Relation between Prolonged Cardiopulmonary Bypass Time in Cardiac Surgery in Adult Patients and Post-Operative Acute Kidney Injury

Thesis

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Mohamed Samir Mohamed Salama

List of Contents

List of Tables

List of Figures

List of Figures Cont...

List of Abbreviations

Abb.	Full term
ACE	Angiotensin-converting enzyme
AKI	Acute kidney injury
AKIN	Acute Kidney Injury Network criteria
ARBs	Angiotensin-receptor blockers
AV	Aortic valve
CABG	Coronary artery bypass grafting
CKD	Chronic Kidney Disease
CPB	Cardiopulmonary bypass
CSA-AKI	Cardiac-surgery associated acute kidney injury
DM	Diabetic mellitus
e-GFR	Estimated glomerular filtrations rate
GFR	Glomerular filtration rate
HbA1C	Hemoglobin A1c
HCV	Hepatitis C
HES	Hydroxyethyl starch
HK	High– molecular-weight kininogen
HO1	Haem oxygenase 1
HTN	Hypertension
I/R injury	Ischemia-reperfusion injury
IABP	Intra-aortic ballon pump
ICU	Intensive care unit
IHD	Ischemic heart disease
IRI	Ischaemia–reperfusion injury
KDIGO	Kidney Disease Improving Global Outcome
KIM1	Kidney injury molecule 1
LPS	Lipopolysaccharide

List of Abbreviations Cont...

Abb.	Full term
LV	Left ventricular
MODS	Multiple organ dysfunction syndrome
MOF	Multiple organ failure
MV	Mitral valve
NGAL	Neutrophil gelatinase-associated lipocalin
RCTs	Randomized controlled trials
RHD	Rheumatic heart disease
RIFLE	Risk, injury, failure, loss end-stage kidney disease
RRT	Renal replacement therapy
SIRS	Systemic inflammatory response syndrome
TF	Tissue factor
TV	tricuspid valve

INTRODUCTION

Cardiac-surgery associated acute kidney injury (CSA-AKI) remains an important and frequent complication in patients undergoing cardiac surgery and is associated with a poor short- and long-term prognosis. The incidence for CSA-AKI according to Acute Kidney Injury Network criteria (AKIN) varies between 3% and 50% ***(Chertow et al., 1997).*** Cardiac-surgery associated acute kidney injury requiring temporary renal replacement therapy (RRT) occurs in 5% to 20% of these patients and is associated with a high mortality rate ***(Seitz et al., 2013).***

To decrease the incidence AKI after cardiac surgery, numerous interventions have been tested, but none has proved efficient. In the absence of proven interventions, a reasonable strategy would be to identify modifiable risk factors for AKI in this setting. These modifiable risk factors might serve as therapeutic targets for preventing AKI.

Previous studies have identified several important risk factors for AKI after cardiac surgery. Patient-related risk factors like female gender, chronic obstructive pulmonary disease, diabetes mellitus, peripheral vascular disease, renal insufficiency, congestive heart failure, left ventricular (LV) ejection fraction <35%, need for emergent surgery, cardiogenic shock requiring intra-aortic ballon pump (IABP), total circulatory arrest, left main

coronary artery disease, etc., are the important factors associated with CSA-AKI ***(Thakar et al., 2005).***

Risk factors pertaining to procedures that increase the likelihood of CSA-AKI are the cardiopulmonary bypass (CPB) machine, On-pump versus off-pump CABG, hemolysis, and hemodilution ***(Rosner and Okusa, 2006).***.

Unlike nephropathies that reflect a single source of insult (e.g. contrast-induced nephropathy), post-cardiac surgery AKI reflects the cumulative consequences of numerous potential perioperative factors. One of the most important factors affecting perioperative renal function is the cardiopulmonary bypass which induce renal insult by several mechanisms ***(Mehta et al., 2007):***

1. Systemic inflammatory response syndrome caused by the CPB in the picture of activation of complement and neutrophils, release of cytokines and production of oxygen free radicals which lead to renal dysfunction.

2. Despite adequate heparinization, the bypass circuit is a potent activator of the coagulation system with generation of factor Xa, thrombin and micro emboli formation that lead to endothelial damage of renal capillaries causing renal dysfunction.

3. The non-pulsatile flow of the CPB with hemodilution produce elevated levels of hormones that affect vascular

tone, renal blood flow and glomerular filtration rate exposes the renal parenchyma to reduced oxygen tension contributing to ischemia-reperfusion injury.

4. Cardiopulmonary bypass induced erythrocyte hemolysis lead to increase concentration of free erythrocytes constituents like haemoglobin and iron and subsequent exhaustion of their scavengers such as transeferrin and haptoglobin during CPB lead to alternations of systemic vascular resistance, platelets function and renal tubular damage.

Aim of the Study

The aim of this study was to detect the relation between prolonged cardiopulmonary bypass time in cardiac surgery and the incidence of post-operative acute kidney injury.

Chapter 1

CARDIOPULMONARY BYPASS INDUCED INFLAMMATORY RESPONSE

Cardiac surgery had begun slowly in the 1940s with just a handful operations that could be done without the use of cardiopulmonary bypass: closure of a patent ductus, coarctation repair, the Blalock-Taussig shunt, mitral commisurotomy and in the early 1950s closure of atrial septal defects with the use of hypothermia. However, by 1950 it became obvious to those interested in cardiac operations that a heart-lung machine would be required to deal with the majority of congenital cardiac malformations and valvular heart disease ***(Stoney, 2009)***.

The first attempts at cardiopulmonary bypass during those years were a series of disasters with a very high mortality rate. Many years later, Walton Lillehei reviewed all of the open heart operations reported in the surgical literature between 1951 and 1955. During those 4 years, 18 patients were reported to have had an operation using cardiopulmonary bypass at 6 different centers. There were 17 deaths and only 1 survivor. The type of oxygenators used were film (8 patients), bubble (4 patients), monkey lung (5 patients), and autologous lung (1 patient) ***(Gravlee et al., 2015).***

The first successful cardiac surgery to be done using cardiopulmonary bypass machine was for 18-year-old female

colleague student with repeated episodes of right heart failure. Cardiac catheterization confirmed that she had an atrial septal defect. The operation was done on May 6, 1953 by John Gibbon (professor and chairman of the Department of Surgery at Jefferson Medical College) ***(Stoney, 2009).***

In order to talk about cardiopulmonary bypass induced inflammatory response and it's injurious effect on tissues we have to know that Inflammation is the initial, nonspecific response of vascularized tissue to a variety of injuries and represents the body's attempt to protect itself from an injuring agent. Irrespective of the cause, the inflammatory response follows qualitatively similar patterns of activation, involving both humoral and cellular inflammatory pathways. While aiming to be protective, the inflammatory response can on occasions become exaggerated, damaging the host it aims to protect.

The inflammatory response witnessed in CPB-assisted cardiac surgery is no different. Major surgery and its associated prolonged anesthesia cause the body to undergo a major inflammatory response. Cardiopulmonary bypass, an inherently unnatural process, magnifies this reaction. The pump and oxygenator both function in a nonphysiologic manner; thus, intravascular pressures and blood gas composition stray outside normal ranges. Significant hemodilution occurs, causing intercompartmental fluid shifts, significant fluid retention, and dilution and denaturing of important plasma proteins; blood is exposed to nonendothelial surfaces and abnormal shear