بسم الله الرحمن الرحيم

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بقسم التوثيق الإلكتروني بمركز الشبكات وتكنولوجيا المعلومات دون أدنى مسئولية عن محتوى هذه الرسالة.

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Ain Shams University
Faculty of Pharmacy

Evaluation of Warfarin Initiation at 3mg versus 5mg for Anticoagulation of Mechanical Mitral Valve Replacement Patients

A Thesis

Submitted for the fulfillment of Ph.D. degree in

Pharmaceutical Sciences
(Clinical Pharmacy)

Submitted by:

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Master of Pharmaceutical Sciences, 2016
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2022

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Sarah Sabry

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List of Abbreviations

Abbreviation	Stands for
ACC	American College of Cardiology
ACCP	American College of Chest Physicians
ACE	Angiotensin-Converting Enzyme
AF	Atrial Fibrillation
AHA	American Heart Association
ALT	Alanine Aminotransferase
AMS	Anticoagulation Management Services
ANCOVA	ANalysis of COVAriance.
ASA	Acetyl Salicylic Acid
AST	Aspartate Aminotransferase
ASU	Ain Shams University
AVR	Aortic Valve Replacement
BMI	Body Mass Index
CAD	Coronary Artery Disease
CI	Confidence Interval
CMR	Cardiac Magnetic Resonance
CONSORT	Consolidated Standards of Reporting Trials
CT	Computed Tomography
CVC	Cardiovascular Center
CVD	Cardiovascular Disease
CYP	Cytochrome
DVT	Deep Venous Thrombosis
EACTS	European Association for Cardio-Thoracic Surgery
ECG	Electrocardiogram
ESC	European Society of Cardiology
GSK	GlaxoSmithKline Company
HF	Heart Failure
ICU	Intensive Care Unit
IE	Infective Endocarditis
IMR	Ischemic Mitral Regurgitation
INR	International Normalized Ratio

IQR	Interquartile Range
LA	Left Atrium
L.E.	Egyptian Pound
LMWH	Low Molecular Weight Heparin
LV	Left Ventricle
MAQI2	Michigan Anticoagulation Quality Improvement Initiative 2
MR	Mitral Regurgitation
MS	Mitral Stenosis
MVP	Mitral Valve Prolapse
MVR	Mitral Valve Replacement
NCI-CTCAE v4.03	National Cancer Institute Common Terminology Criteria for Adverse Events Version 4.03
OAC	Oral Anticoagulation
OTC	Over The Counter
PE	Pulmonary Embolism
PET	Positron Emission Tomography
PM	Papillary Muscle
PT	Prothrombin time
PTTR	Proportion Of Time Spent in Therapeutic Range
PVT	Prosthetic valve thrombosis
RF	Rheumatic Fever
RHD	Rheumatic Heart Disease
RV	Right Ventricle
SD	Standard Deviation
SE	Systemic Embolisms
STS	Society Of Thoracic Surgeons
TAVI	Transcatheter Aortic Valve Implantation
TE	Thromboembolism
TEE	Trans Esophageal Echocardiography
TRT	Time To Reach Therapeutic INR Range
TTE	Transthoracic Echocardiography
UFH	Unfractionated Heparin
VHD	Valvular Heart Disease
VKA	Vitamin K Antagonist

VTE	Venous Thromboembolism
WHO	World health organization

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Abstract

Abstract

Abstract

Purpose: The increased warfarin sensitivity observed after mechanical mitral valve replacement (MVR) operations dictates clinical discretion in warfarin dose initiation. Evidence is still lacking with regards to anticoagulation management of MVR patients. This study aimed to compare initiating warfarin at the recommended dosing versus empirically lowered doses intended to account for the variation in warfarin sensitivity.

Methods: A prospective randomized comparative study was conducted on postoperative MVR patients. Patients were randomly assigned to either the 5 mg group (n = 25) or 3 mg group (n = 25) and were initiated on 5 mg or 3 mg warfarin dose, respectively. Time to target INR, time in therapeutic range, the occurrence of bleeding/thromboembolic events, and cost of bridging with enoxaparin were assessed for both groups.

Results: Target INR was achieved earlier in the 5 mg group than the 3 mg group (p = 0.033), with a mean ± SD of 5.3±2.0 and 6.6±2.0, respectively (95% confidence interval of the mean difference 1.022 – 1.890). Bleeding events did not differ significantly between the two groups. The Cost of enoxaparin consumption per patient was significantly higher in the 3 mg group versus the 5 mg group (p = 0.002).

Conclusions: The initiation of warfarin at 5 mg dose in MVR patients was more efficacious than the 3 mg dose in terms of time to reach target INR. Moreover, the

cost of enoxaparin bridging was significantly reduced with a 5 mg warfarin initiation dose. Bleeding events were comparable.

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Keywords:

Anticoagulation Initiation, Mitral Valve Replacement, Warfarin, Bridging, Time to therapeutic INR, Bridging, Time to therapeutic INR

Introduction