Mohamed**, Lecturer of General and Vascular Surgery, Ain Shams University, for his continuous guidance, advice, unlimited help, encouragement, and sincere support.*

***Finally**, I wish to extend my great thanks and gratitude to all my staff members and to my colleagues in Vascular Surgery Department for the various help, support and facilities offered by them during the progress of this work.*

List of Contents

	Page
LIST OF ABBREVIATIONS	I
LIST OF TABLES	III
LIST OF FIGURES	V
Introduction	1
Aim of the Work	5
REVIEW OF LITERATURE	
☒ Anatomy of the Venous System of the Lower Limb	6
☒ Pathophysiology of DVT	20
☒ Complications of DVT of the lower limb	44
☒ Diagnosis of DVT	55
☒ Treatment of DVT	89
Summary and Conclusion	156
References	159
Arabic Summary	-

List of Abbreviations

ACCP	: American college of chest physicians.
ACL	: Anticardiolipin antibodies.
ACT	: Activated clotting time.
AHRQ	: The Agency for Healthcare Research and Quality.
APC	: Activated Protein C.
aPTT	: Activated partial thromboplastin time.
AVF	: Arteriovenous fistula.
CDDUS	: Colored Doppler Duplex Ultra-Sound.
CDRs	: Clinical decision rules.
CDT	: Catheter directed thrombolysis.
CFV	: Common Femoral Vein.
CIA	: Common Iliac Artery.
CTEPH	: Chronic thrombo-embolic pulmonary hypertension.
CTPA	: CT pulmonary angiography.
CTV	: Computed tomography venography.
CVH	: Chronic venous hypertension
DIC	: Disseminated intravascular coagulation.
DTIs	: Direct thrombin inhibitors.
ELISA	: Enzyme-linked immunosorbent assay.
GCS	: Graduated compression stockings.
GPIIb	: Glycoprotein Ib.
GSV	: Great saphenous vein.
HIT	: Heparin-induced thrombocytopenia.
INR	: International normalized ratio.
IPC	: Intermittent pneumatic compression.
IPG	: Impedance plethysmography.
ISPMT	: Isolated segmental pharmacomechanical thrombolysis.
IVC	: Inferior vena cava.
LMWH	: Low molecular weight heparin.

List of Abbreviations

MRV	: Magnetic resonance venography.
PA	Pulmonary Artery.
PAI	: Plasminogen activator-inhibitor.
PCD	Phelegmasia Cerula Dolens.
PE	: Pulmonary embolism.
PEEP	: Positive end-expiration pressure.
PMT	: Pharmaco-mechanical thrombectomy.
PT	: Prothrombin time.
PTS	: The post-thrombotic syndrome.
rt-PA	: Recombinant Tissue Plasminogen Activator.
SFJ	: Saphenofemoral junction.
SPJ	Saphenopopliteal junction.
SSV	: Small saphenous vein.
tPA	: Tissue plasminogen activator.
TXA2	: Thromboxane A2.
UFH	: Unfractionated heparin.
VKA	: Vitamin K antagonists.
VTE	: Venous thrombo-embolism.

List of Tables

No.	Table	Page
<i>Chapter (2):</i>		
1-	Risk factors for acute deep venous thrombosis and pulmonary embolism	28
2-	Risk of Postoperative Deep Venous Thrombosis	35
3-	Thrombophilias Identified in Patients Presenting with DVT or PE	37
<i>Chapter (3):</i>		
1-	Complications Associated with Proximal (Iliofemoral) Deep Venous Thrombosis	45
2-	Clinical features of the post-thrombotic syndrome	51
<i>Chapter (4):</i>		
1-	Wells Clinical Decision Rule	58
2-	Diagnostic criteria that aid in distinguishing between acute and chronic DVT	70
3-	Thrombophilia Testing Recommendations	81
<i>Chapter (5):</i>		
1-	Percentage risks venous thrombosis	90
2-	Features of an Ideal Prophylactic Method for Venous Thromboembolism	91
3-	Advantages and disadvantages of heparin use	95

List of Tables

No.	Table	Page
4-	Advantages and disadvantages of warfarin use	98
5-	Advantages of Low-Molecular-Weight Heparin over Unfractionated Heparin	106
6-	Criteria for Outpatient Management of VTE Clinical Criteria	108
7-	Venous thrombectomy; comparison of old and contemporary techniques	116
8-	Overview of the Technique of Contemporary Venous Thrombectomy	118

List of Figures

No.	Figure	Page
<i>Chapter (1):</i>		
1-	Anatomy of the great saphenous vein	7
2-	Anatomy of the short saphenous vein	9
3-	Deep venous system of L.L	10
4-	Anatomy of the popliteal vein	12
5-	Anatomy of iliac veins	15
6-	Abdominopelvic computed tomography representing duplication of inferior vena cava	19
<i>Chapter (2):</i>		
1-	Thrombogenesis, Virchow s triad	23
<i>Chapter (3):</i>		
1-	Selective pulmonary angiogram	48
2-	CT pulmonary angiography (CTPA)	49
3-	Large saddle embolus seen at PA	49
4-	Post phlebitis syndrome	51
5-	Large venous ulcer	52
<i>Chapter (4):</i>		
1-	A deep vein thrombosis of the right leg	59
2-	Phlegmasia cerulae dolens	59
3-	Normal phlebography	62

List of Figures

No.	Figure	Page
4-	Color duplex showing normal vein	68
5-	Color duplex showing Thrombotic vein	70
6-	Abdominal computed tomographic scan	76
7-	Algorithm for evaluation of suspected acute DVT in symptomatic outpatients	88
<i>Chapter (5):</i>		
1-	Cannulation of the popliteal vein using ultrasound-guided venous puncture techniques with the patient in the prone position	126
2-	Thrombolysis of iliac vein thrombosis before (a) and after therapy (b)	127
3-	Thrombolysis: A tiny catheter is entered into the clot and delivers a "clot- busting" drug directly into the clot	127
4-	Angiojet catheter and pump drive	136
5-	(A) Venogram demonstrating complete superficial vein thrombosis. (B) Completion venogram demonstrating complete thrombus removal following Angiojet thrombectomy	137
6-	(A) In the PMT therapy, the thrombolytic agent is first administered into the venous thrombus by shutting off the outflow channel. (B) After a period of 15 minutes has elapsed to allow thrombolytic therapy to take effect, the outflow channel is opened	138
7-	Technique of thrombolysis	140
8-	EKOS System, consisting of a multi-lumen infusion catheter with removable coaxial ultrasound core and a control unit, simultaneously delivers high-frequency	143

List of Figures

No.	Figure	Page
9-	Trellis thrombectomy catheter	147
10-	Repeat venography demonstrated a patent iliac system but (A) segmental continued segmental obstruction of the proximal femoral vein. Venoplasty resulted in recoil	152
11-	Operative exposure revealed a markedly inflamed and thickened vein wall measuring 4 mm in thickness (A)	153

INTRODUCTION

Deep venous thrombosis (DVT) of the lower limb is a serious, even life-threatening condition requiring treatment primarily to avoid the morbidity and mortality associated with its most serious acute complication pulmonary embolism (PE) (*Gogalniceanu et al., 2009*).

Significant complications associated with dvt include pulmonary emboli which cause 10% of inpatient deaths, phlegmasia caerulea dolens (PCD) leading to limb- threatening venous gangrene and sever morbidity secondary to chronic venous hypertention and post – thrombotic syndrome (PTS) (*Gogalniceanu et al., 2009*).

PCD is characterized by limb cyanosis and swelling as a result of thrombosis at a capillary level. This is of clinical importance as it has an associated mortality and many survivors ultimately develop venous ulceration (*Gogalniceanu et al., 2009*).

Unfortunately few are fully aware of the delayed complication of acute DVT postthrombotic syndrome which can occur month to years following acute DVT (*Mark and Signe, 2000*).

PTS is caused by chronic venous hypertension secondary to venous reflux, venous obstruction and valvular dysfunction with the clinical sequelae of leg pain, oedema, venous trophic

changes and chronic ulceration. It is estimated that up to 80% of patients with a DVT may go on to develop symptoms of PTS, 4-15% progress to leg ulceration (*Gogalniceanu et al., 2009*).

Ilio-femoral DVTs are most likely to lead to PTS as the ilio-femoral segment of the venous system is the single outflow channel for the lower extremity. Occlusion of this outflow tract leads to high venous pressures and post-thrombotic morbidity as long term sequelae (*Comerota et al., 2012*).

Treatment of this condition is constantly changing, the ideal goals of therapy for acute DVT are elimination of the embolic potential of existing thrombus, restoration of unobstructed flow, preservation of venous valve function. Meeting these goals will not only prevent PE but will also minimize the long-term sequelae of venous hypertension and the development of PTS (*Mark and Signe, 2000*).

Multiple treatment options including anticoagulation, surgical venous thrombectomy and thrombolytic therapy achieve these goals to a variable degree. Standard treatment of DVTs involves anticoagulation with low molecular weight heparine (LMWH) or unfractionated heparin (UH), followed by long term therapy with vitamin k antagonists, such as warfarin. This has been shown to effectively reduce the risk of thrombus propagation or recurrence, pulmonary embolism and death. Nevertheless, anticoagulants have little impact on reducing

thrombus size in the short term, being ineffective in the management of PCD. Furthermore, their inability to cause thrombus dissolution may not prevent the development of post-thrombotic limb syndrome in the long term in many patients (*Mark and Signe, 2000*).

Treatment strategies aimed at eliminating or reducing the risk of PTS should focus on preserving valvular function and eliminating the risk of continued venous obstruction following acute DVT. Surgical removal by means of thrombectomy techniques combined with creation of arteriovenous fistulas have been employed successfully in Europe and the United States, but overall such procedures have not been commonly performed (*Mark and Signe, 2000*).

The feasibility of more invasive techniques aimed at reducing thrombus burden has gained increasing interest in recent years. Initially, systemic thrombolysis (with urokinase, streptokinase or tissue plasminogen activator) demonstrated adequate clot lysis, but exposed patients to unacceptable side-effects, including intracranial haemorrhage, significant retroperitoneal haematomas (*Suresh et al., 2002*).

Catheter directed thrombolysis (CDT) involves a focused delivery of plasminogen activating agents directly into the thrombus. This may be more effective in local thrombolysis and restoring venous patency, whilst reducing the risks associated with systemic therapy (*Guan-Hua et al., 2013*).

CDT in combination with percutaneous mechanical thrombectomy with or without stent placement, has become increasingly important because of its effectiveness in achieving venous patency and in preventing secondary venous insufficiency. Ultrasound – accelerated thrombolysis (UAT) is a novel modality of thrombolytic therapy (*Reginald et al., 2012*).