

EFFECT OF DIABETES MELLITUS ON GRAFT DISEASE PATTERN AFTER CORONARY ARTERY BYPASS GRAFT SURGERY IN SYMPTOMATIC PATIENTS DETECTED BY MULTI SLICE CORONARY COMPUTED TOMOGRAPHY ANGIOGRAPHY

By

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ABSTRACT

Background: Surgical revascularization of the coronary arteries is one of the most frequent surgical procedures performed worldwide. Although the procedure is one of the major successes of modern medicine, it does not treat the disease underlying the symptoms (atherosclerosis), but only the clinical presentation of coronary artery disease. Multi detector computed tomography (MDCT) accuracy in coronary artery bypass grafting (CABG) patency and stenosis assessment is excellent compared with angiography. Its safety advantages have led to rapidly increasing usage in both native and grafted vessel evaluation.

Objective: To evaluate the impact of diabetes mellitus on the patency of arterial and venous grafts after coronary artery bypass surgery assessed by multi slice CT coronary angiography.

Patients and methods: One hundred post CABG patients were included, and divided into two groups: Group A (sixty diabetic patients) from which thirty two had NIDDM (53.3% of diabetic patients), twenty eight (46.6% of diabetic patients) had IDDM, and group B (forty non diabetic patients). Patients subjected to our study were symptomatic with recurrent typical chest pain or angina equivalent. All included patients had sinus rhythm, heart rate less than 70 bpm, weight less than 150 kg and serum creatinine <1.5 mg/dl. Patients were investigated by Seimens Somatom Definition Flash 64- dual source MDCT at least 12 months after the surgery.

Results: The most common risk factor in our studied population was hypertension affecting 55% of studied population followed by smoking which was prevalent at 54% of studied population. Comparison of the number of diseased grafts in the two study groups according to hypertension showed a statistically significant difference in group A (diabetic group). Comparison of the number of diseased grafts in the two study groups according to dyslipidemia showed a statistically significant difference in group A. Comparison of the number of diseased grafts in the two study groups according to smoking showed a statistically significant difference in group B (non- diabetic group). 101 arterial grafts had been evaluated for patency, 96 LIMA and 5 radial arteries. There were 59 LIMA in diabetic patients and 37 LIMA in non-diabetic patients evaluated. There was no statistically significant LIMA occlusion in group A and group B. In our study, 141 venous grafts were evaluated for patency: 83 venous grafts in diabetic patients, and 58 venous grafts in non-diabetic patients. Comparison of the two study groups as regards patency of venous grafts showed a statistically significant in group A, and revealed also more occluded grafts at diabetic group. There was a statistically significant graft occlusion with longer duration of diabetes mellitus and higher glycosylated hemoglobin HbA1c.

Conclusion: Multi-slice CT coronary angiography has an important role in evaluation patency of coronary grafts after coronary artery bypass surgery. Graft occlusions were more common among diabetics compared with non-diabetics. Diabetes was associated with lower vein graft patency but similar arterial graft patency in comparison to non-diabetics. Uncontrolled diabetes mellitus and long duration of disease was found to be a significant predictor for graft occlusion.

Keywords: Diabetes Mellitus, Graft disease pattern, Coronary Artery Bypass Graft surgery, MDCT.

INTRODUCTION

Coronary artery bypass grafting (CABG) remains one of the most commonly performed major surgical procedures worldwide and the most common procedure performed by cardiac surgeons (*D'Agostino et al., 2018*).

The reduction or disappearance of angina, the improved tolerability of physical exercise and the overall improvement in quality of life and life expectancy have been the motivations underlying its use since the first the procedure was performed in the 1950. Although the procedure is one of the major successes of modern medicine, it doesn't eliminate the disease underlying the symptoms (atherosclerosis) only the clinical presentation of coronary artery disease (*Cademartiri et al., 2012*).

The large number of patients suffering a recurrence of angina after surgical revascularization represents a significant issue in clinical cardiology. Recurrence of angina can be present in association with myocardial ischemia both in previously reperfused and non reperfused regions. These patients should therefore undergo clinical and instrumental monitoring and some cases a repeat procedure is needed, which unfortunately is encumbered by a higher percentage of post procedure complications (*Borges et al., 2010*).

An important predictor of long-term success in CABG is graft patency. This is

especially true in diabetic patients because they are prone to diffuse and rapidly progressive atherosclerosis (*Aronson and Edelman, 2010*).

Multi-detector computed tomography has become an alternative to coronary angiography to diagnose graft occlusion and stenosis after coronary artery bypass. In addition, multi-detector CT has the added advantage over traditional angiographic evaluation of simultaneously allowing evaluation for alternate postoperative complications that may also manifest with chest pain and dyspnea and recurrent angina (*Khedr et al., 2013*).

Multi slice computed tomography (MDCT) is a result of progress spatial resolution through thinner slice collimation and to increased temporal resolution through faster gantry rotation. MDCT angiography is a non-invasive imaging technique that in the scanner technology which led to improved can be performed on ambulatory patients (*Hamon et al., 2010*).

The introduction of 64-slice MDCT and dual-source CT permitted improved temporal resolution, spatial resolution, and reduction of both cardiac and respiratory motion, leading to improved assessment of arterial and venous graft stenosis and occlusion. Reports on diagnostic accuracy of MDCT in CABG have shown values of sensitivity and specificity over 95% for the presence of lesions in these vessels. However, the investigation of native

vessels showed that sensitivity and specificity are significantly lower than in patients with suspected coronary artery disease (*Shaw et al., 2012*).

The aim of our study was to evaluate the impact of diabetes mellitus on the patency of arterial and venous grafts after coronary artery bypass surgery assessed by multi slice CT coronary angiography.

PATIENTS AND METHODS

This study included 100 post CABG patients in the span of one year from November 2018 to November 2019 at National Heart Institute, and Al-Hussein University Hospital, and complaining of ischemic symptoms.

All hundred patients were divided into two groups: **Group A** (sixty diabetic patients) and **group B** (forty non diabetic patients), and investigated by Seimens Somatom Definition Flash 64- dual source MDCT at least 12 months after the surgery.

Inclusion Criteria:

Symptomatic post CABG with at least of 12 months from surgery either diabetic or not diabetic.

All symptomatic patients presented with recurrent exertional chest pain or angina equivalent were eligible for inclusion in the study, and fulfilling: Sinus rhythm, their heart rate less than 70 bpm spontaneously or beta-blocker induced, can hold breath for more than 14 seconds, weight less than 150 kg. and serum creatinine <1.5 mg/dl.

Exclusion Criteria:

Patients known to have high serum creatinine and not for regular dialysis (S.

creatinine >1.5mg/dl), patients with invaluable images due to artifacts e.g. obese patients, motion artifacts due to inadequate breath holding or arrhythmia e.g. atrial fibrillation (AF), frequent premature atrial contractions (PVCs), previous coronary stenting, repeated bypass surgery (REDO), patients presented with acute coronary syndrome (ACS), hypersensitivity to iodinated contrast agent and history of allergies or allergic reactions to other medications

All the patients were subjected to the following:

- **Personal data collection and risk factors assay** such as age, gender, presence or absence of hypertension, diabetes, smoking, dyslipidemia, and to ensure that there was no obstacles to undergo MSCT such as history of bronchial asthma (which would contraindicate the administration of beta blockers).
- **Clinical examination** including vital signs with general, chest, and cardiac examination.
- **12- Lead ECG:** to detect ischemic changes and exclude non sinus rhythm.
- **Echocardiography;** Variables of left ventricular performance that were measured included LV internal diameter during end-diastole (LVIDd), LV internal diameter during end-systole (LVIDs), LVEF, left atrial diameter, LV mass, septal wall thickness and posterior wall thickness.
- **Routine lab investigations:**
 1. Blood glucose level for patients not known to be diabetic: Diabetes was diagnosed according to the criteria

set by *American Diabetes Association (2018)*: Classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥ 200 mg/dl. Fasting plasma glucose level of ≥ 126 mg/dl. The 2-h plasma glucose (2-h PG) value after a 75-g oral glucose tolerance test (OGTT) ≥ 200 mg/dl. Glycosylated Hemoglobin (HBA1C) of greater than or equal to 6.5.

2. Serum creatinine.
3. Lipid Profile.

All patients underwent MDCTA after one year, at least, post CABG using 64-dual source Siemens Flash definition scanner. The contrast was injected intravenously and a non-ionic low osmolar contrast was used. The test bolus technique was used. Scanning started after determining the delay time. The entire scans were ECG gated.

MDCT data were evaluated using the transaxial images, as well as other reconstruction modalities; maximal intensity projection (MIP) and curved

multiplanar reconstruction (MPR). Each graft was classified as patent (flow visible), occluded, or not analyzable (graft was obscured by a metal ligature clip or because the image quality was poor).

Informed written consent was obtained from every participant.

Statistical Analysis:

Data were collected, revised, coded and entered to the Statistical Package for the Social Sciences (IBM SPSS) version 20. Descriptive statistics were done for numerical parametric data as mean and minimum & maximum of the range, while they were done for categorical data as number and percentage. Inferential analysis was done for quantitative variables using independent t-test in cases of two independent groups with parametric data. Inferential analysis was done for qualitative data using Chi square. The confidence interval was set to 95% and the margin of error accepted was set to 5%. P-value was considered significant when $P \leq 0.05$.

RESULTS

This study included 242 grafts from one hundred symptomatic post CABG patients, randomized into group A (n= 60) which was diabetic, and group B (n=40) which was non-diabetic, All of them underwent Multi-detector Computed Tomography (MDCT) to evaluate grafts patency.

Comparison of the two study groups as regards age showed a statistically non-significant difference (P-value = 0.099). The comparison of the two study groups as regards gender showed a

statistically non-significant difference (P-value = 0.610). Comparison of the two study groups as regards prevalence of smoking shows insignificant difference (P-value: 0.512). Comparison of the two study groups as regards prevalence of hypertension showed non-statistically significant difference (P-value = 0.682). Comparison of the two study groups as regards prevalence of dyslipidemia showed non-statistically significant difference (P-value=0.741).

Comparison of the two study groups according to number of diseased grafts demonstrated a statistically significant

difference at the diabetic group (P-value=0.002). Number of occluded grafts was more in diabetic group (Table 1).

Table (1): Comparison of the two groups as regards age, gender, smoking, hypertension and dyslipidemia and number of disease grafts

Parameters \ Groups	Diabetic N=60		Not Diabetic N=40		P-value		
	Age:						
Range	37	-	82	43	-	77	0.099
Mean ±SD	58.700	±	9.367	61.750	±	8.357	
	Diabetic		Not Diabetic		Total		
	N=60	%	N=40	%	N	%	
Gender:							
Female	13	21.67	7	17.50	20	20.00	0.610
Male	47	78.33	33	82.50	80	80.00	
Smoking:							
Non-smoker	26	43.33	20	50.00	46	46.00	0.512
Smoker	34	56.67	20	50.00	54	54.00	
Hypertension:							
No HTN	26	43.33	19	47.50	45	45.00	0.682
HTN	34	56.67	21	52.50	55	55.00	
Dyslipidemia:							
Not Dyslipidemia	34	56.67	24	60.00	58	58.00	0.741
Dyslipidemia	26	43.33	16	40.00	42	42.00	
Grafts status:							
Patent	89	60.54	76	80.00	165	68.18	0.002
Occluded	58	39.46	19	20.00	77	31.82	

Comparison of the two study groups as regards patency of arterial graft showed insignificant difference in group A and in group B (P-value = 0.171) while comparison of the two study groups as

regards patency of venous grafts showed statistically significant in group A and revealed also more occluded grafts at diabetic group (P-value=0.002) (Table 2).

Table (2): Comparison of the two study groups according to patency of arterial and venous grafts

Grafts Type	Grafts status	Groups						Chi-Square	
		Diabetic		Not Diabetic		Total		X ²	P value
		N	%	N	%	N	%		
Venous	Patent	41	49.40	44	75.86	85	60.28	9.987	0.002
	Occluded	42	50.60	14	24.14	56	39.72		
Arterial	Patent	48	75.00	32	86.49	80	79.21	1.878	0.171
	Occluded	16	25.00	5	13.51	21	20.79		

Comparison of the number of diseased grafts in the two study groups according to duration after CABG more than 10 years demonstrated non statistically significant difference (p-value =0.0.074), while comparison of the number of

diseased grafts in the two study groups according to duration after CABG less than 10 years was demonstrated statistically significant difference (p-value =0.007) (**Table3**).

Table (3): Comparison of the number of diseased grafts in the two study groups according to duration after CABG.

Duration of CABG	Grafts status	Groups						Chi-Square	
		Diabetic		Not Diabetic		Total		X ²	P-value
		N	%	N	%	N	%		
<10 Years	Patent	74	61.67	57	80.28	131	68.59	7.174	0.007
	Occluded	46	38.33	14	19.72	60	31.41		
>10 Years	Patent	15	55.56	19	79.17	34	66.67	3.188	0.074
	Occluded	12	44.44	5	20.83	17	33.33		
Chi-Square	X ²	0.345		0.014					
	P-value	0.557		0.906					

Comparison of the number of diseased grafts according to type of treatment of DM that showed a statistically non-

significant difference (P-value=0.506) (**Table 4**).

Table (4): Comparison of the number of diseased grafts according to type of treatment of DM

Treatment of DM Grafts status	OHG		Insulin		Total		Chi-Square	
	N	%	N	%	N	%	X ²	P-value
Patent	51	62.96	38	57.58	89	60.54	0.442	0.506
Occluded	30	37.04	28	42.42	58	39.46		
Total	81	100.00	66	100.00	147	100.00		

Comparison of the number of diseased grafts according to duration of DM demonstrated a statistically significant difference (P-value <0.001), and revealed

that there are more occluded grafts at the diabetic group of duration more than five years (**Table 5**).

Table (5): Comparison of the number of diseased grafts according to duration of DM

Duration of DM Grafts status	Duration of DM						Chi-Square	
	<5 Years		>5 Years		Total		X ²	P-value
	N	%	N	%	N	%		
Patent	50	79.37	39	46.43	89	60.54	16.348	<0.001
Occluded	13	20.63	45	53.57	58	39.46		
Total	63	100.00	84	100.00	147	100.00		

Comparison of the number of diseased grafts according to HbA1c demonstrated a statistically significant difference (P-value = 0.033) in patients with HbA1c > 7

and revealed that there were more occluded grafts at diabetic patients with higher HbA1C more than 7 (Table 6).

Table (6): Comparison of the number of diseased grafts according to HbA1c

Grafts status \ HbA1c	HbA1c						Chi-Square	
	<7 HbA1c		>7 HbA1c		Total		X ²	P-value
	N	%	N	%	N	%		
Patent	45	70.31	44	53.01	89	60.54	4.528	0.033
Occluded	19	29.69	39	46.99	58	39.46		
Total	64	100.00	83	100.00	147	100.00		

DISCUSSION

The mean age for the non-diabetic group was 61.75±8.35, and the diabetic group was 58.7±9.36. The gender predominance was mostly males (in the non-diabetic group they were 82.5%, while in the diabetic group they were 78.3%). Other studies showed more male patients with a mean age of 62.6±10.3 for non-diabetics and 63.5±9.7 for the diabetic group (Weiss et al., 2013).

The most common risk factor in our studied population was hypertension affecting 55 % of studied population, correlating with the study done by Sunman et al. (2013), in which hypertension was the most common risk factor affecting 63% of studied population. In Li et al. (2011) study smoking was the most common risk factor affecting 60% of studied population which is not correlated with our study due to different group samples of different studies.

In our study, comparison of the number of diseased grafts in the two study groups according to hypertension showed statistically significant difference in group A, with non-significant difference in

group B, this was in agreement with the study done by Muath et al. (2011), where 75% of hypertensive patients developed graft occlusion. So, hypertension with diabetes mellitus increases risk of graft occlusion. A post hoc analysis of the Clopidogrel after surgery for coronary artery disease (CASCADE) trial was done by Dai et al. (2013), where hypertension correlates with the development of graft hyperplasia and occlusion.

In our study, comparison of the number of diseased grafts in the two study groups according to dyslipidemia showed a statistically significant difference in group A, with statistically non-significant difference in group B. This was in agreement with the study done by Jerzewski et al. (2013), within the CASCADE trial population which demonstrated that lower HDL levels were associated with trends towards more graft occlusions 12 months following CABG. In the study done by Muath et al. (2011) found a strong correlation between high triglycerides, high LDL and graft occlusion.

In our study, 101 arterial grafts had been evaluated for patency, 96 LIMA and 5 radial arteries. There were 59 LIMA in

diabetic patients and 37 LIMA in non-diabetic patients evaluated. Comparison of the two study groups as regards patency of arterial graft showed no statistically significant difference in group A and in group B. This was in agreement with *Yang et al. (2018)* who found that suffering from diabetes mellitus yielded significant higher graft failure of SVG, but not for LIMA graft, correlating with our study. Also, our study was in agreement with *Raza et al. (2017)* revealed that LIMA patency was stable over time and similar in patients with and without diabetes.

In our study, 141 venous grafts were evaluated for patency, 83 venous grafts in diabetic patients and 58 venous grafts in non-diabetic patients. Our study showed statistically significance in group A, and revealed also more occluded grafts at diabetic group and was in agreement with the study done by *Deb et al. (2014)*. *Deb et al. (2014)* showed that SV graft patency was lower in diabetics than the non-diabetics. Also our study came in agreement with the study done by *Azizi et al. (2016)*.

In our study, comparison of the number of diseased grafts in the two study groups according to duration of CABG more than 10 years demonstrated non-statistically significant difference. This was in agreement with *Raza et al. (2017)* which revealed that the long-term patency of bypass grafts was similar between diabetic and non-diabetic patients. However, a study by *Ayan et al. (2015)*. DM was associated with higher graft stenosis and occlusion compared to non-DM in contrast to our study.

In our study, as regard to the type of treatment of DM either (insulin or oral

hypoglycemic drug), there was no statistically significant difference at the number of diseased grafts between diabetic patients on insulin and those on oral hypoglycemic drugs, which was in agreement with a study done by *Koshizaka et al. (2014)*. *Koshizaka et al. (2014)* revealed that there was no significant difference of severity of graft lesion and number of diseased grafts between patients with diabetes requiring insulin and those treated with other therapies.

In our study, the number of diseased grafts is in direct relation to duration of DM and showed a statistically significant difference at the diabetic group of duration more than five years which was in agreement with study done by *Saleem et al. (2010)* that showed strong correlation between the duration of DM with severity of graft occlusion and coronary artery disease.

In our study, the number of diseased grafts was in-direct relation to glycosylated hemoglobin and showed a statistically significant difference in patients with HbA1c more than 7. This was in agreement with study done by *Nystrom et al. (2015)* patients undergoing surgical revascularization with a median follow-up of 4.7 years. They showed that increasing levels of HbA1c resulted in increasing rates of death and major cardiovascular events (MI, heart failure or repeat revascularization). However, our study was in contrast to a previous study done by *Lau et al. (2006)* who assessed Graft patency by multi slice computed tomographic (CT) angiography and found that poor diabetic control was not

independent predictor of graft non-patency.

CONCLUSION

Multi-slice CT coronary angiography has an important role in evaluation patency of coronary grafts after coronary artery bypass surgery. Uncontrolled diabetes mellitus and long duration of disease was found to be a significant predictor for graft occlusion. Diabetes is associated with lower vein graft patency but similar arterial graft patency in comparison to non-diabetics. Type of treatment of diabetes mellitus has no role in graft patency.

RECOMMENDATION

In view of the small number of the studied cases and lack of long-term follow-up data, further studies including larger number of patients and focusing on long-term clinical outcomes is recommended.

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تأثير داء السكري على قصور الوصلات للشرايين التاجية بعد جراحة القلب المفتوح المقيمة بالأشعة المقطعية متعددة المقاطع

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خلفية البحث: عملياته اعاده مسار الشرايين التاجيه باستخدام الوصلات الشريانيه والوريديه تعد من اكثر العمليات الجراحية شيوعا فالعالم اجمع على الرغم من ان جراحه القلب المفتوح لتكوين الوصلات تعد من اهم النجاحات فى الطب الحديث الا انها لا تعالج سبب قصور الشرايين التاجيه الا وهو تصلب الشرايين ولكنها تخفف من اعراض قصور الشرايين مثل الام الصدر. التنبؤ بالتقدم المرضى لايعتمد على الاجراء الجراحى فقط ولكنه يعتمد ايضا على تقدم المرض ذاته فى الشرايين التاجيه نفسها وفى الوصلات. ومن المعلوم ان مرض السكرى يصاحب نشاط زائد للصفائح الدمويه وارتفاع لعوامل التجلط وخمول لتأثير الاسبرين مما يعطى اشاره لزيادة فشل الوصلات فى مرضى السكرى.

الهدف من البحث: نحن نهدف من هذه الدراسة إلى تقييم تأثير داء السكري على سالكية الوصلات الشرايين التاجية سواء وصلات شريانية او وريدية بعد جراحة القلب المفتوح مقيمة بالأشعة المقطعية متعددة الكواشف.

المرضى وطرق البحث: لقد اشتملت دراستنا على مائة من المرضى الذين اجروا جراحة قلب مفتوح لعمل وصلات للشرايين التاجية و يعانون من الاعراض التي تستدعي عمل أشعة مقطعية على الشرايين التاجية متعددة المقاطع وذلك فى خلال عام فى مستشفى الحسين الجامعى ومعهد القلب القومى، حيث تم تقسيم المرضى الى مجموعتين كالتالى مجموعة (أ) مرضى بول سكرى (وتشمل ستين مريضا) ينقسمون بدورهم الى اثنين وثلاثين مريض لا يعتمدون على الانسولين وثمانية وعشرين مريضا يعتمدون على الانسولين ومجموعة (ب) مرضى لا يعانون من مرض البول السكرى (وتشمل اربعين مريض).

نتائج البحث: إرتفاع الضغط هو عامل الخطورة الاكثر شيوعا فى عينة المرضى الخاصه بالدراسة وذلك بنسبه تصل الى 55% يتبعه التدخين بنسبة 54% من اجمالى مرضى الدراسة. وقد اظهرت دراستنا ايضا ان نسبة الوصلات المسدوده اعلى بنسب هامة احصائيا فى مرضى الضغط وارتفاع نسبة الدهون من المجموعه (أ) عن اولئك من المجموعه (ب). بينما نسبة الوصلات المسدوده اعلى بنسب هامة احصائيا فى المدخنين من المجموعه ب عن اولئك من المجموعه أ. كما أظهرت الدراسة كذلك ان نسبة الوصلات المسدوده اعلى بنسب هامة احصائيا فى مرضى البول السكرى عن اولئك الذين لا يعانون من المرض. أظهرت الدراسة ايضا ان نسبة الوصلات الشريانيه المسدوده لا تختلف بشكل احصائى هام بين مرضى المجموعه ا والمجموعه ب ولكن العكس بالنسبة للوصلات الوريدية حيث ان نسبه الوصلات الوريدية المسدوده تزيد بشكل احصائى اكبر فى مرضى المجموعه (أ) عن المجموعه (ب).

الإستنتاج: مرضى البول السكرى اكثر عرضة لانسداد الوصلات للشرايين التاجية اكثر من المرضى الذين لا يعانون من البول السكرى سواء كانت الوصلات شريانية او وريدية. عدم تنظيم نسبة السكر بالدم وطول فترة المرض عاملان يؤثران بالسلب على سالكية وصلات الشرايين التاجية. نوع العلاج بالنسبة لمريض البول السكرى سواء انسولين او اقراص لا يؤثر على سالكية الوصلات. الوصلات الشريانية اقل عرضة للانسداد عن الوصلات الوريدية فى مرضى البول السكرى.