Original Research Article

Drug Eluting Stents Versus Coronary Artery Bypass Graft Surgery for Patients with Diabetes Mellitus and Multivessel Disease

Abstract

Background: Coronary revascularization can be achieved using either coronary artery bypass graft (CABG) or percutaneous coronary intervention (PCI) with stenting. Diabetics represent a difficult subset for both treatments. The aim of this work was to estimate clinical outcome in diabetic patients with multiple vessels disease who had either PCI or CABG over 30 days.

Methods: This ~~**prospective**~~ **potential** study was carried out on 200 patients with diabetes mellitus, multivessel disease ~~**defined as**~~ **with** severe stenosis. Patients were classified into two equal groups: Group (A) [underwent CABG], and group (B) [underwent PCI with Drug Eluting Stents (DES)]. All patients were ~~**subjected to**~~ full history taking, complete clinical examination, resting twelve-leads electrocardiogram, transthoracic echocardiography, coronary angiographic, SYNTAX score and Euro score.

Results: Age, dual antiplatelet therapy, statin, ACE-I/ARB and β- -blocker was significantly higher in CABG than PCI groups. Death, myocardial infarction (MI), stroke and myocardial infarction were significantly higher in PCI than CABG group. PCI, MI and repeated revascularization were significantly higher in PCI than CABG group.

Conclusions: DES have dramatically altered the management of coronary artery disease (CAD) and are increasingly used to treat complex CAD, including left main or multivessel

CAD. Patients with high surgical risk tend to prefer PCI over CABG because of a shorter hospital stay, a quicker recovery time and a potentially lower incidence of stroke.

Keywords: Drug Eluting Stents, Coronary Artery Bypass Graft Surgery, Diabetes Mellitus, Multivessel Disease, Percutaneous Coronary Intervention **. β- -blockers**

Introduction:

Diabetes Mellitus (DM) is **hormonal and metabolic disorders** and consider a major risk factor for coronary artery disease (CAD), making patients prone to diffuse, multiple and rapidly progressive CAD [1]. About 25% of patients with significant CAD who undergo percutaneous coronary intervention (PCI) procedure or coronary artery bypass graft surgery (CABG) have DM. DM is significantly associated with higher rates of ischemic complications and repeat revascularization procedure in these patients [2].

In the past decade, advancements in both PCI and cardiac surgical techniques have continued to improve methods of coronary **angiogenesis** ~~**revascularization**~~. Although there is evidence to suggest that these ~~**advancements**~~ **progress** have improved outcomes in diabetic patients, ~~**this population still experiences significantly worse outcomes compared with general population, and the optimal revascularization strategy in diabetic patients remains unclear**~~ [3].

The optimal method of ~~**revascularization**~~ **neovascularization** for diabetic patients with multivessel CAD is a topic of debate. Coronary revascularization can be achieved using either CABG or PCI with stenting. Diabetics represent a difficult subset for both treatments. While PCI is more commonly used in patients affected with single vessel CAD, the best strategy for patients with multivessel disease is remain not **understood** ~~**determined,**~~ due to higher repeat revascularization rate at 1-year follow-up in patients treated by PCI with stenting [4].

Coronary artery bypass graft (CABG) surgery was first attempted in humans in 1960 using the internal mammary artery (IMA)[5]. Subsequently, percutaneous coronary intervention (PCI) using transluminal balloon angioplasty was introduced as alternative method for coronary artery revascularization in 1977 [6]. Over the years, percutaneous and surgical revascularization techniques complement advances in medical therapies to provide effective

treatment of acute coronary syndromes (ACS) and stable coronary artery disease (SCAD) to improve angina, and quality of life (QoL) [7]. In patients with left main disease (LMS) and multi vessel disease (MVD), coronary revascularization has been shown to prolong survival [7]. Historically, CABG was considered the treatment of choice for MVD and LMD. However, remarkable advances in PCI led to higher procedural success rates, decreased procedural myocardial infarction (MI), target lesion revascularization (TLR), in-stent thrombosis, and in-stent restenosis rates. As such PCI became a viable alternative to CABG in treatment of LMD and MVD [8]. Multiple moderate size randomized controlled trials comparing both treatment strategies for LMD and MVD interventions revealed an increase in periprocedural cardiac and cerebrovascular events with CABG but higher long-term need for repeat revascularization in patients managed with PCI [9]. The aim of this work was to estimate clinical outcome in diabetic patients with multiple vessels disease who had either PCI or CABG over 30 days.

Patients and Methods:

This prospective study was carried out on 200 patients with diabetes mellitus, multivessel disease defined as severe stenosis (≥ 70%) in at least 2 major epicardial coronary arteries, angiographic characteristics amenable to both PCI/DES and CABG with complete revascularization in one section and patients undergoing PCI with implantation of DES or those undergoing CABG.

The study was conducted at The Department of Cardiology, Tanta University Hospitals and National Heart Institute through 6 months from April 2020 to September 2020. A written informed consent was obtained from all the patients included and the study was approved by the Ethics Committee of Faculty of Medicine, Tanta University.

Exclusion criteria were revascularization within 1 year before the index procedure, prior cardiac surgery (CABG or valve surgery), prior PCI, severe left main coronary artery disease

(degree of stenosis ≥ 50%) and MI within 24 hours preceding the index procedure because these patients preferentially undergo PCI; and unstable hemodynamic or in cardiogenic shock.

Patients were classified into two equal number groups: group (A) **[**underwent CABG] and Group (B) [underwent PCI with DES].

All patients were subjected to full history taking, complete clinical examination, resting twelve-leads electrocardiogram, transthoracic echocardiography and coronary angiographic.

PCI: include number and types of stents and number of vessels which had been stented. **CABG:** include types of grafts (venous or arterial) and numbers of grafts used. **Syntax score**: The SYNTAX Trial is a manufacturer-funded trial with a primary endpoint of death, patients were randomized to either CABG surgery or a drug-eluting stent (the Boston Scientific TAXUS paclitaxel-eluting stent). SYNTAX found the two strategies to be similar for hard endpoints (death and MI). Those receiving PCI required more repeat revascularization (hence the primary endpoint analysis did not find PCI to be non-inferior), but those undergoing CABG had significantly more strokes pre or perioperatively. Use of the SYNTAX risk score is being investigated as a method of identifying those multivessel disease patients in whom PCI is a reasonable option vs those in whom CABG remains the preferred strategy.

Add reference

Euro score: Euro SCORE (European System for Cardiac Operative Risk Evaluation) is a risk model which allows the calculation of the risk of death after a heart operation. The model asks for 17 items of information about the patient, the state of the heart and the proposed operation, and uses logistic regression to calculate the risk of death. Add reference

The primary outcome was all-cause death. The secondary outcomes were MI, stroke, and repeat revascularization tabulated separately.

Statistical analysis

Statistical analysis was done by SPSS v25 (IBM Inc., Chicago, IL, USA). The qualitative data were presented as number and percentages while quantitative data were presented as mean, standard deviations and ranges when their distribution found parametric. The comparison between two groups with qualitative data were done by using Chi-square test and/or Fisher exact test was used instead of Chi-square test when the expected count in any cell was found less than 5. The comparison between two independent groups with quantitative data and parametric distribution was done by using independent t-test. A two tailed P value < 0.05 was considered significant.

Results:

Sex, smoker, DM, oral medications, require insulin, HTN, hypercholesterolemia and clinical presentation were insignificant different between CABG and PCI groups. Age was significantly higher in CABG than PCI groups. **Table 1**

Table 1: Comparison between CABG and PCI regarding age, sex, BMI, smoker, DM, oral medications, require insulin, HTN, hypercholesterolemia and clinical presentation

		CABG (n= 100)	PCI (n= 100)	P-value
Age(years)		46.56 ± 6.97	42.52 ± 10.73	**0.002***
Sex	**Female**	40 (40.0%)	48 (48.0%)	0.254
	Male	60 (60.0%)	52 (52.0%)	
BMI		28.75 ± 2.90	29.46 ± 2.91	0.089
Smoker		16 (16.0%)	8 (8.0%)	0.082
DM		100 (100.0%)	100 (100.0%)	NA
Oral medications		56 (56.0%)	68 (68.0%)	0.080
Require insulin		44 (44.0%)	32 (32.0%)	0.080
HTN		68 (68.0%)	64 (64.0%)	0.550
Hypercholesterolemia		60 (60.0%)	64 (64.0%)	0.560
Clinical presentation	**Stable angina**	40(40%)	44(44%)	0.567
	Acute coronary syndrome	64(64%)	60(60%)	0.560
	Prior myocardial infarction	40(40%)	36(36%)	0.560
	Prior stroke	8(8%)	12(12%)	0.346
	Peripheral artery disease	20(20%)	16(16%)	0.462
	Chronic pulmonary disease	12(12%)	16(16%)	0.415
	Chronic kidney disease	8(8%)	12(12%)	0.346
	Left ventricular dysfunction	12(12%)	8(8%)	0.346

Data are presented as mean ± SD or frequency (%), BMI: Body mass index, HTN: hypertension, DM: diabetes mellitus, *: significant difference at p<0.05.

Diseased vessel, SYNTAX score, Euro SCORE, follow-up (30 days), total cholesterol, mg/dL, LDL-C, mg/dL, HDL-C, mg/dL and triglyceride, mg/dL were insignificant different between CABG and PCI groups. HbA1c (NGSP), % was significantly lower in CABG than PCI group while LVEF, % was significantly higher in CABG than PCI groups. **Table 2**

Table 2: Comparison between CABG and PCI regarding diseased vessel, SYNTAX score, Euro SCORE, follow-up (30 days), total cholesterol, mg/dL, LDL-C, mg/dL, HDL-C, mg/dL, triglyceride, mg/dL, HbA1c (NGSP), % and LVEF, %.

		CABG (n= 100)	PCI (n= 100)	P-value
Diseased vessel	**Proximal LAD disease**	60 (60.0%)	52 (52.0%)	0.254
	Left main disease	36 (36.0%)	40 (40.0%)	0.560
	Multivessel disease	64 (64.0%)	60 (60.0%)	0.560
SYNTAX score		29.80 ± 7.72	28.53 ± 6.26	0.205
Euro SCORE		7.58 ± 1.36	7.56 ± 1.40	0.886
Follow-up (30 days)		4.24 ± 1.72	4.30 ± 1.74	0.807
Total cholesterol, mg/dL		183.16 ± 38.42	179.83 ± 36.50	0.530
LDL-C, mg/dL		111.74 ± 23.74	106.74 ± 34.12	0.231
HDL-C, mg/dL		44.92 ± 11.50	46.44 ± 10.43	0.330
Triglyceride, mg/dL		134.02 ± 62.04	133.47 ± 54.48	0.947
HbA1c (NGSP), %		7.03 ± 1.36	7.99 ± 1.47	**< 0.001***
LVEF, %		64.17 ± 9.99	51.50 ± 16.87	**< 0.001***

Data are presented as mean ± SD or frequency (%), LAD: Left anterior descending artery. *: significant difference at p <0.05.

Death from any cause, death from cardiac cause, Stroke and repeat revascularization were insignificant different between two groups, while death, MI, stroke and myocardial infarction were significantly higher in PCI than CABG groups. **Table 3**

Table 3: Comparison between CABG and PCI regarding primary outcome and secondary outcome.

	CABG (n= 100)	PCI (n= 100)	P-value
Death, MI, Stroke	28(28%)	44(44%)	**0.018***
Secondary outcome			
Death from any cause	20(20%)	24(24%)	0.495
Death from cardiac cause	12(12%)	16(16%)	0.415
Myocardial infarction	4(4%)	12(12%)	**0.037***
Stroke	8(8%)	4(4%)	0.234
Repeat revascularization	28(28%)	28(28%)	1.000

Data are presented as mean ± SD or frequency (%), LAD: Left anterior descending artery. *: significant difference at p <0.05.

Aspirin and CABG were insignificant different between CABG and PCI groups. Dual antiplatelet therapy, Statin, ACE-I/ARB and β- -blocker were significantly higher in CABG than PCI groups, while PCI was significantly lower in CABG than PCI groups. **Table 4**

Table 4: Comparison between CABG and PCI regarding medication and PCI and CABG

Medication	CABG (n= 100)	PCI (n= 100)	P-value
Aspirin	96(96%)	16(16%)	0.234
Dual antiplatelet therapy	96(96%)	16(16%)	**< 0.001***
Statin	68(68%)	24(24%)	**< 0.001***
ACE-I/ARB	52(52%)	24(24%)	**< 0.001***
β-blocker	56(56%)	28(28%)	**< 0.001***
PCI	8 (8.0%)	52 (52.0%)	**< 0.001***
CABG	16 (16.0%)	20 (20.0%)	0.462

Data are presented as frequency (%), PCI: percutaneous coronary intervention, CABG: coronary artery bypass grafting surgery, *: significant difference at p <0.05. ACE-I: angiotensin converting enzyme inhibitors, ARBs: angiotensin-receptor blockers

Stroke and death were insignificant different between groups. MI and Repeated revascularization were significantly higher in PCI than CABG groups. **Table 5**

Table 5: Comparison between CABG and PCI regarding 30-days Outcome

30-days Outcome	CABG (n= 100)	PCI (n= 100)	P-value
MI	4(4%)	16(16%)	**0.005***
Repeated revascularization	4(4%)	12(12%)	**0.037***
Stroke	4(4%)	4(4%)	1.000
Death	8(8%)	16(16%)	0.082

Data are presented as frequency (%), *: significant difference at p <0.05.MI: myocardial infarction,

Discussion

~~Coronary artery bypass graft (CABG) surgery was first attempted in humans in 1960 using the internal mammary artery (IMA) [5].~~ **Repeated as mentioned in introduction**

Subsequently, percutaneous coronary intervention (PCI) using transluminal balloon angioplasty was introduced as alternative method for coronary artery revascularization in 1977[6]. Over the years, percutaneous and surgical revascularization techniques complement advances in medical therapies to provide effective treatment of acute coronary syndromes (ACS) and stable coronary artery disease (SCAD) to improve angina, and quality of life (QoL) [7]. In patients with left main disease (LMS) and multi vessel disease (MVD), coronary revascularization has been shown to prolong survival [7].

Our study revealed no statistically significant difference between the two groups (PCI and CABG) regarding Primary, secondary and 30 days follow up outcomes.

A meta-analysis by Lee et al. [10]. comparing PCI and CABG in patients with DM and MVD demonstrated that there was no significant difference in mortality or MI between the two procedures. In contrast, a large-scale randomized study by Farkouh et al. [11]. with 1900 patients with DM and MVD showed that mortality and MI rates were better with the CABG procedure than PCI.

Several studies Foundation and Serruys [12, 13] have compared PCI and CABG in patients with multivessel CAD. Early studies have demonstrated that long-term clinical outcomes were equivalent in patients who underwent PCI or CABG, although the subsequent revascularization rate was significantly higher in the PCI group.

In the bare metal stent era, PCI with bare metal stent or balloon angioplasty and CABG for multivessel CAD exhibited similar rates of mortality and a composite of mortality or MI; however, CABG demonstrated a survival advantage in patients with diabetes or older patients [14].

In the DES era, the FREEDOM trial by Farkouh et al. [11] showed that CABG was superior to PCI with DES in that CABG significantly reduced mortality rates and MI in patients with diabetes and multivessel CAD.

Likewise, CABG, as compared with PCI with DES by Chang et al. [15] significantly reduced the long-term risk of mortality in nondiabetic patients with multivessel CAD. Therefore, in the DES era, despite advances in stent technology, CABG demonstrated improved clinical outcomes of mortality in patients with multivessel CAD compared to PCI, [11] [15, 16]supporting the hypothesis that CABG is the preferred strategy for the majority of patients with multivessel CAD.

The CARDia trial was the first examining the treatment of CAD in a subgroup of diabetic patients, demonstrating the superiority of CABG in this subset with combined rates of mortality, MI, stroke and repeated revascularization of 11.3% in the CABG group and 19.3% in the PCI group at 1 year [17]. The FREEDOM trial confirmed these findings in 1,900 patients with complex MVD and diabetes, demonstrating comparatively worse 5-year rates of a composite outcome, including death from any cause, nonfatal MI, or nonfatal stroke, in the PCI group (26.6% vs. 18.7% in the CABG group). Despite the incidence of stroke being higher in CABG cohort, death and MI were significantly higher in the PCI group, leading to the conclusion that diabetic population would best benefit from CABG rather than PCI [11].

Subsequently, the VA-CARDS investigators reported the results of a randomized trial comparing interventions exclusively with drug-eluting stents and surgery in patients with diabetes and high-complex CAD. Despite being underpowered, all-cause mortality was 5.0% for CABG and 21% for PCI at 2 years follow-up, while the risk for nonfatal MI was 15% for CABG and 6.2% for PCI [18].

Sipahi and colleagues [19]. performed another review including six randomized studies (N = 6,055), with their meta-analysis illustrating a significant reduction in total mortality, MI, and

repeat revascularization with CABG compared with PCI. However, unlike the previous studies, these authors found a trend toward excess strokes with CABG, but this was not significant. The conclusions drawn suggest CABG as the best treatment option in patients with MVD compared with PCI, given the undisputable reduction in long-term mortality, MIs and repeat revascularizations, irrespective of the presence of diabetes.

An interesting work has been recently reported by Fanari and colleagues [20], who performed a meta-analysis of six RCTs and investigated the results of the long-term follow-up of the studies. Despite potential bias due to the presence of an additional RCT involving unprotected LM disease [21] this study demonstrated that at 1 year, PCI was associated with a significantly higher incidence of target vessel revascularization, lower incidence of stroke and no difference in death or MI compared to CABG. However, at 5 years, PCI was associated with a higher incidence of death and MI. Increased mortality in the PCI group was mainly found in diabetics [20].

In a meta-regression analysis using event rates as a dependent variable to test for an interaction between baseline clinical features (i.e., age, gender, diabetes mellitus, previous MI and ejection fraction) and choice of revascularization, D'Ascenzo et al. [22]concluded that PCI significantly reduces the risk of stroke compared to CABG particularly in female patients, but the risk of revascularization is increased with PCI, especially in women and in those with diabetes.

An interesting point has been raised in meta-analyses and systematic reviews on CAD with respect to the comparison of outcomes in complete or incomplete revascularization. A large preliminary investigation, including 35 studies and 89,883 patients, demonstrated that complete revascularization is more commonly achieved with CABG rather than PCI, and that incompleteness of revascularization is associated to increased mortality and repeated revascularization independently on the mode of treatment [23].

In a pooled analysis of individual patient-level data of the SYNTAX and BEST randomized trials, Cavalcante et al [24]analysed the outcomes of 1,166 patients in which 577 were randomized to PCI and 589 to CABG. In patients with MVD with proximal left anterior descending artery (LAD) involvement, CABG is associated with a significantly lower rate of cardiac death, MI and all-cause revascularization when compared with DES-PCI. There was no difference among the groups as far as all-cause mortality and stroke were concerned, but the combined outcome of major adverse cardiovascular and cerebro vascular events (i.e., all-cause death, MI, stroke, revascularization) favoured CABG. The authors concluded that in patients with MVD CABG was superior in terms of survival and cardiovascular events to drug-eluting stents at 5 years of follow-up.

Nevertheless, a systematic review by Head et al. [25]. featured in The Lancet by Head and colleagues, including 11 randomized trials and involving a total of 11,518 patients, illustrated equivalence in the long-term safety outcomes between the modalities of revascularization for unprotected LM disease. Conversely, the benefit of CABG was restricted to complex MVD and diabetic patients.

Finally, our study has some limitations: The sample size was relatively small and it was a single-center study.

Conclusions:

Both CABG and PCI with DES play a major role in the management of left main or multivessel CAD. DES have dramatically altered the management of CAD and are increasingly used to treat complex CAD, including left main or multivessel CAD. Patients with high surgical risk tend to prefer PCI over CABG because of a shorter hospital stay, a quicker recovery time and a potentially lower incidence of stroke.

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

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