Myocardial perfusion in patients with total occlusion of a single coronary artery with and without collateral circulation

Thesis
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Presented by
Maged Saad Mohamed El-Gantiry
M.B., B.C.H.

Under the supervision of
Professor Doctor Salah El-Din Hamdy Demerdash
Professor of Cardiology
Ain Shams University

Doctor Mona Rayyan
Assistant Professor of Cardiology
Ain Shams University

Doctor Ramy Raymond
Lecturer of Cardiology
Ain Shams University

Faculty of Medicine
Ain Shams University
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Protocol

Introduction

Anastomotic channels, known as collateral vessels, can develop in the heart as an adaptation to ischemia *(Fujita et al., 1999 and Tayebjee et al., 2004)*. They serve as conduits which bridge severe stenoses or connect a territory supplied by one epicardial coronary artery with that of another *(Levin et al., 1974)*. Collaterals therefore provide an alternative source of blood supply to myocardium jeopardized by occlusive coronary artery disease and they can help to preserve myocardial function in the setting of a chronic total coronary occlusion *(Werner et al., 2001)*.

The clinical and pathophysiologic determinants of collateral recruitment are poorly understood. Although primarily thought to be initiated by ischemia, appreciable collateral perfusion is present in some patients who do not have coronary disease *(Wustmann et al., 2003)*.

Studies of transient coronary occlusion during balloon angioplasty have found that the following independent clinical and angiographic variables are correlated with increases in collateral flow *(Werner et al., 2001and Pohl et al., 2001)*.

- Longer duration of angina.
- Greater level of long-term physical activity during leisure time.
- Greater lesion severity.
- Proximal lesion location.
- Greater duration of lesion occlusion.

(*Piek et al., 1997 and Senti et al., 1998)*

In patients with a chronically occluded artery, collateral flow to the territory of a CTO artery is influenced by the extent and the anatomical distribution of the donor artery, microvascular function, the duration of vessel occlusion and left ventricular function *(Gatzov et al., 2003 and Werner et al., 2003).*

Collateral recruitment may be diminished in the elderly. In a study of over 1900 patients undergoing angiography within 72 hours after an acute myocardial infarction, the prevalence of collaterals decreased from 48 percent in patients <50 years of age to 34 percent in patients ≥70 years of age *(Kurotobi et al., 2004)* .

Evaluation of coronary collateral arteries can be performed by different non-invasive testing including myocardial contrast echocardiography (MCE), magnetic resonance imaging (MRI), Multi-slice computed tomography (CT), Positron emission tomography (PET) and myocardial perfusion imaging after radionuclide injection. Exercise myocardial perfusion imaging can be used to demonstrate coronary insufficiency, via the presence and extent of perfusion defects *(Colin et al., 2007)*. Myocardial perfusion imaging after 99mTc-Sestamibi radionuclide injection during PCI has also been used to quantify collateral supply by evaluation of the extent of ischaemia *(Colin et al., 2007).*

Despite decades of study, the functional role of the coronary collateral circulation remains controversial *(Helfant et al., 1971)*. Although myocardium supplied by well-developed collaterals may maintain normal resting perfusion, patients may still have myocardial ischemia, as manifested by anginal symptoms, ischemic electrocardiographic (ECG) changes, or abnormal myocardial perfusion studies *(He et al., 2001)*.

Discordance in the results of prior studies is partly due to inclusion of a non-uniform patient population, often with multivessel coronary artery disease, prior myocardial infarction (MI), various degrees of incomplete coronary occlusion, or a combination of these factors. Because blood flow distal to a chronic total occlusion (CTO) would be entirely collateral dependent, Gregg and Patterson suggested that patients with single-vessel CTO in the absence of MI would be the optimal subset in which to study human coronary collaterals during stress *(Gregg et al., 1980)*.

Aim of the work

In this study we will investigate the relationship between angiographic collateral circulation and myocardial perfusion in patients with total occlusion of a single coronary artery, in the absence of myocardial infarction or significant stenosis in the other coronary arteries supplying the same myocardial territory.

Patients and Methods

Patients: Forty patients with chronic total occlusion (CTO) of a single coronary artery as diagnosed by coronary angiography will be included. The patients will be divided into 2 groups according to the presence (Group A) or absence (Group B) of collateral circulation.

Exclusion Criteria: Include a prior myocardial infarction (MI) by history or ECG, previous bypass surgery or significant stenosis in other coronary arteries supplying the same myocardial territory.

Methods: The patients will undergo the following:

History: All patients will be subjected to detailed full history with special emphasis on:

- Age and gender.
- Risk factors including diabetes mellitus, dyslipidemias, hypertension, Smoking and family history of premature coronary artery.
- Type of presentation.
- History of previous MI or
- History of previous revascularization (PCI & CABG).

Examination: All patients will be subjected to detailed general and cardiac examination with special emphasis on:

- Pulmonary venous congestion e.g. basal pulmonary rales
- Systemic venous congestion e.g. congested neck veins
- Extra heart sounds e.g. S3 gallop.
- Additional murmurs e.g. mitral regurgitation murmur.

Electrocardiogram (ECG): All patients will undergo ECG recording with detailed analysis with special emphasis on:

- QRS morphology and duration (Q waves and Bundle branch block).
- Presence of ST segment deviation (Amplitude & leads affected).
- T-wave changes.
- Dysrhythmias.

Echocardiography: All patients will undergo echocardiographic examination with special emphasis on:

- Assessment of systolic and diastolic function.
- Assessment of left ventricular dimensions.
- Presence of regional wall motion abnormality (RWMA)
- Presence of concomitant valvular heart disease.

Stress myocardial perfusion imaging by SPECT: All patients will undergo stress myocardial imaging, using technetium 99-m scan.

- The Patient will exercise on a motor-driven treadmill using standard Bruce protocol. Chest pain and ECG changes will be carefully monitored during exercise.

- Radiotracer will be injected at peak exercise. Distribution of sestamibi myocardial uptake will be imaged with a gamma camera. Rest images will be obtained first 60 minutes after injection. Stress images will be obtained 30 minutes post-stress.

- Tomographic images will be performed over 180 degrees. Images will be analyzed in the short axis, vertical long axis and horizontal long axis.

Left sided catheterization with coronary angiography: All patients will have detailed analysis with special emphasis on:

- Location of the chronic total occlusion in the vessel (Proximal, mid or distal).
- Collateral fillings (if present) will be graded from 1 to 3: 1 = filling of side branches only; 2 = partial filling of the epicardial segment; 3 = complete filling of epicardial segment *(Rentrop et al., 1985).*
- Presence of myocardial blush flow.

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%	Percentage
ACEI	Angiotensin converting enzyme inhibitor
AM	Acute marginal
ASA	Acetyl salicylic acid
ASTAMI	The Autologous Stem Cell Transplantation in Acute Myocardial Infarction
AV	Atrioventricular
BMC	Bone marrow cells
CABG	Coronary artery bypass grafting
CAD	Coronary artery disease
CFI	Collateral flow index
CT	Computed Tomography
CTO	Chronic total occlusion
ECG	Electrocardiogram
EF	Ejection fraction
FFRcoll	Collateral fractional flow reserve
FH	Family history
GCSF	Granulocyte colony-stimulating factor
LAD	Left anterior descending
LAO	Left anterior oblique
LBBB	Left bundle branch block
LCx	Left circumflex
LM	Left main
LV	Left ventricle
LVEF	Left ventricular EF
MCE	Myocardial contrast echocardiography

mCi	Millicurie
METs	Metabolic equivalents
MI	Myocardial infarction
MPI	Myocardial perfusion imaging
MRI	Magnetic resonance imaging
OM	Obtuse Marginal
PCI	Percutaneous coronary intervention
PDA	Posterior descending artery
PET	Positron emission tomography
PLV	Posterior left ventricular
PTCA	Percutaneous transluminal coronary angioplasty
RAO	Right anterior oblique
RCA	Right coronary artery
RColl	Collateral resistance
REPAIR-AMI	Reinfusion of Enriched Progenitor Cells & Infarct Remodeling in Acute Myocardial Infarction
RV	Right ventricular
S3	Third heart sound
SA	Sinoatrial
SD	Standard deviation
SPECT	Single photon emission computed tomography
SSS	Summed stress score
STEMI	ST elevation myocardial infarction
Tc	Technetium
TIMI	Thrombolysis in myocardial infarction
Tl	Thallium
(X)	Mean

Introduction

Introduction

Cardiovascular diseases, in particular coronary artery disease (CAD), are the leading cause of death in industrialized countries. Established options for revascularization include angioplasty and surgical bypass, both of which are not suitable in 20–30% of patients in whom the extent of coronary atherosclerosis is especially severe. An alternative treatment strategy for revascularization is therefore warranted both to control symptoms as well as to alter the course of advanced CAD *(Seiler et al., 2003)*.

An ideal candidate to fill in this gap is therapeutic promotion of coronary collateral growth—that is, the induction of natural bypasses. In order to reach this goal, a comprehensive understanding of the human coronary collateral circulation with regard to its relevance, accurate assessment, the pathogenetic and pathophysiological aspects, and the different therapeutic options is mandatory *(Seiler et al., 2003)*.

Coronary collaterals are anastomotic channels, known as collateral vessels, can develop in the heart as an adaptation to ischemia *(Tayebjee et al., 2004)*. They serve as conduits which bridge severe stenoses or connect a territory supplied by one epicardial coronary artery with that of another *(Levin et al., 1974)*. Collaterals therefore provide an alternative source of blood supply to myocardium jeopardized by occlusive coronary artery disease and they can help to preserve myocardial function in the setting of a chronic total coronary occlusion *(Werner et al., 2001)*.

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