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Perioperative Beta Blocker in High Risk Patients Undergoing Major Abdominal Surgery and its Effect on Cardiovascular Mortality and Morbidity

Thesis

Submitted for the Partial Fulfillment of M.D. Degree in Anesthesia

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2019

Acknowledgment

First and foremost, I feel always indebted to **GOD,** *the Most Kind and Most Merciful.*

I'd like to express my respectful thanks and profound gratitude to **Prof. Dr. Gehan Fouad Kamel,** *Professor of Anesthesia, Intensive Care and Pain Management Faculty of Medicine, Ain Shams University for her keen guidance, kind supervision, valuable advice and continuous encouragement, which made possible the completion of this work.*

I am also delighted to express my deepest gratitude and thanks to **Prof. Dr. Adel Mohamad Alansary,** *Assistant Professor of Anesthesia, Intensive Care and Pain Management Faculty of Medicine, Ain Shams University, for his kind care, continuous supervision, valuable instructions, constant help and great assistance throughout this work.*

I am deeply thankful to **Dr. Hoda Shokry Abdelsamie,** *Assistant Professor of Anesthesia, Intensive Care and Pain Management Faculty of Medicine, Ain Shams University, for her great help, active participation and guidance.*

I wish to introduce my deep respect and thanks to **Dr. Rasha Mahmoud Hassan,** *Lecturer of Anesthesia, Intensive Care and Pain Management Faculty of Medicine, Ain Shams University, for her kindness, supervision and cooperation in this work.*

Lydia Edward Aziz Zakhary

List of Contents

Title	Page No.

List of Tables

Table No.	Title	Page No.

List of Figures

Fig. No.	Title	Page No.

List of Abbreviations

Abb.	Full term
AAA	Abdominal aortic aneurysm
ABP	Arterial blood pressure
AC	Adenyl cyclase
ACC/ AHA	American College of Cardiology/American Heart Association
ACEIs	Angiotensin converting enzyme inhibitors
AF	Atrial Fibrillation
AR	Aortic
AS	Aortic Stenosis
ATP	Adenosine triphosphate
AV	Atrioventricular
AVR	Aortic valve replacement
BB	Beta blocker
βNP	β-Natriuretic peptide
CAD	Coronary artery disease
cAMP	Cyclic adenosine monophosphate
CNS	Central nervous system
COP	Cardiac output
COPD	Chronic obstructive pulmonary disease
DBP	Diastolic blood pressure
ECG	Electrocardiogram
EF	Ejection fraction
ESC/ESA	European Society of Cardiology/ European Society of Anesthesiology
EVAR	Endovascular AAA repair
GFR	Glomerular filtration rate
HF	Heart failure
HR	Heart rate
ICU	Intensive care unit
IHD	Ischemic heart disease

List of Abbreviations Cont...

Abb.	Full term
ISA	Intrinsic sympathomimetic activity
LV	Left ventricle
MAC	Minimal alveolar concentration
MACE	Major adverse cardiac events
MET	Metabolic equivalent
MI	Myocardial infarction
MICA	Myocardial infarction or cardiac arrest
MR	Mitral Regurgitations
MS	Mitral Stenosis
NSQIP	National Surgical Quality Improvement Plan
POISE	PeriOperative ISchemic Evaluation
PVCs	Premature ventricular contractions
RCRI	Revised cardiac risk index
RV	Right ventricle
SBP	Systolic blood pressure
SpO2	Peripheral oxygen saturation
SVR	Systemic vascular resistance
TAVR	Trans-catheter aortic valve replacement
UFH	Un-fractioned heparin
VT	Ventricular tachycardia

INTRODUCTION

Worldwide it is estimated that around 200 million people undergo non-cardiac surgery annually. Cardiovascular complications account for majority of the cause of postoperative morbidity and mortality with incidence ranging from 0.5% to 30% ***(Bakker et al., 2011).***

Non-cardiac surgery causes a rise in catecholamine concentrations that results in an increase in heart rate, blood pressure, and free fatty acid concentrations, which in turn increases myocardial oxygen demand. The cardiovascular effects of general anesthesia include changes in the arterial and central venous pressures, cardiac output, and varying heart rhythms, which occur by the following mechanisms: decreased systemic vascular resistance, decreased myocardial contractility, decreased stroke volume, and increased myocardial irritability. Induction of general anesthesia lowers systemic arterial pressures by 20-30%, tracheal intubation increases the blood pressure by 20-30 mm Hg, and inhalational agents lower cardiac output by 15% ***(Hübner et al., 2013).***

A previously stable patient may decompensate postoperatively, leading to significant postoperative morbidity and mortality. A substantial number of all deaths among patients undergoing noncardiac surgery are caused by cardiovascular complications ***(Augoustides et al., 2013).***

The high prevalence of cardiac events associated with noncardiac surgery reflects the high prevalence of underlying Coronary artery disease in the general population, upon which the additional stresses of surgery are overlaid ***(Smeili and Lotufo, 2015).***

The pathophysiology of perioperative myocardial infarction is complex, but may include myocardial oxygen demand/supply mismatch associated with tachycardia, hypertension, and pain ***(Meltzer et al., 2013).***

Aim of the Work

To study the effects of perioperatively administered beta-blockers for prevention of surgery-related mortality and morbidity in patients undergoing major abdominal surgery while under general anesthesia.

Chapter 1

RISK FACTORS IN CARDIAC PATIENTS UNDERGOING NON-CARDIAC SURGERY

Surgical Risk for Cardiac Events:

Cardiac complications after non-cardiac surgery depend on specific risk factors and the type of surgery with the circumstances under which it takes place. Surgical factors that influence cardiac risk are related to the urgency, magnitude, type, and duration of the procedure, as well as the change in body core temperature, blood loss, and fluid shifts ***(Kheterpa et al., 2009).***

Every operation elicits a stress response. This response is initiated by tissue injury and mediated by neuroendocrine factors, and may induce tachycardia and hypertension. Fluid shifts in the perioperative period add to the surgical stress. This stress increases myocardial oxygen demand ***(Poldermans et al., 2010).***

Surgery causes alterations in the balance between prothrombotic and fibrinolytic factors, resulting in hypercoagulability and possible coronary thrombosis (elevation of fibrinogen and other coagulation factors, increased platelet activation and aggregation, and reduced fibrinolysis). The extent of such changes is proportionate to the extent and duration of the intervention. All these factors may cause myocardial ischemia and heart failure (HF) by causing coronary thrombosis and interrupting blood flow to the myocardium. Certainly in patients with high risk, attention to these factors should be given and lead, if indicated, to adaptations in the surgical plan ***(Poldermans et al., 2010).***

Although patient specific factors are more important than surgery specific factors in predicting the cardiac risk for non-cardiac surgical procedures, the type of surgery cannot be ignored when evaluating a particular patient undergoing an intervention. With regard to cardiac risk, surgical interventions can be divided into low risk, intermediate risk, and high risk groups with estimated 30-day cardiac event rates (cardiac death and MI) of <1, 1–5, and >5%, respectively. This risk stratification provides a good indication of the need for cardiac evaluation, drug treatment, and assessment of risk for cardiac events ***(Kristensen et al., 2014).***

Table (1): Surgical risk estimate according to type of surgery ***(Kennon and Archbold, 2017).***

Low-risk: < 1%	Intermediate-risk: 1-5%	High-risk: > 5%
• Superficial surgery • Breast • Dental • Endocrine: thyroid • Eye • Reconstructive • Carotid asymptomatic (CEA or CAS) • Gynaecology: minor • Orthopaedic: minor (meniscectomy) • Urological: minor (transurethral resection of the prostate)	• Intraperitoneal: splenectomy, hiatal hernia repair, cholecystectomy • Carotid symptomatic (CEA or CAS) • Peripheral arterial angioplasty • Endovascular aneurysm repair • Head and neck surgery • Neurological or orthopaedic: major (hip and spine surgery) • Urological or gynaecological: major • Renal transplant • Intra-thoracic: non-major	• Aortic and major vascular surgery • Open lower limb revascularization or amputation or thromboembolectomy • Duodeno-pancreatic surgery • Liver resection, bile duct surgery • Oesophagectomy • Repair of perforated bowel • Adrenal resection • Total cystectomy • Pneumonectomy • Pulmonary or liver transplant

The high-risk group consists of major vascular interventions. In the intermediate risk category the risk also depends on the magnitude, duration, location, blood loss, and fluid shifts related to the specific procedure. In the low risk category the cardiac risk is negligible unless strong patient specific risk factors are present (Table 1) ***(Kennon and Archbold, 2017).***

The need for and the value of preoperative cardiac evaluation also depend on the urgency of surgery. In the case of emergency surgical procedures, such as those for ruptured abdominal aortic aneurysm (AAA), major trauma or for perforated viscus, cardiac evaluation will not change the course and result of the intervention but may influence the management in the immediate postoperative period ***(Fleisher et al., 2008).***

In non-emergent but urgent untreated surgical conditions such as bypass for acute limb ischemia or treatment of bowel obstruction, the morbidity and mortality of the untreated underlying condition will outweigh the potential cardiac risk related to the intervention. In these cases, cardiac evaluation may influence the perioperative measures taken to reduce the cardiac risk, but will not influence the decision to perform the intervention ***(De Hert et al., 2018).***

In some cases, the cardiac risk can also influence the type of operation and guide the choice to less invasive interventions, such as peripheral arterial angioplasty instead of infra-inguinal bypass, or extra-anatomic reconstruction instead of aortic procedure, even when these may yield less favorable results in the long term ***(De Hert et al., 2018).***

Lastly, the cardiac evaluation should be taken into consideration even when deciding whether to perform an intervention or not. This is the case in certain prophylactic interventions such as the treatment of small AAAs or asymptomatic carotid stenosis where the life expectancy of the patient and the risk of the operation are important factors in evaluating the potential benefit of the surgical intervention ***(Kennon and Archbold, 2017).***

- **Type of Surgery:**

In general, endoscopic and endovascular techniques speed recovery, decrease hospital stay and reduce the rate of complications. However, randomized clinical trials comparing laparoscopic with open techniques exclude older, sicker, and urgent patients, the results have shown no significant differences in conversion rate, pain, complications, length of hospital stay or re-admissions ***(Wang et al., 2014).***

1. Endovascular vs. Open Vascular Procedures:

Vascular interventions are of specific interest, not only because they carry the highest risk of cardiac complications, explained by the high probability that the atherosclerotic process also affects the coronary arteries, but also because of the many studies that have shown that this risk can be influenced by adequate perioperative measures in these patients ***(Bauer et al., 2010).***

Open aortic and infra-inguinal procedures have both to be considered as high risk procedures. Although a less extensive intervention, infra-inguinal revascularization entails a cardiac risk similar to or even higher than aortic procedures. This can be explained by the higher incidence of diabetes, renal dysfunction, ischemic heart disease, and advanced age in this patient group. This also explains why the risk related to peripheral artery angioplasties, which are minimally invasive procedures, is not negligible ***(Kristensen et al., 2014).***

Endovascular AAA repair (EVAR) has been associated with lower operative mortality and morbidity than open repair but this advantage decreases with time, due to more frequent graft related complications and re-interventions in patients who underwent EVAR, resulting in similar long term AAA related total mortality ***(Paravastu et al., 2014).***

Therefore, multiple factors must be taken into consideration when deciding which type of procedure serves the patient best. An endovascular-first approach may be advisable in patients with significant comorbidity, whereas a bypass procedure may be offered as a first line interventional treatment for fit patients with a longer life expectancy ***(Kristensen et al., 2014).***

Several randomized trials, as well as community based studies, have shown that the cardiac risk is substantially lower after endovascular aortic aneurysm repair compared with open