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Original Research Article

Effect of Kidney Dysfunction on Results of Revascularization of Multivessel Coronary Disease

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Abstract

Kidney dysfunction is a risk factor for interventional procedures in coronary artery disease. We analyzed this point. We studied 120 patients who had objective and angiographic evidence of myocardial ischemia and significant coronary artery disease (lesion > 70%) in two or more vessels. Forty patients underwent Percutaneous Coronary Intervention (PCI) of the significant lesions beside optimal medical therapy (PCI group II), 40 received optimal medical therapy alone (medical-therapy group III) and 40 were subjected to CABG (Group I). The choice between PCI and CABG was based on the Syntax score. The 40 pts on medical therapy alone either refused surgery (18), or were not suitable for surgery (12) or the lesions were not severe as assessed by FFR (7) or failed stenting (3). The primary outcome was death from any cause and nonfatal myocardial infarction during a follow-up period of 1 year. There was no significant difference between the three groups as regards incidence of diabetes, hypertension, dyslipidemia or age. Renal dysfunction (creatinine >2) was present in 18 pts (10+4+4). The highest was 2.28 mg/dl. Results comparing pts with creatinine >2 (18 pts) with those with creatinine < 2 (102 pts): Death 0 vs 4 (NS), non fatal MI 3 vs 8 (NS), heart failure 0 vs 10 (NS), recurrence of chest pain 3 vs 7 (NS). Conclusion: In 120 patients with multivessel disease treated by CABG or PCI or medical therapy, the presence of creatinine >2 and < 2.3 did not affect the results or prognosis or incidence of complications.

Key words: Multivessel coronary disease, PCI, optimum medical therapy, renal dysfunction

INTRODUCTION

Approximately 60% of patients with CAD have symptomatic multivessel disease that could be treated by either percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG) surgery or Medical therapy (MT) (Bucher et al., 2000; Emond et al., 2004; King et al., 2000; Henderson et al., 2003; Bucher et al., 2000; Emond et al., 2004; King et al., 2000; Sianos et al., 2005; Lloyd, 2006; Serruys et al., 2001).

Revascularization strategies of multivessel coronary artery disease: Among patients with coronary artery disease (CAD), multivessel stenoses are a more frequent occurrence than single-vessel disease. Coronary artery bypass surgery (CABG) and percutaneous coronary intervention (PCI) are both established treatment modalities of revascularization in patients with multivessel CAD. Medical therapy for patients with multivessel CAD has changed considerably in recent years. Current therapeutic strategies, including aggressive modification of risk factors and intermittent use of nitrates, beta-blockers, calcium channel blockers, Angiotensin-converting enzyme inhibitors, and 3-hydroxy-3-methylglutarylcoenzyme A reductase inhibitors (Statins), have improved the outcomes of patients with CAD.

CABG was first performed in 1962 and has been used in multivessel and left main stem disease for almost 40years. In contrast, PCI has been around for almost

three decades (first used in 1977) and has been used in multivessel and left main disease for about 10 years. Both PCI and CABG have benefited from improved medical therapy, including aspirin, statins, and Angiotensin-converting enzyme inhibitors, and both have witnessed technologic advances such as arterial grafts and off-pump surgery for CABG and drug-eluting stents for PCI (Percutaneous coronary intervention versus bypass surgery in patients with diabetes and multivessel coronary disease, 2014; Revascularization strategies for patients with stable coronary artery disease, 2014; Verma et al., 2013; Sako et al., 2014; Hannan et al., 2014).

The role of kidney dysfunction on prognosis of patients subjected to CABG or PCI or medical therapy was studied by some authors (16-21). We opted to analyze data as regards mild renal impairment.

AIM OF THE WORK

In the present work we aim to investigate the outcome of patients with multivessel coronary heart disease treated with coronary artery bypass grafting (CABG) to those treated with aggressive medical therapy or PCI to the culprit lesion followed for one year minimally. Kidney dysfunction is a risk factor for interventional procedures in coronary artery disease. We analyzed this point.

PATIENTS AND METHODS

The present study included 120 patients with angiographically documented multivessel coronary artery disease; in the form of presence of two major vessels with narrowing more than 60%, or three or more vessels with more than 50% narrowing by visual assessment and documented ischemia; by either stress testing or presence of typical ischemic signs and symptoms, all were candidates for CABG. Patients were enrolled and randomized after agreement between surgeon and interventionist that revascularization could be attained through either strategies.

- Patients were collected from the Main University Hospital of Texas Health Science Center at San Antonio, United States of America from 2008 to 2010.
- The University of Texas Institutional Review Board and The University Health System Clinical Research Department approved the study.
- Patients gave written, informed consent to be a part of a research study. Selection of the therapy to each patient; whether surgery or PCI or medical therapy was done after explaining the different modes of therapy and clarifying its benefits & hazards.
- Patients were divided into:-
- Group I: included 40 patients who were treated by coronary artery bypass grafting (CABG). (Those who accepted surgery)
- Group II: included 40 patients who accepted to undergo PCI to the culprit lesion.

Group III: included 40 patients who were treated by medical therapy. The choice between PCI and CABG was based on the Syntax score (8). The 40 pts on medical therapy alone either refused surgery (18), or were not suitable for surgery (12) or the lesions were not severe as assessed by FFR (7) or failed stenting (3). (Those who refused any intervention, or were not suitable for surgery or their lesions were not severe as assessed by FFR or those with failed stenting).

- Inclusion criteria: Presence of two major vessels with coronary narrowing more than 60% or three or more vessels with > 50% lesion.

Exclusion criteria: Primary myocardial disease, Valvular heart, disease. Patients who had undergone percutaneous coronary intervention

All subjects were subjected to the following: Thorough clinical examination and history taking, Routine laboratory investigations, Basic resting electrocardiogram. Resting transthoracic echocardiographic study: for assessment of LV function, wall motion abnormalities and for estimating ejection fraction (EF) by planimetry (area length method).

Diagnostic coronary angiogram: To estimate the condition of coronary arteries, the severity of the lesion and number of vessels stenosed. Exercise stress, electrocardiographic study: Exercise stress electrocardiographic study was done after therapy for follow up of the cases.

Dobutamine stress echocardiography: Selected patients were subjected to dobutamine echocardiographic study before revascularization or medical therapy to assess myocardial viability

Medical Therapy: All patients received: Antiplatelet therapy with Aspirin at a dose of 81 to 325 mg per day or 75 mg of Clopidogrel per day, if aspirin intolerance was present. Patients undergoing PCI or CABG received aspirin and clopidogrel, in accordance with accepted treatment guidelines and established practice standards. Medical anti-ischemic therapy included long-acting Beta Blockers, Calcium channel blockers, and Nitrates, alone or in combination, along with either Angiotensin converting enzyme inhibitor or Angiotensin receptor blocker as standard secondary prevention. Aggressive therapy to lower low-density lipoprotein (LDL) cholesterol levels (statin alone or in combination with Ezetimibe) with a target level of 60 to 85 mg per deciliter.

- An attempt was made to raise the level of high-density lipoprotein (HDL) cholesterol to a level above 40 mg per deciliter and lower triglyceride to a level below 150 mg per deciliter with exercise, extended-release Niacin, or fibrates, alone or in combination. Hydroxymethylglutaryl-coenzyme A reductase inhibitors were also prescribed, along with a low-fat diet on an individual basis.
- Patients were then divided to continue with aggressive medical therapy alone or to undergo PCI or CABG concurrently with Medical Therapy

Table 1. Comparison between the three groups

	GI CABG	GII PCI	GIII Medical	p value (GI vs GII)	p value (GI vs GIII)	p value (GII vs GIII)
Death	0%	2.5%	5%	NS	NS	NS
Non fatal MI	7.5%	7.5%	7.5%	NS	NS	NS
Need for revascularization 1y	0%	12.5%	7.5%	0.02	NS	NS
Hospitalization	7.5%	12.5%	15%	NS	NS	NS
Heart failure	2.5%	12.5%	12.5%	NS	NS	NS
Recurrence of chest pain	2.5%	12.5%	20%	0.01	0.01	NS
Strokes	2.5%	0%	0%	NS	NS	NS
Kidney creatinine >1.4	21	14	17	NS	NS	NS
Kidney creatinine ≥ 2	10	4	4	0.01	0.01	NS

Table 2. Comparison of patients with creatinine higher and lower than 2 mg/dl

	Creatinine >2 (n = 18)	Creatinine <2 (n = 102)	p
Death	0 (0.0%)	0+2+2= 4 (3.9%)	NS
Non fatal MI	1+2+0=3 (16.6%)	2+3+3=8 (7.8%)	NS
Heart failure	0 (0.0%)	4+3+3=10 (9.8%)	NS
Recurrence of chest pain	3 (16.6%)	1+3+3=7 (6.8%)	NS
Revascularization	0 (0.0%)	3+2+3=8 (7.7%)	NS
Diabetes	4+0+2=6 (33.3%)	13+17+14=44 (43.1%)	NS

CABG Technique: In patients who underwent CABG, Complete revascularization was accomplished, if technically feasible, with saphenous vein grafts, internal mammary arteries, and other conduits such as radial or gastroepiploic arteries. Standard surgical techniques were used under hypothermic arrest with blood cardioplegia. No off-pump CABG was performed.

PCI technique: Patients undergoing PCI, culprit-lesion revascularization was always attempted, and complete revascularization was performed as clinically appropriate. Success after PCI as seen on angiography was defined as normal coronary artery flow after coronary stent implantation, as assessed by visual estimation of the angiograms before and after the procedure.

- PCI was performed according to the standard techniques via femoral approach using either bare metal stents or drug eluting stents. Direct stenting or predilatation was dependent on lesion characteristics. Weight adjusted heparin 70 unit per Kg was given at the beginning of the procedure with further dose monitoring by activated clotting time to keep it above 25 seconds.

Follow up: Each Patient was followed up for one year minimally and assessed for: Death: Either cardiovascular or non-cardiovascular death. Recurrence of chest pain: Chest pain was graded according to the Canadian Cardiovascular Society classification of angina pectoris (CCS), patients with grade II or more were recruited. Hospital admissions: Development of major adverse outcomes as infarction, failure, admission to hospital. Need for revascularization for those assigned to medical treatment. Follow up data were collected through: Hospital Electronic Data Records Systems, Phone Calls, Admission Records and Hospital Telemetry Records.

RESULTS

There was no significant difference between the three groups as regards incidence of diabetes, hypertension, dyslipidemia or age. Renal dysfunction (creatinine $\geq$2) was present in 18 pts (10+4+4). The highest was 2.28 mg/dl. The present study is distinct in that it included patients with two or more vessel disease no single vessel disease was included.

Follow up outcome: tables 1, 2

Mortality: G1: none, G2: one patient, G2: 2 patients. P= NS.

Non fatal MI: G1 3 patients, G2 3 patients, G3 3 patients. P=NS.

Need for revascularization: G1 none, G2 5 patients. G3 3 patients. P between G1 and G2 = <0.02

Hospitalization: G1 3 patients, G2 5 pts, G3 6 pts. P=NS

Heart failure: G1 one pt, G2 5 pts, G3 5 pts. P = NS.

Recurrence of chest pain: G1 1 pt, G2 5 pts, G3 8 pts. P between G1, G3 < 0.01

Strokes: one pt in G1, none in G2 or 3.

Follow up exercise test: Negative in G1 in 37.5%, G2 in 17%, G3 in 5%. P between G1 and G3 < 001.

The presence of creatinine ≥2 and < 2.3 did not affect the results or prognosis or incidence of complications. Revascularization or recurrences of chest pain were not increased because of higher creatinine.

DISCUSSION

Charytan et al 2007 studied effect of kidney disease on long term results of stenting. They analysed results from 1228 patients enrolled in four separate, randomized, controlled clinical trials who underwent elective coronary angioplasty with stenting and were prospectively followed for 5 years after the index procedure. They found that mild to moderate CKD was associated with a non-significantly increased risk of late TLR (HR 1.40, 95% CI 0.73-2.69). They concluded that coronary stenting appears to be similarly effective in patients with mild to moderate CKD and patients with normal renal function. They stated that while target lesion revascularization is rarely needed beyond the first year after revascularization, long-term results of coronary stenting may be less-favourable in patients with CKD

Aoki et al 2005 compared coronary stent implantation and bypass surgery for multivessel coronary disease in patients with renal insufficiency (insights from ARTS trial). In the ARTS trial, 142 moderate renal insufficient patients (Ccr<60 mL/min) with multivessel coronary disease were randomly assigned to stent implantation (n=69) or CABG (n=73). At 5 years, there was no significant difference between the two groups in terms of mortality (14.5% in the stent group vs. 12.3% in the CABG group, P=0.81), or combined endpoint of death, cerebrovascular accident (CVA), or myocardial infarction (MI) (30.4% in the stent group vs. 23.3% in the CABG group, P=0.35). They reached the finding that at 5 years, the differences in mortality and combined incidence of death, CVA, and MI between coronary stenting and surgery did not reach statistically significant level. However, the occurrence of MACCE in the stent group was higher than in the CABG group, mainly driven by the higher incidence of repeat revascularization in the stent group.

In our study we found no difference in results between those with normal kidney function and those with mild renal insufficiency. Whether in the stent group or CABG group; but we had follow up one year only. We tried to divide the 120 pts to 3 groups, with normal creatinine (<1.4), with creatinine 1.4 to 1.99 and > 2. Again there was no increase in events with any of the groups with higher creatinine.

CONCLUSIONS

The study included 120 pts with multivessel coronary disease treated by CABG or PCI or medical therapy and followed for one year. The study showed the following:

1. The rate of improvement in follow up stress test was significantly higher in CABG group than both PCI and Medical Therapy group.
2. No significant difference was found in rate of death or in acute MI among patients treated with CABG, PCI or medical therapy.
3. Medical therapy is a reasonable alternative for patients with multivessel CAD who refuse surgical therapy or when the latter is not feasible
4. Additional need for revascularization procedure was found in patients who underwent PCI. Therefore, patients should be aware of the possibility that further revascularization procedure might be required during the follow up period.
5. Aggressive medical therapy and lifestyle prescriptions with comprehensive risk factors modifications enhance medical therapy strategy in treating multivessel coronary artery disease.
6. The presence of creatinine ≥2 and < 2.3 did not affect the results or prognosis or incidence of complications.

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