MAJOR CLINICAL AND ANGIOGRAPHIC OUT-COME OF DRUG ELUTING STENTS IN OSTIAL CORONARY ARTERY DISEASE

A Thesis

Submitted For Partial Fulfillment Of
MD
In

Cardiology
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2008

Abstract

Since the first application of percutaneous transluminal coronary angioplasty (PTCA) in humans in 1977, catheter-based revascularization has exhibited tremendous growth. The indications have been expanded; innovative technologies emerged; knowledge about the pathophysiology of tissue reactions increased; and new frontiers in pharmaceutical and molecular biology research chartered.

The rapid evolution of stent design, deployment approaches, and adjunctive therapy have led to changes in clinical practice patterns and has broadened the scope of patients that can be approached by PCI beyond those that could be safely treated by PTCA alone.

Key Words :

Posterior Descending Artery - saphenous Vein Graft - Aorto-Ostial .

ACKNOWLEGMENT

To my family, for giving me the power and patience to complete my work.

I would like to express my deepest gratitude and sincere appreciation to ***Prof. Dr. Khaled Sorour,*** Professor of Cardiology, Faculty of Medicine, Cairo University, for his patience, guidance and encouragement throughout this study.

I would like also to express my greatest gratitude and sincere appreciation to ***Prof. Dr.Hisham Boushra Mahmoud,*** Assistant Professor of Cardiology, Faculty of Medicine, Beni Suief University, for his support, supervision and motivation throughout my work. It is also important to mention that he helped me getting the fellowship position.

Finally yet importantly, I would like to express my gratitude, my sincere appreciation and respect to ***Prof.Dr.Jonathan Clague***, Professor of Cardiology, Royal Brompton Hospital, Imperial College, London, for his support and encouragement during my entire work.

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List of Abbreviations

*A-O (Aorto-Ostial)
*LMCA (Left Main Coronary Artery)
*LAD (Left Anterior Descending)
*OM (Obtuse Marginal)
*D (Diagonal Branch)
*PDA (Posterior Descending Artery)
*SVG (saphenous Vein Graft)
*TLR (total Lesion revascularisation)
*DES (Drug Eluting Stent)
*BMS (Bare Metal stent)
*MIHC (Major in Hospital Complications)
*PCI (Percutaneous Coronary Intervention)
*QCA (Quantitative Coronary Angiography)
*GP (Glycoprotein)
*RCA (right Coronary Artery)
*LCX (left Circumflex Coronary artery)
*MACE (Major Adverse Cardiac Events)
*MI (Myocardial Infarction)
*CK (Creatine Kinase)
*DCA (Directional coronary Atherectomy)
*PTCA (Percutaneous Coronary Angioplasty)
*IVUS (Intra Vascular Ultra Sound)
*CABG (Coronary Artery By-pass Graft)
*VLDL (Very Low Density Lipoproteins)
*LDL (Low Density Lipoproteins)
*HDL (High density Lipoproteins)
*CASS (coronary artery Surgery Study)
*NIH (Neointemal Hyperplasia)
*ISR (In-Stent Resteosis)
*mTOR (mammalian Target of Rapamycin)
*SMCs (Smooth Muscle Cells)
* PEVA (Polyethylenevinylacetate)
* PBMA (Polybutylmethacrylate)
*SES (Sirolimus Eluting stents)
*PES (Paclitaxel Eluting Stents)
*ACS (Acute Coronary Syndrome)
* MACCE (Major Adverse Cardiac and Cerebrovascular Events)
* MPA (Mycophenolic Acid)
*ADP (Adenosine Di Phosphate)
*MLD (Minimal Lumen Diameter)
* EEM CSA (External Elastic Membrane Cross Section Area)
* PDGF (platelet-derived growth factor)
* FGF (Fibroblast Growth Factor)
* PMN (Polymorphonuclear Leukocytes)
*RVD (Reference Vessel Diameter)
*CMV (Cytomegalo Virus)
*LST (Late in-Stent Restenosis)

*ECs (Endothelial Cells)
*NO (Nitric Oxide)
*VBT (Vascular Brachytherapy)
*eNOS (endothelial Nitric Oxide Synthase)
*VEGF (Vascular Endothelial Growth Factor)
*IRT (Intracoronary Radiation Therapy)
*TIMI (Thrombolysis In Myocardial Infarction)

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Introduction

Ostial coronary artery lesions constitute a distinct substrate for percutaneous intervention, as they differ from other lesion sites in management strategies and in clinical out-come. The high concentration of elastic muscle fibers around the ostium, and the presence of atherosclerosis and fibrosis of the aortic wall in case of aorto-ostial (A-O) and proximal left main coronary artery (LMCA), has been proposed as a possible mechanisms of elastic recoil and high restenosis rate in these sites (1,2). In addition, the presence of ostial calcification contributes to further lesions rigidity (3). Hence these lesions appear to be both rigid and elastic at the same time (4).

Aorto-ostial lesions were found to be 3%-5% of all patients undergoing cardiac catheterization for ischemic chest pain, congestive heart failure or cardiogenic shock (5).

Ostial stenosis of the left anterior descending coronary artery (LAD) remains the only discrete coronary stenosis often referred to cardiac surgery, even in patients with single vessel disease (6).

Percutaneous intervention of both native and saphenous venous graft (SVG) aorto-ostial (A-O) lesions have been associated with lower procedural success rates of 70%-97%, more frequent in-hospital complications of 5%-12%, and greater likelihood of late restenosis of

28%-52% when compared with treatment of non aorta-ostial lesions (7,8).

Various strategies including high-pressure dilatation, cutting balloon angioplasty and debulking techniques have been used in an attempt to over come ostial coronary artery lesions. Excimer laser coronary angioplasty had a high initial angiographic and clinical success rates but restenosis was a limitation (7). Similarly, although, rotational or transluminal extraction atherectomy were associated with high procedural success rates and low incidence of complications, but the restenosis rates remained high (9).

The beneficial action of stents has been attributed to maximizing the initial luminal gain and overcoming the aorto-ostial elastic recoil (10, 11).

Silvestri et al., on 2000 (12) confirmed the feasibility and safety of stent-supported angioplasty of the left main coronary artery leading to acceptable morbidity, with a 6 month target lesion revascularization (TLR) rate of 17%.

Stenting of ostial left anterior descending artery lesions were associated with better event-free survival, and less target lesion revascularization of 10.5% compared to directional atherectomy alone 50% (13).

Stenting of saphenous venous graft aorto-ostial lesions were associated with a high procedural success rates, and long term follow-up as compared to stents inserted into the body of the vein graft.

Two recent studies by Lakovou et al., on 2004 (14) and Maniyal et at., on 2005 (15), concluded that implantation of drug eluting stents (DES) in aorto-ostial coronary lesions compared to bare metal stents (BMS), appeared safe and effective in all clinical situations, with no increase in major in-hospital complications (MIHC), with significant improvement in restenosis rate and late target lesions revascularization (TLR) at 10 month follow-up.

Drug eluting stents have a potent anti-inflammatory, immunosuppressive, and anti-prolefrative effect (16, 17). A study done on 2003 by Muzaffer et al. (18), concluded that, implantation of DES does not induce a significant vessel response at the edge of the segment, and the vessel lumen, plaque and vessel volume remained stable over 6 month follow-up.

A number of large randomized studies have demonstrated that both Rapamycin and Paclitaxel eluting stents significantly decrease restenosis rates, in a variety of coronary lesions. A study done by Luis et al., on 2004 (19), he concluded that both stents demonstrated similar safety profiles for complex lesions, no significant difference in restenosis rate over long-time follow-up period, and that neointimal

proliferation was the only mechanism of restenosis in patients treated by drug eluting stents (20).

Hypothesis:

- There are a limited number of studies and of short duration follow-up based on evaluating the efficacy of implantation of drug eluting stents (Sirolimus or Paclitaxel) in aorto-ostial coronary artery lesions, in terms of clinical, non-invasive testing and angiographic follow-up.
- Drug eluting stents have been shown to reduce the incidence of restenosis even in very complex lesions (21, 22) but critical aorto-ostial lesions were not included in many trails (23-25).
- We hypothesize that insertion of drug eluting stents in the known highly elastic and rigid aorto-ostial lesions will be safe, with better clinical and angiographic out-come in both early and late follow-up as compared to data obtained from previous studies of bare metal stents in the same critical lesions, where they appeared to be of higher restenosis rate in ostial lesions as compared to other sites (21).

Aim of the Study:

- To evaluate the efficacy of drug eluting stents in aorto-ostial (A-O) coronary artery lesions, in terms of early and late restenosis rate, clinical assessment, non-invasive stress testing and angiographic follow-up.
- To compare the results of implantation of drug eluting stents to that of bare metal stents in aorto-ostial lesions done over the last 5 years in Royal Brompton Hospital

Chapter One

Coronary Ostial Lesions

I-Aorto-Ostial Lesions:

Ostial atherosclerotic lesions, either in native vessels or grafts constitute a distinct substrate for percutaneous interventions, as they differ from the other lesion sites in management strategies and in clinical outcomes. High-pressure dilatation and debulking techniques such as atherectomy, rotablation and cutting balloon angioplasty (28) are sometimes used to modify the lesion morphology.

Histological data from pathologic series (29) and atherectomy specimens (30) showed that ostial lesions are frequently heavily calcified, fibrotic, and sclerotic. It has also been suggested that there may be more elastic recoil even after stent implantation at ostial sites because of the highly elastic tissue in the adjacent aortic wall (31). In fact, many previous investigators noted that aorto-ostial lesions are essentially aortic wall lesions that have encroached on the ostium of the coronary arteries (32). The fundamentally elastic behavior of the thick aortic wall may account for the increased tendency for elastic recoil, which may be the primary mechanism contributing to the increased residual stenosis. These mechanisms may also explain the poorer results reported by other investigators in the dilatation of aorta ostial lesions (33) when compared to non-aorta ostial lesions (34).

A study done by Mun et al in 1995 (35) on why do aorto-ostial lesions behave differently than non-aorto-ostial lesions, they compared directional coronary atherectomy (DCA) samples from patients with aorto-ostial lesions to randomly selected samples of non-aorto-ostial lesions. The study concluded that:

1- The aorto-ostial lesions seems to experience greater spontaneous trauma and stimulus for proliferation, as evidenced by the more abundant reactive cellular component, and this may explain the increased restenosis rate observed in this lesions.

2- The aorto-ostial lesions are more unstable, with a trend for more thrombotic component, and this may explain the high procedural complications during angioplasty of aorto-ostial lesions.

3- DCA specimens from the aorto-ostial lesions tended to have greater amount of adventitia, another potential source for procedural complications and increased restenosis.

A. Ostial Left Main Coronary artery:

The anatomic and physiologic uniqueness of left main coronary artery was studied in a postmortem analysis in 1965 by Broucek et al (36). The study showed that the aortic elastic-muscle fibers were continuous with the left main artery, and sometimes even extended into the proximal left anterior descending artery. The frequency with which these fibers reach the left main bifurcation may depend on left main length and thus impact on stenosis development.