ANAESTHESIA AND MYOCARDIAL ISCHAEMIA/REPERFUSION INJURY

Essay

Submitted for partial fulfillment of Master degree in
Anesthesiology and ICU

By

Abeer Riad Aly Fawzy
M.B.B.Ch

Under Supervision Of

Prof./ Amir Ibrahim Salah
Professor of Anaesthesiology and ICU
Faculty of medicine, Ain Shams University

Dr./ Ahmed Mohamed Shafik Hamed
Assistant Professor of Anaesthesiology and ICU
Faculty of medicine, Ain Shams University

Dr./ Mostafa Gamal El-Din Ahmed Mahran
Lecturer of Anaesthesiology and ICU
Faculty of medicine, Ain Shams University

Faculty of medicine
Ain Shams University
2011

Chapter 1

INTRODUCTION

Prevention and adequate treatment of peri-operative myocardial ischaemia and its consequences are the frequent challenges of current anaesthetic practice. The main goal in the therapy of myocardial ischaemia is to restore perfusion to the ischaemic tissue. However, reperfusion itself can induce additional cellular damage that can exceed that caused by the ischaemic injury, even resulting in death. This phenomenon is called lethal reperfusion injury. *Rosenkranz and Buckberg in 1983* defined lethal reperfusion injury as an irreversible deterioration of the myocardium, which can be reduced by modifications of the conditions of reperfusion. However, not only modifications of reperfusion conditions but also the application of interventions before the occurrence of myocardial ischaemia may help to reduce the extent of ischaemic damage and subsequent reperfusion injury. Interestingly, the use of certain anaesthetic drugs seems to represent one such intervention *(Gross and Auchampach, 2007)*.

There are three time frames in which protection against ischaemia-reperfusion injury can be induced: before ischaemia occurs, during ischaemia, and after the ischaemia at the onset of reperfusion. The first report that sublethal ischaemia before otherwise lethal ischaemia induces strong cardioprotection was published *in 1986 by Murry and colleagues.*

This preconditioning typically consists of two distinct phases: the early phase which starts immediately after the ischaemic stimulus and protects the myocardium for 2-3hrs, followed by a late protection period occurring after 12-24hrs and lasting for 2-3 days. The latter is called *the late pre-conditioning phase*. It has since been shown that the application of short ischaemic episodes interspersed by short periods of reperfusion after the longer period of myocardial ischaemia was also associated with a protective effect on the extent of myocardial damage and post-ischaemic dysfunction. This phenomenon was called post-conditioning *(Zhao et al., 2003)*.

Evidence has now accumulated that anaesthetics and some narcotics may be cardioprotective. While experimental findings are increasingly being applied to clinical practice, continuing efforts are directed towards

the unravelling of the underlying mechanisms. The understanding of the underlying signal transduction cascade is of special importance because there is conflicting clinical evidence concerning the relative contributions of early or late pre- and post-conditioning to clinical cardioprotection provided by anaesthetic agents. Several factors may be responsible for this conflicting evidence such as the differences in the extent and degree of myocardial ischaemia between different studies, possible interference by the use of other drugs, and the presence of co-existing disease such as diabetes. This review will focus on the translation of laboratory evidence of anaesthetic-induced cardioprotection into daily clinical practice *(Fräßdorf et al., 2009)*.

Chapter 2

ANATOMY OF BLOOD SUPPLY OF THE HEART

The circulatory system is an organ system that passes nutrients (such as amino acids and electrolytes), gases, hormones, blood cells, nitrogen waste products, etc. to and from cells in the body to help fight diseases and help stabilize body temperature and pH to maintain homeostasis. This system may be seen strictly as a blood distribution network, but some consider the circulatory system as composed of the cardiovascular system, which distributes blood, and the lymphatic system, which distributes lymph *(Peter and Savage, 2007)*.

The main components of the cardiovascular system are the heart, arteries, arterioles, capillaries, venules, and veins. Adults have approximately 60,000 miles (96,000km) of blood vessels *(Arialdi et al., 2007)*.

I) Coronary circulation:

Is the circulation of blood in the blood vessels of the heart muscle. Although blood fills the chambers of the heart, the muscle tissue of the heart (the myocardium) is so thick that it requires coronary

blood vessels to deliver blood deep into it. The coronary arteries that run on the surface of the heart are called epicardial coronary arteries. These arteries, when healthy, are capable of auto-regulation to maintain coronary blood flow at levels appropriate to the needs of the heart muscle. These relatively narrow vessels are commonly affected by atherosclerosis and can become blocked, causing angina or a myocardial infarction. The coronary arteries that run deep within the myocardium are referred to as subendocardial *(Prasad et al., 2009)*.

The coronary arteries are classified as "end circulation", since they represent the only source of blood supply to the myocardium: there is very little redundant blood supply, which is why blockage of these vessels can be so critical *(Kaimkhani et al., 2005)*.

A. Coronary anatomy: (Fig. 1)

The exact anatomy of the myocardial blood supply system varies considerably from person to person. A full evaluation of the coronary arteries requires cardiac catheterization or CT coronary angiography.

In general there are two main coronary arteries, the left and right:

- Right coronary artery.
- Left coronary artery

Both of these arteries originate from the beginning (root) of the aorta, immediately above the aortic valve. The left coronary artery originates from the left aortic sinus, while the right coronary artery originates from the right aortic sinus ***(Escaned et al., 2009)***.

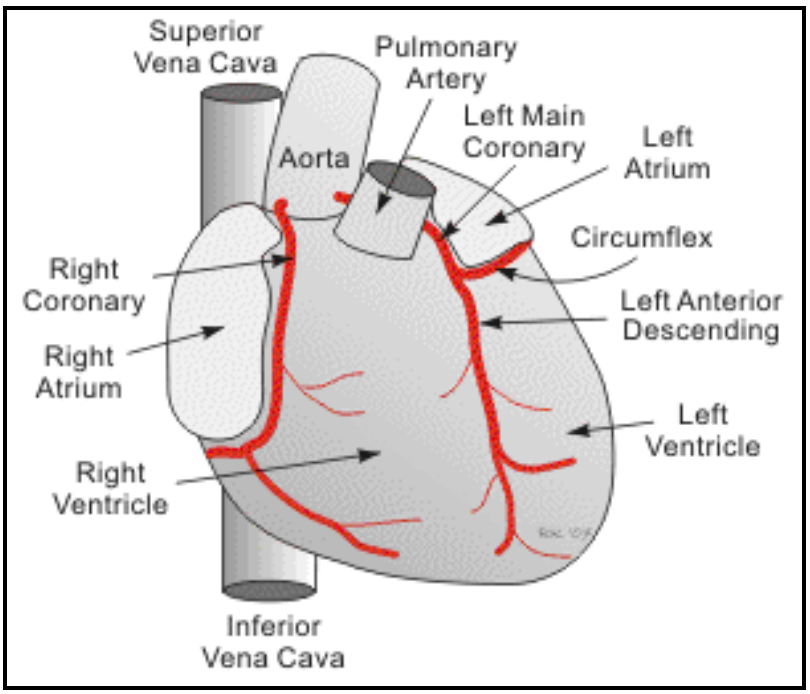

Fig. (1): Coronary anatomy ***(Escaned et al., 2009)***.

1. Right Coronary Artery (RCA):

The right coronary artery branches into:

- Right marginal artery.
- Posterior descending artery.

The right coronary artery supplies:

- Right atrium.
- Right ventricle.
- Bottom portion of both ventricles and back of the septum

The main portion of the right coronary artery provides blood to the right side of the heart, which pumps blood to the lungs. The rest of the right coronary artery and its main branch, the posterior descending artery, together with the branches of the circumflex artery, run across the surface of the heart's underside, supplying the bottom portion of the left ventricle and back of the septum ***(Michael et al., 2009)***.

2. Left Main Coronary Artery (also called the left main trunk): (Hamilos et al., 2009)

The left main coronary artery branches into:

- Circumflex artery.
- Left Anterior Descending artery (LAD).

The left coronary arteries supply:

- Circumflex artery-supplies blood to the left atrium, side and back of the left ventricle.
- Left Anterior Descending artery (LAD)-supplies the front and bottom of the left ventricle and the front of the septum.

B. Variations:

Four percent of people have a third, the posterior coronary artery. In rare cases, a person will have one coronary artery that runs around the root of the aorta.

Occasionally, a coronary artery will exist as a double structure (i.e., there are two arteries, parallel to each other, where ordinarily there would be one) *(Xiao and Lubo zhang, 2009)*.

C. Coronary artery dominance:

The artery that supplies the posterior descending artery (PDA) (posterior interventricular artery) determines the coronary dominance.

- If the posterior descending artery (PDA) is supplied by the right coronary artery (RCA), then the coronary circulation can be classified as "right-dominant".
- If the posterior descending artery (PDA) is supplied by the circumflex artery (CX), a branch of the left

artery, then the coronary circulation can be classified as "left-dominant".

- If the posterior descending artery (PDA) is supplied by both the right coronary artery (RCA) and the circumflex artery, then the coronary circulation can be classified as "co-dominant".

Approximately 70% of the general population are right-dominant, 20% are co-dominant, and 10% are left-dominant *(Ganz and Priscilla, 2009)*.

D. Coronary flow:

During contraction of the ventricular myocardium (systole), the subendocardial coronary vessels (the vessels that enter the myocardium) are compressed due to the high intraventricular pressures. However, the epicardial coronary vessels (the vessels that run along the outer surface of the heart) remain patent. Because of this, blood flow in the subendocardium stops. As a result most myocardial perfusion occurs during heart relaxation (diastole) when the subendocardial coronary vessels are patent and under low pressure. This contributes to the filling difficulties of the coronary arteries. Failure of oxygen delivery caused by a decrease in blood flow in front of increased oxygen demand of the heart results in tissue ischaemia, a condition of oxygen

debt. Brief ischaemia is associated with intense chest pain, known as angina. Severe ischaemia can cause the heart muscle to die of oxygen starvation, called a myocardial infarction. Chronic moderate ischaemia causes contraction of the heart to weaken, known as myocardial hibernation *(Wustmann et al., 2003)*.

In addition to metabolism, the coronary circulation possesses unique pharmacologic characteristics. Prominent among these is its reactivity to adrenergic stimulation. The majority of vasculature in the body constricts to norepinephrine, a sympathetic neurotransmitter the body uses to increase blood pressure. In the coronary circulation, norepinephrine elicits vasodilation, due to the predominance of beta-adrenergic receptors in the coronary circulation. Agonists of alpha-receptors, such as phenylephrine, elicit very little constriction in the coronary circulation *(Williams and Wilkins, 2005)*.

E. Anastomosis: (Fig. 2)

When two arteries of the coronary circulation join, dual blood flow to a certain area of the myocardium occurs. These junctions are called anastomosis. If one coronary artery is obstructed by an atheroma, the second artery is still able to supply oxygenated blood to the myocardium. However this

can only occur if the atheroma progresses slowly, giving the anastomosis a chance to proliferate. Under the most common configuration of coronary arteries, there exist two anastomosis on the posterior side of the heart. More superiorly, there is an anastomosis between the circumflex artery (a branch of the left coronary artery) and the right coronary artery. More inferiorly, there is an anastomosis between the anterior interventricular artery (a branch of the left coronary artery) and the posterior interventricular artery (a branch of the right coronary artery) *(Billinger et al., 2004)*.

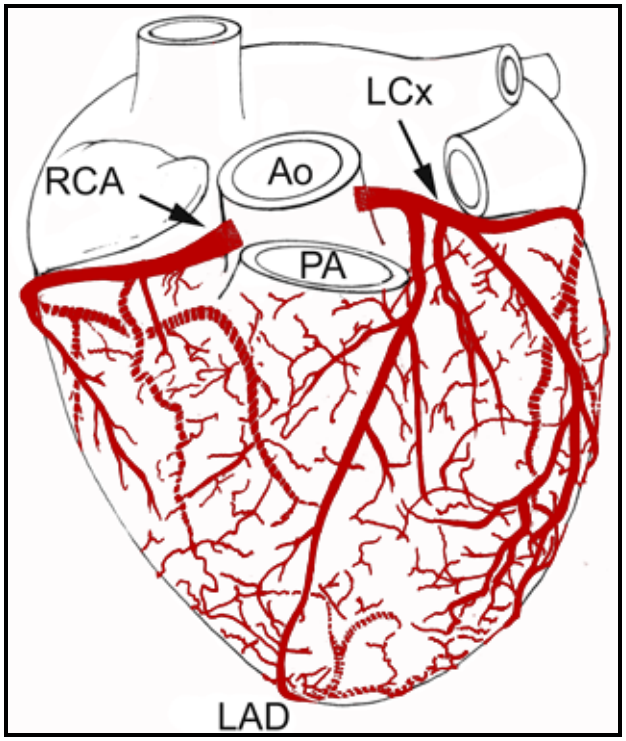

Fig. (2): Coronary anastomosis *(Billinger et al., 2004)*.

II) Cardiovascular Physiology Concepts

The myocardium has a very limited anaerobic capacity, and the heart is dependent on a continuous supply of oxygen from the coronary circulation. Myocardial oxygen consumption increases whenever there is tachycardia and may increase fivefold in the transition from rest to exercise. Powerful mechanisms increase coronary blood flow whenever myocardial oxygen consumption is increased. Without these mechanisms, decreased cardiac output, hypotension, arrhythmias, and death would result *(Duncker and Bache, 2008)*.

A. Oxygen Supply:

The delivery of oxygen (DO_2) to the myocardium (oxygen supply) is determined by two factors: coronary blood flow (CBF) and the oxygen content (concentration) of the arterial blood (CaO_2) *(Zong et al., 2005)*.

$$O_2 \text{ Delivery} = CBF \times CaO_2$$

where CBF = ml/min and CaO_2= ml O_2/ml blood

Therefore, the units for O_2 delivery are ml O_2/min. The normal oxygen concentration in arterial blood is about 20ml O_2/100 ml blood (0.2ml O_2/ml

blood), or 20 vol %. CBF, expressed per 100g of tissue weight is about 80 ml/min per 100g at resting heart rates. Therefore, the oxygen delivery to the heart under resting conditions is about 16ml O_2/min per 100g *(Duncker and Merkus, 2007)*.

Coronary blood flow is determined by hemodynamic factors such as perfusion pressure and vascular resistance. The latter is determined by vascular anatomy and structure, as well as by changes in diameter of the vascular lumen resulting from contraction and relaxation of vascular smooth muscle *(Lavallee and Thorin, 2003)*.

B. Oxygen Demand:

Oxygen demand is a concept that is closely related to the oxygen consumption of an organ. The two terms are often used interchangeably although they are not equivalent. Demand is related to need, whereas consumption is the actual amount of oxygen consumed per minute. Under some conditions, demand may exceed consumption because the latter may be limited by the delivery of oxygen to the myocardium *(Priebe and Skarvans, 2000)*.

C. Myocardial oxygen consumption and its major determinates

Myocardial oxygen consumption (MVO2) is required to regenerate ATP that is utilized by membrane transport mechanisms (e.g., Na^+/K^+-ATPase pump) and by myocyte contraction and relaxation (e.g., myosin ATPase). The following table (1) gives MVO2 values in different cardiac states (*Westerhof et al., 2006)*.

Table (1): Myocardial oxygen consumption value (*Westerhof et al., 2006)*

Cardiac State	MVO_2 (ml O_2/min/100g)
Arrested heart	2
Resting heart rate	8
Heavy exercise	70

By comparison, the oxygen consumption (ml O2/min/100g) for other organs is shown in (Table 2) (*Westerhof et al., 2006)*.