A Comparative Study between Custodiol and Warm Blood Cardioplegia in Coronary Artery Bypass Graft Operation with Poor Left Ventricular Function

Thesis

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List of Abbreviations

A	: Indicates appropriate
AA	: Antianginal
ACPE	: Adverse cardiopulmonary events
ARTS II	: The Arterial Revascularization Therapies Study II
BB	: beta blockers
BMI	: Body mass index
CABG	: Coronary artery bypass grafting
CAD	: Coronary heart disease
CKMB	: Creatine kinase-MB
COPD	: Chronic obstructive pulmonary disease
COPD	: Chronic obstructive pulmonary disease;
COR	: Class of recommendation;
CPB	: Cardiopulmonary bypass
D	: Diagonal artery
DM	: Diabetes mellitus
EF	: Ejection fraction;
ERK	: Extracellular-regulated kinase
FFR	: Fractional flow reserve;
GSK-3	: Glycogen synthase kinase-3
HFrEF	: Reduced left ventricular ejection fraction
HTK	: Histidine- tryptophan- ketoglutarate
ICU	: Intensive care unit
LAD	: Left anterior descending
LCX	: Left Circumflex
LIMA	: Left internal mammary artery;
LIMA	: Left Internal Mammary Artery
LM	: Left main
LOE	: Level of evidence;
LV	: Left ventricular;
LVEDD	: Left ventricular end diastolic volume
LVESD	: Left ventricular end systolic volume
M	: May be appropriate;

MACCE	: Major adverse cardiac and cerebrovascular events
MI	: Myocardial infarction
MPTP	: The mitochondrial permeability transition pore
MvO2	: Minimizing myocardial oxygen requirement
N/A	: Not available;
NS	: Non-significant
OM	: Obtuse marginal
PCI	: Percutaneous coronary intervention
PDA	: Posterior descending artery
PI3K	: Phosphatidylinositol 3 kinase
R	: Rarely appropriate.
RCA	: Right coronary artery
RISK	: The reperfusion injury salvage kinases
ROS	: Reactive oxygen species
S	: Significant
SAFE	: Survivor activating factor enhancement
SIHD	: Stable ischemic heart disease;
STEMI	: ST-elevation myocardial infarction;
STS	: Society of Thoracic Surgeons;
SVG	: Saphenous vein graft
SYNTAX	: Synergy between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery;
TAVR	: Transcatheter aortic valve replacement.
TIMI	: Thrombolysis In Myocardial Infarction;
TNFa	: Tumor necrosis factor alpha
TVS	: (replacement or repair of aortic, mitral and tricuspid valve)
UA/NSTEMI	:unstable angina/non–ST-elevation myocardial infarction;
UPLM	: Unprotected left main disease; and
VT	: Ventricular tachycardia.

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ABSTRACT

Introduction:

Cardioplagia, a solution used to achieve diastolic arrest of the heart, is an essential tool for open cardiac surgery. The ideal cardioplagia solution should provide excellent myocardial protection especially in patient with poor left ventricular function. Various solutions have been prepared to achieve this among which warm blood cardioplagia and Bretschneider solution .

Methods:

This comparative prospective, unicenter study (National Heart Institute) in the period From Jan 2018 to jan2019 included 53 patients who had IHD were scheduled for CABG using on pump method. They were divided into 2 groups A (27 patients) for CABG operation with Bretschneider solution "Custodiol", and group B (26 patients) for CABG operation with warm blood cardioplagia.

Results:

Mortality was 1 (3.7%) for *group A* and was 2 (7.69%)for *group B* P-value 0.53 (NS) , adverse cardiopulmonary events 15 (55.55%)for *group A* and 6 (23.08%)for *group* B P-value 0.016 (S) , **post operation % Ejection fraction** for *group A* 46.43± 15.64and *group B* were 41.06± 17.17 P-value 0.26 (NS).

Patient receiving inotropic support in first 48 hours were 18 (66.7%) in *group A* while 21 (80.77%) for *group B* P-value 0.24 (NS) , **Mean number of grafts** *group A* 2.96±1.091and *group B* 2.65±0.937 P-value 0.27(NS) **IABP support** *group A* was 4 (14.81%)while *group B* were 3 (11.54%) P-value 1.00 (NS) , **Weaning from ventilator** *group A* were 17± 23.39 hours and *group B* were 20.9± 30.7hours P-value 0.62 (NS) , **ICU stay** for *group A* were 75.2 hours and 92.88 hours for *group B* P-value 0.22 (NS).

Conclusion:

Overall rates of mortality showed a statistically non-significant difference between the two groups, while overall rates of adverse cardiopulmonary events (ACPE) were significantly higher in group A .

The only superiority of custodiol was found to be single dose administration

Aim of the work

Study Objectives/Specific Aims

Overall Goal:

To compare the outcome of using HTK "custodial" versus warm blood cardioplegia during coronary artery bypass grafting in patients with poor left ventricular function.

Coronary Artery Bypass Grafts Surgery

Introduction

Coronary artery disease represents the most common cause of insufficient oxygen delivery to the myocardium, referred to as myocardial ischemia. Understanding the pathophysiology of arterial disease with sub intimal atheroma and plaque Formation has been a breakthrough of modern medicine. Even with our advanced understanding of heart disease, it remains the most common cause of death. Cardiovascular disease claims more lives (men and women) than cancer, trauma, and pulmonary disease combined[(1)].

Historical review Coronary artery bypass graft surgery, In 1958 Manson Sones et al at The Cleveland Clinic performed the first selective coronary angiography, which led to the application of direct myocardial revascularization[(2)].

In 1962[(3)], by Senning[(4)]was able to repair a tight narrowing of the left main trunk of the coronary artery by using the patch graft technique developed. However, the mortality when applying this technique was extremely high. In 1963 Sabiston performed a coronary bypass from the aorta to the right coronary artery using an autologous saphenous vein[(5)].

In 1965 Kolessov in Russia performed the first anastomosis between LIMA and LAD[6]. In 1967 Favaloro successfully reconstructed the right coronary artery by interposing a segment of SV and later on he started using SV graft direct from the aorta to the coronary arteries. Afterwards, significant progress occurred when Favaloro and his group were able to perform double bypass, emergency revascularization and even combined operation[7] until 1970 they had performed 1086 CABG in 951 patients with an overall mortality of 4.2%. The first coronary bypass operation in Sweden was performed in June 1970 at the Karolinska Hospital, Stockholm[8].

In the 1980 several studies published by Campeau[9], Bourassa[10] and Grondin[11] demonstrated that severe atherosclerotic deterioration of SV graft occurs between 6 and 11 years. They proposed that aortocoronary surgery, with the use of saphenous vein grafts, should eventually be reconsidered and suggested that modifications of harvesting techniques and pharmacological intervention might improve the durability of aortocoronary vein grafts.

At the same time Loop[12] in a great number of patients, showed a clear advantage of using IMA over the SV. A few years later they suggested[13] the benefit from expanded internal thoracic artery grafting techniques by using bilateral, free and sequential[14] anastomoses. Until 1980, only 13% of the surgeons were using mammary grafts (Since the mid-80s the number of users has increased steadily and today most surgeons employ them. Due to the

excellent results of the internal mammary artery grafts, surgeons looked for other sources of arterial conduits. In 1987,[15,16] and (Attum, 1987) reported the first studies on the use of the gastroepiploic artery for direct myocardial revascularization. In 1990,[17] introduced the use of inferior epigastria artery. In 1971, Carpentier introduced the radial artery as an alternative conduit for CABG, however, the initial results were disappointing[18] After the modification of the harvesting technique and with the use of preoperative calcium channel blockers, the results were significantly improved[19] .

Indications for Coronary Artery Bypass Grafting[20]:

2017 Appropriate Use Criteria for Coronary Revascularization in Patients With Stable Ischemic Heart Disease.

A Report of the American College of Cardiology Appropriate Use Criteria Task Force, American Association for Thoracic Surgery, American Heart Association, American Society of Echocardiography, American Society of Nuclear Cardiology, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, and Society of Thoracic Surgeons

Table 1 A [20]: Revascularization to improve survival compared with medical therapy therapies to improve survival in patients with SIHD are outlined in detail in the 2012 SIHD guideline.

Anatomic sitting	COR	LOE
UPLM or complex CAD		
CABG and PCI	I—Heart Team approach recommended	C
CABG and PCI	IIa—Calculation of STS and SYNTAX scores	B
UPLM*		
CABG	I	B
PCI	IIa—For SIHD when *both* of the following are present: n Anatomic conditions associated with a low risk of PCI procedural complications and a high likelihood of good long-term outcome (e.g., a low SYNTAX score of #22, ostial or trunk left main CAD) n Clinical characteristics that predict a signi*fi*cantly increased risk of adverse surgical outcomes (e.g., STS-predicted risk of operative mortality $5%)	B
	IIa—For UA/NSTEMI if not a CABG candidate	B

	IIa—For STEMI when distal coronary *flow* is TIMI *flow* grade <3 and PCI can be performed more rapidly and safely than CABG	C
	IIb—For SIHD when *both* of the following are present: n Anatomic conditions associated with a low to intermediate risk of PCI procedural complications and an intermediate to high likelihood of good long-term outcome (e.g., low-intermediate SYNTAX score of <33, bifurcation left main CAD) n Clinical characteristics that predict an increased risk of adverse surgical outcomes (e.g., moderate—severe COPD, disability from prior stroke, or prior cardiac surgery; STS-predicted operative mortality >2%)	B
	III: Harm—For SIHD in patients (versus performing CABG) with unfavorable anatomy for PCI and who are good candidates for CABG	B
3-vessel disease with or without proximal LAD artery disease*		
CABG	I	B
	IIa—It is reasonable to choose CABG over PCI in patients with complex 3-vessel CAD (e.g., SYNTAX score >22) who are good candidates for CABG.	B
PCI	IIb—Of uncertain bene*fit*	B
2-vessel disease with proximal LAD artery disease*		
CABG	I	B
PCI	IIb—Of uncertain bene*fit*	B
2-vessel disease without proximal LAD artery disease*		
CABG	IIa—With extensive ischemia	B
	IIb—Of uncertain bene*fit* without extensive ischemia	C
PCI	IIb—Of uncertain bene*fit*	B
1-vessel proximal LAD artery disease		
CABG	IIa—With LIMA for long-term bene*fit*	B
PCI	IIb—Of uncertain bene*fit*	B
vessel disease without proximal LAD artery involvement		
CABG	III: Harm	B