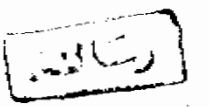
EFFECT OF INTRAVENOUS STREPTOKINASE ON THE RELATION BETWEEN INITIAL ST-PREDICTED SIZE AND FINAL QRS ESTIMATED SIZE OF ACUTE MYOCARDIAL INFARCTS



Thesis Submitted for Partial Fulfillment of Master Degree of Cardiology

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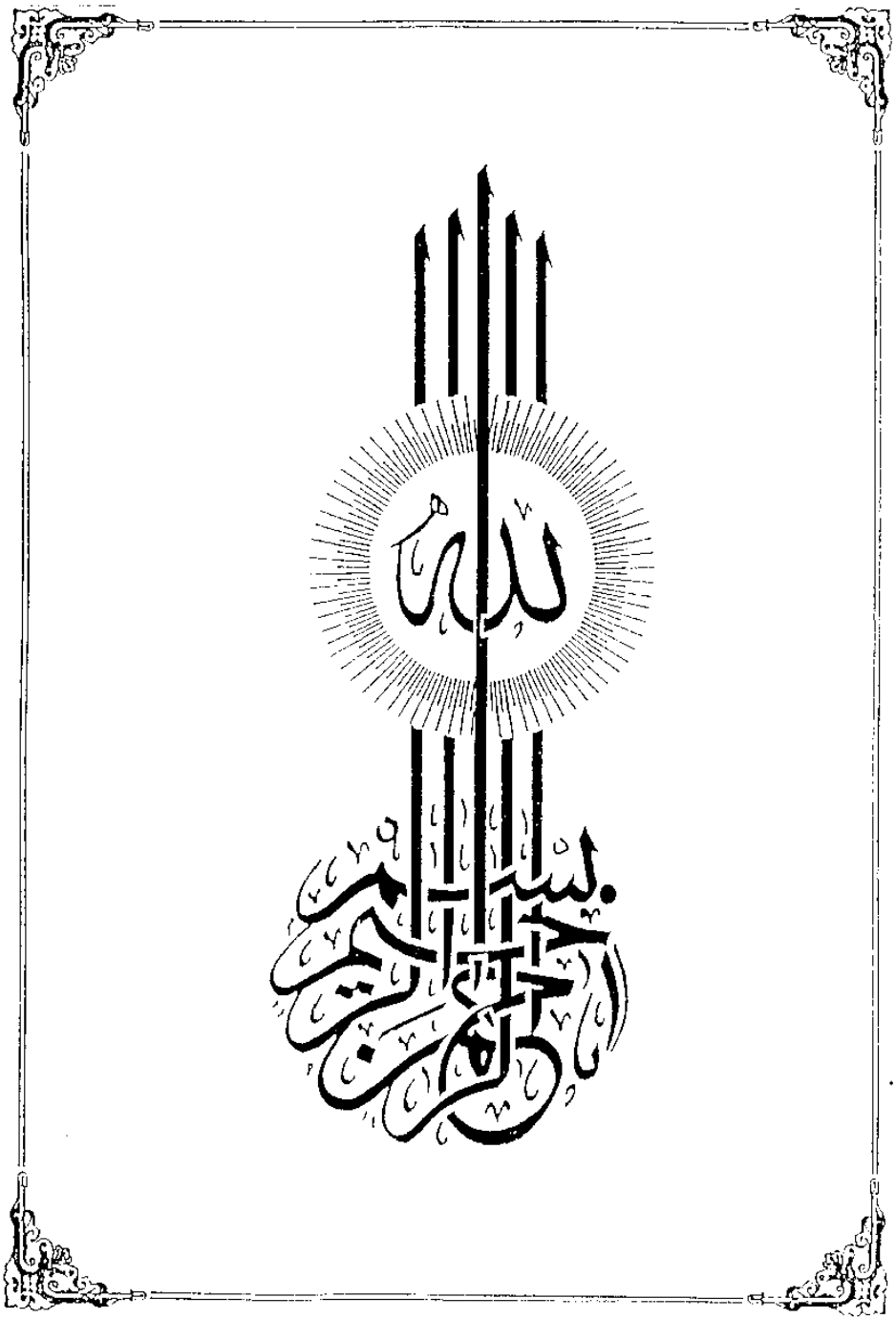

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ERRATA

Page	Line	Wrong	Correct
1	Fig. I-1	PROTHROMBIN ↓ Plasmin	PLASMINOGEN ↓ Plasmin
41	20	Table II	Table III - 2
63	24	Table V-I (Title)	Table V - 1
		ST Segment Criteria from Admition ECG:	
		1. ST ↑ ≥ 1 mm in ≥ 1 lead	
		2. Max ST ↑ ≥ Max ST ↓ or Max ST ↓ in V1 - V3	
		3. ST ↑ in V1 > V2	
64	5	story	stay
76	10	Reperfusion	Incidence of
76	13	Reperfusion (delete)	-------
112	7	**Kerschat**	**Kersschat**
112	13	**Posternak**	**Pasternak**
112	16	**Wibber**	**Wilber**
113	11	r= 0.746	r=0.76 (Fig. 12.A, p. 88)
113	13	(73%)	(3.3%)
113	21	--------	(add) Fig. 12.B, p. 89
114	4	--------	(add) Fig. 12.C, p. 89
116	8	--------	(add) patients with no myocardial Salvage may be better to do PTCA.

ERRATA

Page	Line	Wrong	Correct
CONTENTS	15	Infarts	Infarcts
(II)	3	machanism	mechanism.
(II)	7	Paramter	Parameter.
(II)	19	Precent	Percent.
(II)	21	Salavge	Salvage.
(V)	14	compete	complete.
11	13	Form patients	From patients
26	15	Infraction	Infarction.
27	12	Infraction	Infarction.
49	23	***Adb Elhameed***	***Abd Elhameed.***
50	7	***Adb Elhameed***	***Abd Elhameed.***
63	18	transnural	transmural
71	19	propertions	proportions.
72	7	Smookers	Smokers
73	5	rang	range
73	6	femal	female
73	7	femal	female
73	9	Smookers	Smokers.
73	11	hypertention	hypertension
73	17	admistion	admission.
75	24	dissapeared	disappeared.
76	2	Intervension	intervention
76	5,6,8	dissapearance	disappearance
77	18,19	M1	M.I.
77	20,24	M1	M.I.
77	25,27	M1	M.I.

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ABBREVIATIONS

AMI = Acute Myocardial infarction.
MI size = Myocardial infarct size.
% dif. = Percentile difference.
AF = Atrial Fibrilation.
PAC = Premature atrial contraction.
PVC = Premature ventricular contraction.
VT = Ventricular tachycardia.
VF = Ventricular Fibrilation.
Pt. = Patients.
ant. = Anterior.
Inf. = Inferior.
LBBB = Left Bundle Branch Block.
RBBB = Right Bundle Branch Block.
CHB = Compete Heart Block.
Σ = Sum
Δ = Deviation (Delta)
ST ($\uparrow$) = ST-segment elevation
ST ($\downarrow$) = ST-segment depression
no. = Number
Inferior leads = II, III, aVF
Non inferior leads = I, aVL, $V_{1\text{-}6}$ (aVR excluded)
Fig. = Figure
ECG = Electrocardiography

PART ONE

REVIEW OF LITERATURE

INTRODUCTION

With the advent of thrombolytic therapy, there is now a major focus on limiting the size of acute myocardial infarcts ***(Shah et al, 1986)***.

Several clinical techniques ***(Mcpherson et al, 1985)*** including serum enzymes, and scintigraphic and magnetic resonance imaging ***(White et al, 1988)*** have been used to evaluate the functional and anatomic extent of single and multiple myocardial infarcts. Previous studies documented the correlation between the Selvester QRS scoring system applied to the standard 12-lead electrocardiogram and anatomically measured percent left ventricular infarction in patients with single anterior ***(Ideker et al, 1982)***, inferior ***(Roark et al, 1983)*** and posterolateral ***(Ward et al, 1984)*** locations.

Thrombolytic therapy has been shown to reduce final infarct size in patients with acute myocardial infarction ***(The ISAM Study Group 1986; Simoons et al 1986; Kennedy et al 1983)***. As so, the reduction in infarct size has resulted in improvement of both the left ventricular function and the prognosis of patients ***(GISSI, 1986; ISIS-2, 1988;Res et al 1986; Stak et al, 1983)***.

In the absence of reperfusion therapy, previous studies ***(Askenazi et al 1977; Yusuf et al 1979; Aldrich et al 1988)*** have established the relation between the acute myocardial infarct size predicted by initial ST segment changes and that established by final QRS score.

Aldrich et al (1988) has presented formulas describing this relation [the initial predicted and the final estimated] for both anterior and inferior acute infarct location.

In an independent study by Clemmensen et al (1988, 1991), the formula for anterior location was validated and that for inferior location modified to include consideration of the full spectrum of electrocardiographic (ECG) leads.

So, if the size of an acute myocardial infarction were limited by either spontaneous or therapeutic reperfusion, these relation should be invalidated. The aim of the present study is to test this hypothesis in control versus streptokinase-treated groups of patients by estimation quantitatively the amount jeopardized myocardium initially predicted by ST-segment changes and finally by Selvester QRS scoring system. Then, the effect of streptokinase on the myocardial salvage could be estimated quantitatively by simple, rapid, easy and cheap method.

The concept that the size of a myocardial infarction can be modified by certain interventions in experimental animals after coronary occlusion has gained support from studies using the method of epicardial ST-segment mapping, correlated with analyses of creatine kinase (CK) activity and histological appearance of myocardial biopsies.

AIM OF THE WORK

This study has been done to quantify the effect of intravenous streptokinase on the relation between the initial ST-predicted size, and final QRS-estimated size of acute myocardial infarcts using the standard 12-lead surface electrocardiograph (ECG), and to identify the threshold for myocardial salvage.

PART ONE

CHAPTER I

THROMBOLYTIC THERAPY

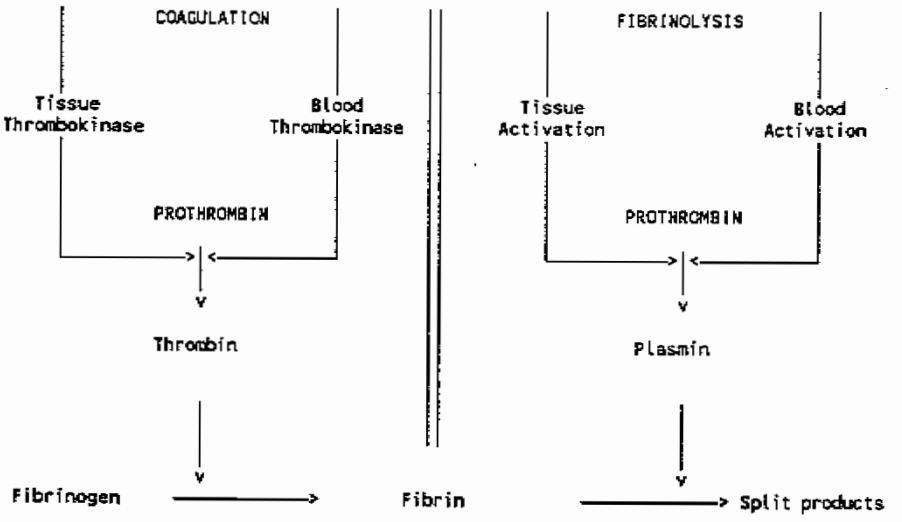
Blood clots which partially or completely obstruct major vessels must be removed in order to restore blood flow. Streptokinase achieve this by dissolving thrombus enzymatically, through activation of the patient's physiological potential for thrombolysis.

Thrombolysis is superior to the use of anticoagulants which only restrict the further deposition of fibrin, but have no direct action on an established thrombus. Thus, the role of anticoagulant therapy is secondary to that of thrombolysis.

Although a surgical approach to removing thrombus or emboli may be considered, the attendant hazards and inconvenience outweigh the possible benefits, which are rarely greater than those attained by thrombolysis. Extensive trials have proven thrombolytic treatment to be of great value.

THE HEMOSTATIC SYSTEM

In the hemostatic system, there is a dynamic equilibrium between coagulation (the formation of fibrin) and fibrinolysis (Fig.1). Coagulation is responsible for the integrity of the vascular system, whereas the fibrinolytic mechanism is concerned with maintaining vascular patency, by preventing excess fibrin accumulation.



(Fig. 1). * Coagulation and Fibrinolysis

THROMBOLYTIC AGENTS

Thrombolysis is mediated by plasmin, a non-specific serine protease generated by activation of the liver-synthesized circulating proenzyme plasminogen. Plasmin degrades fibrin (thrombolysis) as well as other peptides including fibrinogen; clotting factors V, VIII, and XII; and some hormones ***(Sherry et al, 1959).***

Both endogenous (intrinsic and extrinsic) and exogenous activators of plasmin are recognized. The intrinsic activators [which include factor XII, kallikrein, and kinins] circulate in the plasma in precursor state, and the extrinsic plasminogen activators are of tissue or cellular origin (kidney, endothelial cells) and appear to be released and act locally. The exogenous activators are those used for the pharmacologic activations of plasminogen to plasmin. There are three groups of pharmacological activators of plasmin:

(1) Streptokinase and its related agents;
(2) Urokinase and its related agents; and
(3) Tissue plasminogen activator.

I. STREPTOKINASE

Will be discussed later.

II. UROKINASE AND RELATED COMPOUNDS

Urokinase is produced by the human renal tubular cell and therefore is not antigenic to humans ***(Williams, 1951)***. It is a direct activator of the fibrinolytic system and requires no preliminary complexing phase with plasminogen. Its thrombolytic actions are similar to those of streptokinase, but urokinase appears to be slightly more clot specific than streptokinase. The disadvantage of urokinase is its very high price.

Single-chain urokinase, or **prourokinase**, is the zymogen precursor of urokinase. It is relatively clot-selective thrombolytic agent that release urokinase in the presence of fibrin ***(Gurewich et al, 1984)***. In experimental studies and in some clinical trials of patients with acute myocardial infarctions, single-chain urokinase has been an effective thrombolytic agent without pronounced systemic lytic effects ***(Collen et al, 1985; Van de Werf et al, 1986)***.