# *Predictors of Postoperative Atrial Fibrillation after Coronary Artery Bypass Grafting: A Prospective Cohort Study*

***Thesis***

*Submitted for partial fulfillment of Master Degree*
*In General Intensive Care*

*By*


**Mohamed Hassan Mohamed Dabsha**

M.B, B. Ch. Faculty of Medicine, Cairo University- 2012


**Under supervision of**


## Dr. Gamal Eldin Mohammad Ahmad Elewa

*Professor of Anesthesia, Intensive Care, and Pain Management*
*Faculty of Medicine, Ain Shams University*

## Dr. Hanaa Mohamed Abd Allah El Gendy

*Assistant Professor of Anesthesia, Intensive Care, and Pain Management*
*Faculty of Medicine, Ain Shams University*

## Dr. Amr Hosni Hamza Ali

*Lecturer of Anesthesia, Intensive Care, and Pain Management*
*Faculty of Medicine, Ain Shams University*



**Faculty of Medicine**
**Ain Shams University**
**2020**

# *Acknowledgment*

*First of all, I would like to express my deep gratitude and thanks to ALLAH, the most merciful.*

I have great honor that my work was under the supervision of ***Dr. Gamal Eldin Mohammad Ahmad Elewa,*** *Professor of Anesthesia, Intensive Care, and Pain Management, Faculty of Medicine, Ain Shams University*. I would like to express my profound gratitude and sincere appreciation for his kind supervision, continuous encouragement and unlimited support in every step throughout this work.

I would like to express my deepest thanks and sincere appreciation to ***Dr. Hanaa Mohamed Abd Allah El Gendy***, Assistant Professor of *Anesthesia*, *Intensive Care, and Pain Management*, *Faculty of Medicine, Ain Shams University*, for her continuous support, great encouragement, great help, patience and valuable advice in every step throughout this work.

I would like also to thank ***Dr. Amr Hosni Hamza Ali***, lecturer of *Anesthesia, Intensive Care, and Pain Management, Faculty of Medicine, Ain Shams University*, for his valuable advice and encouragement throughout this work.

*Last but not least, I would like to express all my feelings of love and appreciation to all my senior staff and my colleagues for their lovely help throughout this work.*

**Mohamed Hassan Mohamed Dabsha**

# Contents

# List of Figures

# List of Tables

# List of Abbreviations

**AA:** Arachidonic acid

**AAD:** Antiarrhythmic Drug

**ACS:** Acute Coronary Syndrome

**ADP:** Adenosine Diphosphate

**AF:** Atrial Fibrillation

**AFL:** Atrial Flutter

**APTT:** Activated Partial Thromboplastin Time

**ASA:** Acetylsalicylic Acid

**AV:** Atrioventricular

**AVNRT:** Atrioventricular Node Re-entry Tachycardia

**AVRT:** Atrioventricular Re-entry Tachycardia

**BMS:** Bare Metal Stent

**CABG:** Coronary Artery Bypass Graft

**CABS:** Coronary Artery Bypass Surgery

**CAD:** Coronary Artery Disease

**CAIC:** Canadian Association of Interventional Cardiology

**CASS**: Coronary Artery Surgery Study

**CCB:** Calcium Channel Blocker

**CCS:** Canadian Cardiovascular Society

**CI:** Confidence Interval

**CHF:** Congestive Heart Failure

**CKD:** Chronic Kidney Disease`

**COPD:** Chronic Obstructive Pulmonary Disease

**CPB:** Cardio Pulmonary Bypass

**CT:** Computerized Tomography

**CrCl:** Creatinine Clearance

**CV:** Cardioversion

**CVA**: Cerebro-Vascular Accidents

**dC:** Delta Change

**DES:** Drug-Eluting Stent

**DTT:** Diluted Thrombin Time

**ECASS:** European Coronary Artery Surgery Study

**ECG:** Electrocardiogram

**ECT:** Electroconvulsive Therapy

**ED:** Emergency Department

**EF:** Ejection Fraction

**HF:** Heart Failure

**HR:** Hazard Ratio

**Hx:** History

**ICU:** Intensive Care Unit

**IMA:** Internal Mammary Artery

**INR:** International Normalized Ratio

**LA:** Left Atrium

**LAA:** Left Atrial Appendage

**LAD:** Left Anterior Descending Artery

**LIMA:** Left Internal Mammary Artery

**LMWH:** Low Molecular Weight Heparin

**LV:** Left Ventricle

**LVEF:** Left Ventricle Ejection Fraction

**MI:** Myocardial Infarction

**MVR:** Mitral Valve Replacement

**NOAC:** Non-Vitamin K Antagonist Oral Anticoagulant

**NSAIDS:** Nonsteroidal Anti-Inflammatory Drugs

**NSTEACS:** Non ST-Elevation Acute Coronary Syndrome

**NVAF:** Non-Valvular Atrial Fibrillation.

**OAC:** Oral Anticoagulant

**OPCAB:** Off Pump Coronary arterial Bypass

**P-Gp:** P-Glycoprotein

**PAD:** Peripheral Artery Disease

**PALLAS:** Permanent Atrial Fibrillation Outcome Study Using Dronedarone on Top of Standard Therapy Trial

**PCI:** Percutaneous Coronary Intervention

**PIP:** Pill-in-the-Pocket

**PO:** post operative

**PIP-AAD:** "Pill-in-the-Pocket" Anti-Arrhythmic Drug

**POAF:** Postoperative Atrial Fibrillation

**PTCA:** Percutaneous Transluminal Coronary Angioplasty

**QOL:** Quality of Life

**RCA:** Right coronary artery

**RCT:** Randomized Controlled Trial

**SAF:** Severity of Atrial Fibrillation

**SR:** Sinus Rhythm

**STEMI:** ST-Elevation Myocardial Infarction

**TEA:** Thoracic Epidural Anesthesia

**TEE:** Trans-Esophageal Echocardiography

**TIA:** Transient Ischemic Attack

**TT:** Thrombin Time

**TTR:** Time in Therapeutic Range

**UFH:** Unfractionated Heparin

**VF:** Ventricular Fibrillation

# Introduction

Post-operative atrial fibrillation (POAF) is one of the most critical and common complications after cardiovascular surgery, precipitating early and late morbidities. Incidence of POAF after coronary artery bypass graft (CABG) surgery is about 30%, about 40% after valve surgery, and about 50 % after combined CABG and valve replacement/repair surgery, with peaks occurring 2 to 3 days after surgery(**Chebbout et al.**, **2018**).

Although this arrhythmia is usually benign and self-limiting, it may lead to hemodynamic instability, thromboembolic manifestation, more hospital stay, readmissions to intensive care unit (ICU), organ failure, healthcare costs and mortality. So, much attention is focused on the prevention of atrial fibrillation (AF) in high risk patients. (**Maisel et al., 2001; Lahtinen et al., 2004**)

The pathophysiological mechanism of AF is complex and affected by various factors. A variety of diagnostic modalities are useful in predicting POAF(**Lowres et al.**, **2018**). Conventionally, diagnosis and management of AF are focused on patient's medical history, examination, and detection of AF through cardiac monitoring. Multiple investigations and studies have tried to identify demographic risk factors and predictors of POAF after CABG with or without valve replacement(**Dobrev et al.**, **2019**).

# Aim of the Work

The aim of this study was to determine the effect of certain predictors on the incidence of post-operative atrial fibrillation during the ICU stay after coronary artery bypass graft surgery.

# Review of literature

## Coronary Artery Bypass Grafting

Coronary artery bypass grafting (CABG) is an “open-heart surgery in which a section of a blood vessel is grafted from the aorta to the coronary artery to bypass the blocked section of the coronary artery and improve the blood supply to the heart.” pathophysiology of coronary artery disease was identified in 1876 when it was postulated that angina (imbalance of coronary perfusion supply and demand) was caused by interruption of coronary blood supply and that myocardial infarction occurred after the occlusion of at least one coronary artery(**Diodato & Chedrawy**, **2014**).

The 1960s saw great advances in coronary artery surgery. **Goetz et al.** (**1961**) performed the first successful human coronary artery bypass operation. **Proudfit et al.(1966)** produced the first practical cardiac angiography visualizing the coronary arteries. In the 1980s, the prevalence of CABG increased and safety improved. Thoracoscopic harvesting of the Internal mammary artery (IMA) was reported in 1998 by **Duhaylongsod et al.** Minimally invasive and robotic surgery were also developed(**Poffo et al.**, **2017**). The number of CABG is declining from a peak of 519,000 cases in 2000 to about 300,000 operations in 2012(**Diodato & Chedrawy**, **2014**).

Although the fundamental basis of CABG is to reestablish perfusion to the myocardium, there are different approaches to get this aim . The first factor is the utilization of cardiopulmonary bypass or “on pump versus off pump.” Initially, most cardiac surgeries were done on a beating heart, but with the development of cardiopulmonary bypass and cardioplegia, most CABG were done on pump. Off-pump coronary artery bypass (OPCAB) surgery had regained interest in 1990s. **Benetti et al.**(**1991**) **and Buffalo et al.**(**1996**) Did 2000 OPCAB patients with operative safety. Benefits of OPCAB are lower end organ damage, that is, renal failure, cerebrovascular accidents (CVA), fewer cognitive deficits, less psychomotor defects, less transfusion rates, and less systemic inflammation(**Parissis et al.**, **2015**).

The randomized on/off bypass (ROOBY) trial Studied the outcomes for 2.203 patients (99% men) at 18 Veterans Affairs Medical Centers. The primary short-term endpoint, adeath or complications within 30 days of surgery, occurred with similar frequency (5.6% for on-pump CABG; 7.0% for off-pump CABG; $P = 0.19$). The primary long-term endpoint, death from any cause, revascularization procedure, or nonfatal myocardial infarction (MI) within 1 year of surgery, occurred more in off-pump CABG (9.9%) than in those having on-pump CABG (7.4%; $P = 0.04$). Neuropsychological outcomes were not different between the groups, and graft patency was higher in on-pump group (87.8% versus 82.6%; $P = 0.01$) at 12 months(**Shroyer et al.**, **2009**).

**In 2011**, **Forouzannia et al.** compared clinical and economic outcomes of off-pump and on-pump CABG surgery. They analyzed 304 patients undergoing coronary artery bypass surgery and were randomized into conventional on pump and off-pump groups. On-pump coronary artery bypass OPCAB surgery significantly reduced the need for P.O. transfusion requirement ($P < 0.05$). There were no statistically significant differences in surgical reexploration or length of stay. The mean cost for an on-pump surgery was significantly higher than an off-pump surgery.

**Yadava et al.**, (**2011**) reviewed 3500 patients over 8 years, women were 14.6%. In-hospital mortality was higher in women as compared to men; 2.92% versus 1.8%. The most common causes of mortality were low cardiac output and renal failure. Use of OPCAB reduced mortality (1.84% versus 4.5% on pump; $P$ =0.01) in women. Blood transfusions (2.5 ± 1.2 units versus 4.3 ± 1.4; units $P$ < 0.001); ICU stay (29.4 ± 16.4 h versus 38.3 ± 17.3 h; $P$ < 0.0001); and length of stay (6.81 ± 1.6 d versus 8.05 ± 2.1 d; $P$ < 0.0001) were also reduced in OPCAB females.

**Afilalo et al. (2012)** published a meta-analysis comparing on-pump CABG and OPCAB. The primary outcomes were all-cause mortality, stroke, and myocardial infarction. Fifty-nine trials were included with nearly 9000 patients. The study population had a mean age of 63.4 years with a male to female predominance of over 4 : 1. Postoperative CVA was significantly reduced by 30% in the OPCAB group (risk ratio (RR) 0.70, 95% CI: 0.49–0.99). Rate in mortality (RR: 0.90, 95% CI: 0.63–1.30) and myocardial infarction (pooled RR: 0.89, 95% CI: 0.69–1.13) were not different between groups. In the metaregression analysis, clinical outcome was similar regardless of mean age, proportion of females in the trial, number of grafts per patient, and trial publication date.

Minimally invasive and robotic assisted approaches are emerging. Minimally invasive cardiac surgery does not use CPB and can be performed through smaller incisions. This approach has gained popularity and is often used for LIMA to LAD grafts. Other benefits include reduced operative time, reduced recover time, decreased need for blood transfusion, less anesthesia time , decreased length of ICU stay, less pain, and an estimated 40% savings over conventional CABG. However, the total number of bypassable vessels is reduced secondary to exposure making these approaches useful for certain group of patients(**Pettinari et al.**, **2017**).

**Indications:**

The CABG procedure is indicated for relief of symptoms (primarily angina) unresponsive to medical treatment or percutaneous transluminal coronary angioplasty (PTCA), specially if operation will delay unfavorable events (death, MI, angina recurrence) more than other treatment. For angina relief, surgery often succeedes where medical or interventional therapy fails or is not recommended. For survival, the situation is more complex. There is agreement that CABG improves prognosis in early post-surgical years in those patients with symptomatic left main coronary artery stenosis or stenosis of three main coronary vessels, although this advantage is not significant after 10–12 years(**Maier**, **2012**).

For majority of patients with less severe pathology, the prognosis is good without surgery. Furthermore, cardiac surgery has advanced mortality have declined dramatically. Thus, selection among different courses of cardiac therapy is based mainly on measures of quality of life (QOL), including minimization of pain and disability(**Diodato & Chedrawy**, **2014**).

**Outcomes of CABG:**

Prolongation of life as an outcome of CABG was addressed in 3 randomized clinical trials that compared CABG with medical therapy. They include the Veterans Administration Study (VAS), the European Coronary

Artery Surgery Study (ECASS), and the Coronary Artery Surgery Study (CASS). The VAS recruited 1015 patients from 13 centers between 1970 and 1974. Patients were randomly allocated to medical or surgical treatment. There was revealed no significant difference in mortality 4 years after CABG in patients with 1, 2- or 3-vessel disease, but a highly significant increase in survival in patients underwent CABG for left main coronary artery obstruction. The 4-year mortality for CABG patients was 7% (n = 46), compared with 33% for medical treatment (n = 44)(**VA Coronary Artery Bypass Surgery Cooperative Study Group**, **1992**).

The ECASS recruited 768 men below 65-years between 1973 and 1976. Patients were randomized to medical or surgical treatment. The main weakness of this trial was that nothing was known about the original population from which patients were drawn. There was significant improvement in survival for the total CABG population, and for patients with 3-vessel disease, with stenosis in the proximal third of the LAD artery, or with left main coronary disease. After 5 years of follow up, 30 deaths were reported among the 395 patients treated surgically (7.6%), and 61 deaths among the 373 patients treated using medical by (16.3%)(**European Coronary Surgery Study Group**, **1982**).

The CASS recruited 780 patients below 65 years allocated to medical or surgical treatment between 1975 and 1979 (90% male). The 5-year survival in the medical group (92%) and the surgical group (95%) were similar. No significant differences in survival were found between medically and surgically treated groups at baseline in extent of coronary heart disease (CHD) or in ventricular function. In patients with 3-vessel disease and low ejection fractions, a distinct (but not significant) trend for improved 5-year