**Role of Dobutamine Stress Echocardiography in the Evaluation of Coronary Ischemia in Diabetic Patients Before and After Coronary Revascularization In Upper Egypt**

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## **Abstract**

## **Introduction:** Cardiovascular diseases are considered the leading cause of death in patients with diabetes in particular, coronary artery disease (CAD) is the cause of death in more than half of these patients. Diabetes is present in as many as 30% of patients hospitalized because of acute coronary syndromes and is associated with greater mortality during the acute phase of myocardial infarction and a higher morbidity in the post infarction period. Dobutamine stress echocardiography is a safe, cheap and reliable method for coronary artery disease diagnosis and viability and provides important long term prognostic information. The diagnostic accuracy and prognostic power of this technique has been validated by a number of studies on patients with and without diabetes.

## **Aim of the work:**To evaluate the role of the dobutamine stress echocardiography in the evaluation of coronary ischemia before and after coronary revascularization either with PCI (Percutenous Coronary Intervention) or CABG (Coronary Artery Bypass Grafting) in diabetic patients for the detection of the myocardial functional recovery and recurrent ischemia after coronary intervention in Sohag University Hospital.

## **Patients and Methods:** Study design: Prospective single center comparative non randomized clinical study.Patients: During the study period, 150 patients met inclusion criteria for Dobutamine Stress Echocardiography and divided according to the procedure of revascularization into three equal groups (each group involves 50 patients): Group A: Patients treated with CABG, Group B: Patients treated with PCI with DES and Group C: Patients treated with PCI with BMS. Also each group is subdivided into another subgroup according to the presence or absence of DM. Patients in our study, who matched with the selection criteria, were subjected to: 1-History taking and clinical Examination. 2-Laboratory Investigations: Serum glycated HbA1c, Serum creatinine and serum lipogram. 3- 12 lead surface ECG. 4- Baseline Resting Echocardiography. 5-Dobutamine Stress Echocardiography.

## **Result:** Comparing EF between the three groups at baseline (pre-procedure) and after 6 and 12 months post procedure, respectively revealed that EF improved in the three groups. Comparing EF between diabetic and non diabetic patients among the three groups both before procedure, and at 6 and 12 months post procedure showed significant differences in all figures, with diabetics showed always worse EF.Ischemic mitral regurge (IMR) was similar among the three groups at baseline, improved at 6 months and at 12 months; this improvement was highest among CABG, followed by PCI with DES and lastly among PCI with BMS. Comparing Wall motion abnormality (WMA) and Wall Motion Score Index (WMSI) between the three groups at baseline (pre-procedure), and after 6 and 12 months post-procedure, respectively revealed that WMA and WMSI improved in the three groups, but the improvement was higher among cases of the CABG and DES groups compared to BMS groups. Most of cases did not have complications including in addition overall mortality, and this is fixed in the three groups, with no significant difference. Regarding MACE between the three groups, the only significant difference was seen in target lesion revascularization (TLR) at 12 months, with CABG was the best group and BMS was the worst. There was no significant difference between DM and non DM patients in all groups as regards the occurrence of MACE. The only exception was TLR at 12 months, where diabetic patients were significantly worse than non diabetics in all groups. There was no significant difference between DSE positive and negative results in all groups as regards the occurrence of MACE. The only exception was TLR at 12 months, where DSE positive patients were significantly worse in diabetics than non diabetics in all groups.

## **Conclusion:** DSE is essential for the evaluation of coronary ischemia and the impact of different procedures of coronary revascularization in diabetic patients for the assessment of cardiac function and relations of the different parameters of the test to the follow up of improvement of the function and occurrence of MACE.

**Keyword**: Dobutamine, Stress echocardiography, Diabetes, Coronary Revascularization.

##

## **Introduction**

Cardiovascular diseases are considered the leading cause of death in patients with diabetes**(**[**1**](#_ENREF_1)**)**in particular, coronary artery disease (CAD) is the cause of death in more than half of these patients**(**[**2**](#_ENREF_2)**)**.

Diabetes is present in as many as 30% of patients hospitalized because of acute coronary syndromes and is associated with greater mortality during the acute phase of myocardial infarction and a higher morbidity in the post infarction period**(**[**3**](#_ENREF_3)**)**.

The risk of adverse outcome is independent of the conventional risk factors for CAD. Patients with diabetes but without other risk factors for atherosclerosis have a chance of death from CAD two to four times that of age-matched controls**(**[**4**](#_ENREF_4)**)**.

Most guidelines recommend a systematic screening of asymptomatic high risk patients with diabetes for silent ischemia, but the clinical benefit of this strategy has not been demonstrated compared with the simple control of cardiovascular risk factors**(5)**.

Dobutamine stress echocardio-graphy is currently used to predict recovery of regional and global left ventricular systolic function in patients with chronic coronary artery disease. Inotropic stimulation with dobutamine results in a transient amelioration of contractile dysfunction in viable myocardium which is highly predictive of functional recovery following revascularisation**(6)**.

Dobutamine stress echocardio-graphy is a safe, cheap and reliable method for coronary artery disease diagnosis and viability and provides important long term prognostic information. The diagnostic accuracy and prognostic power of this technique has been validated by a number of studies on patients with and without diabetes**(7)**.

##  ***Aim of the work***

To evaluate the role of the dobutamine stress echocardiography in the evaluation of coronary ischemia before and after coronary revascular-ization either with PCI (Percutenous Coronary Intervention) or CABG (Coronary Artery Bypass Grafting) in diabetic patients for the detection of the myocardial functional recovery and recurrent ischemia after coronary intervention in Sohag University Hospital.

##  ***Patients and Methods***

## **Study design:** Prospective single center comparative non randomized clinical study.

**Patients:**During the study period, 150 patients met inclusion criteria for Dobutamine Stress Echocardiography and divided according to the procedure of revascularization into three equal groups (each group involves 50 patients): Group A: Patients treated with CABG, Group B: Patients treated with PCI with DES and Group C: Patients treated with PCI with BMS.Also each group is subdivided into another subgroup according to the presence or absence of DM

The study was done at SohagCathlab Unit of Internal Medicine Department, Sohag University Hospital during the period from 1/1/2013 to 1/11/2014. The study has been approved from Ethical Review Committee for Human Research at Sohag Faculty of Medicine, and informed written consent was taken from all included patients.

**Inclusion criteria:**Diabetic and Non Diabetic Patients with symptomatic ischemic heart disease. Those with limited exercise tolerance.Poor ECG criteria for detection of ischemia .Echocardiography with regional wall motion abnormalities at rest in one or more myocardial segments .

**Exclusion criteria:** Patients with contraindications to DSE and are related to the administration of dobutamine and include:Ventricular arrhythmias, Recent myo­cardial infarction , unstable angina, significant left ventricular outflow obstruction, Aortic dissec­tion.Severe hypertension, Signiﬁcant valvular heart disease. Contraindication to cardiac catheterization, Congenital or rheumatic heart disease, and malignacy.

**Methods:** Patients in our study are matched as regarding age, sex and other cardiovascular risk factors (Hypertension, Smoking, Family history of CAD, Dyslipidemia, obesity) with no significant difference between groups.

Patients in our study, who matched with the selection criteria, were subjected to:

1-History taking and clinical Examination.2-Laboratory Investigat-ions: Serum glycated HbA1c, Serum creatinine and serum lipogram. 3- 12 lead surface ECG . 4- Baseline Resting Echocardiography:The Echocardio-graphies were performed with Vivid S5 instruments, GE, USA with a 2.5-MHz transducer and harmonic imaging with split-screen and quadruple-screen display to facilitate simultaneous compari­son from rest to peak to post-stress images and have the ability to trigger image acquisition based on the ECG.

All echocardiographic results were obtained as a baseline before revascularization.

**Dobutamine Stress Echocadiography:** Patients typically fast for 4 hours prior to the test. All negative chronotropic agents and nitrates should be held 8–12 hours before DSE**.** During a DSE, images of the left ventricle at each echocardio-graphic window are obtained during rest, low-dose dobutamine, peak-dose dobuta-mine, and post-stress. After doing resting Echocardiography; A graded dobutamine infusion is given typically at a starting dose of 5 μg/kg per minute using a mechanical infusion pump. The goal of the dobu­tamine infusion is to achieve a heart rate 85% of the maximal predicted heart rate for the patient’s age. Accordingly; Thedobutamine dose is increased every 3–5 minutes to doses of 10, 20, and 30, and finally to 40 μg/kg per minute.

**Categorization of wall motion abnormalities:**The left ventricular wall was divided into 16 segments and scored using a 4-point scale: 1=normal, 2=hypokinetic,3=akinetic,4=dyskineticA wall motion score index (WMSI) was calculated by adding the numeric value assigned to each segment and dividing by the number of visualized segments. An inducible wall motion abnormality was deﬁned as wall motion worsening in two or more segments.The test was considered positive in case of worse wall motion in dysfunctional segments or new wall motion abnormalities in normokinetic segments. Also we consider evaluation of the possible complications of the test and evaluation of Major Advanced Cardio and/or Cerebrovascular events which includes Death, MI, Stroke and TLR(Target Lesion Revasculari-zation)**(8)**.

**Coronary Revascularization:*Either by Coronary Angiography and PCIor Coronary artery bypass graft (CABG).***

*The Groups are followed up for one year (at 6months then at 12 months) to assess:*

1. Degree of improvement of LV sys-tolic function measured by ejection fraction by DSE to evaluate the impact of the procedure in comparison to the presence or absence of diabetes.
2. Evaluation of wall motion abnormalities.
3. Evaluation of wall motion score index.
4. Evaluation of the impact of the procedure on IMR.
5. Evaluation of the complications of the test.
6. Assessment of complications including in-stent restenosis and graft occlusion.
7. Relation of the different procedures regarding the presence or absence of diabetes to MACE.

**Statistical analysis**

Statistics: Data were collected and analyzed using Statistical Package for Social Science (SPSS). P value was considered insignificant if > 0.05, significant if < 0.05, and highly significant if < 0.01.

## **Results**

Our study included 150 patients, divided into three equal groups, one group treated with CABG, another with PCI with DES and a third treated with PCI and BMS. Each group was divided into two subgroups according to the presence or absence of diabetes mellitus (DM). According to this division, each group was divided into subgroup I (DM) and II (non DM) Table 1.

**Table 1. Groups of the study**

|  |  |  |  |
| --- | --- | --- | --- |
| ***Group*** | ***Subgroup*** | ***Number*** | ***%*** |
| **Group A (CABG)** | **AI (DM)** | **20** | **40%** |
| **AII (non DM)** | **30** | **60%** |
| **Group B (PCI with DES)** | **BI (DM)** | **21** | **42%** |
| **BII (non DM)** | **29** | **58%** |
| **Group C (PCI with BMS)** | **CI (DM)** | **18** | **36%** |
| **CII (non DM)** | **32** | **74%** |
| **Total** | **150** | **-** |

**Chi square = 0.391, P value = 0.822 (NS)**

The mean age of the study groups was around 55.5±6 years, with no significant difference between the three groups. More than 75% of cases were males, with no significant difference between the groups. No significant difference as regard smoking, hypertension, family history, obesity, dyslipidemia and duration of diabetes.

No significant differences as regarding laboratory investigation. The only exception is the significant difference between diabetic and non diabetic patients in HbA1c (*p* value<0.001). Also no significant differences in ECG findings.

Comparing EF between the three groups at baseline (pre-procedure) and after 6 and 12 months post-procedure, respectively revealed that EF improved in the three groups (P value=0.032), but the improvement was higher and more rapid among cases of the CABG (44±4.3 at baseline to 57.3±5 at 12 months, *p* value =0.015)and DES (44.3±3.6.3 at baseline to 56.8±6.6 at 12 months, *p* value=0.039 ) group compared to BMS groups. With no significant changes between CABG and PCI with DES groups (*p* value=0.69).Comparing EF between diabetic and non diabetic patients among the three groups both before procedure, and at 6 and 12 months post-procedure showed significant differences in all figures (*p* value<0.001), with diabetics showed always worse EF. Also, diabetic patients showed delayed improvement as shown by the less improvement at 6 months Table 2.

**Table 2. Comparison between baseline ejection fraction among the three groups**

|  |  |  |  |
| --- | --- | --- | --- |
| **Procedure** | **Baseline EF** | **EF at 6 months** | **EF at 12 months** |
| **CABG** | **44.092±4.303** | **54.180±5.110** | **57.337±5.023** |
| **PCI with DES** | **44.334±3.651** | **53.700±5.738** | **56.885±6.630** |
| **PCI with BMS** | **44.364±3.068** | **51.615±7.287** | **54.480±5.571** |
| **P values** | **CABG vs DES** | **0.745** | **0.695** | **0.696** |
| **CABG vs BMS** | **0.715** | **0.038** | **0.015** |
| **DES vs BMS** | **0.968** | **0.049** | **0.039** |
| **All groups** | **0.923** | **0.087** | **0.032** |

Ischemic mitral regurge (IMR) was similar among the three groups at baseline, improved at 6 months and at 12 months; this improvement was highest among CABG, followed by PCI with DES and lastly among PCI with BMS Table 3.

**Table 3. IMR among the three groups**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Procedure** | **Total** | **P value** |
|  **CABG** | **PCI with DES** | **PCI with BMS** |
| **Baseline IMR** | **No** |  | **35** | **32** | **33** | **100** | **0.371 (NS)** |
| **Mild** |  | **9** | **9** | **8** | **26** |
| **Moderate** |  | **6** | **9** | **9** | **24** |
| **IMR at 6 months** | **No** |  | **42** | **39** | **34** | **115** | **0.105 (NS)** |
| **Mild** |  | **5** | **7** | **9** | **22** |
| **Moderate** |  | **3** | **4** | **7** | **13** |
| **IMR at 12 months** | **No** |  | **43** | **45** | **35** | **124** | **0.090**  |
| **Mild** |  | **4** | **4** | **10** | **19** |  **(NS)** |
| **Moderate** |  | **3** | **1** | **5** | **7** |  |

Comparing Wall motion abnormality (WMA) and Wall Motion Score Index (WMSI) between the three groups at baseline (pre-procedure), and after 6 and 12 months post procedure, respectively revealed improvement in WMA (*p*value=0.017)and WMSI (*p* value<0.001) in the three groups, but the improvement was higher among cases of the CABG and DES groups compared to BMS groups (*p* value<0.001 compared to CABG and 0.026 compared to PCI with DES) At 12 months.There was no significant difference between CABG and PCI with DES groups (*p* value=0.103).

Comparing WMA and WMSI between diabetic and non diabetic patients among the three groups both before procedure and at 6 and 12 months post-intervention showed significant differences in all figures, with diabetics showed worse WMSI. The only exception is the difference between DM and non DM cases at 6 months of BMS group.Comparing WMA and WMSI between before procedure, and at 6 and 12 months post-procedure among diabetic and non diabetic patients of the three groups showed significant to highly significant differences in all figures (*p* value< 0.001). The only exception was the comparison between baseline and after 6 months WMSI and WMA among PCI with BMS which showed no significant difference in both the diabetic and non diabetic groups (*p* value=0.147) Table 4,5.

**Table 4. Wall motion abnormality (WMA) among the three groups**

|  |  |  |
| --- | --- | --- |
|  | **Procedure** | **P value** |
| **CABG** | **PCI with DES** | **PCI with BMS** |
| **Baseline WMA** | **Akinesia** |  | **2(4%)** | **1(2%)** | **0** | **0.657 (NS)** |
| **Hypokinesia** |  | **41(82%)** | **41(82%)** | **44(88%)** |
| **Normal** |  | **7(14%)** | **8(16%)** | **6(12%)** |
| **WMA at 6 months** | **Akinesia** |  | **1(2%)** | **1(2%)** | **0** | **0.272 (NS)** |
| **Hypokinesia** |  | **34(68%)** | **36(72%)** | **43(86%)** |
| **Normal** |  | **15(30%)** | **13(26%)** | **7(14%)** |
| **WMA at 12 months** | **Akinesia** |  | **0** | **0** | **0** | **0.017 (S)** |
| **Hypokinesia** |  | **25(50%)** | **27(54%)** | **38(76%)** |
| **Normal** |  | **25(50%)** | **23(46%)** | **12(24%)** |

**Table 5. Comparison between WMSI among the three groups**

|  |  |  |  |
| --- | --- | --- | --- |
| **Procedure** | **Baseline WMSI** | **WMSI at 6 months** | **WMSI at 12 months** |
| **CABG** |  | **19.88±2.66** | **18.14±1.55** | **17.62±1.31** |
| **PCI with DES** | **19.98±2.16** | **18.30±1.76** | **18.10±1.42** |
| **PCI with BMS** | **19.50±1.95** | **19.34±1.89** | **18.76±1.65** |
| **P values** | **CABG vs DES** | **0.826** | **0.647** | **0.103** |
| **CABG vs BMS** | **0.405** | **0.001** | **<0.001** |
| **DES vs BMS** | **0.455** | **0.003** | **0.026** |
| **All groups** | **0.540** | **<0.001** | **<0.001** |

Most of cases did not have complications including in addition overall mortality, and this is fixed in the three groups, with no significant difference (*p* value=0.352). The non significance difference in graft occlusion may be due to the limited number of graft occlusion cases (only 4 cases) (*p* value=0.641) Figure 1.



**Figure 1:** Complications of Dobutamine Stress Echocardiography

There was significant difference between PCI with DES and PCI with BMS

groups as regards in-stent stenosis, with more cases in the PCI with BMS group developed in stent stenosis compared to PCI with DES. More cases who developed in-stent restenosis were diabetic, in both of the PCI with DES and PCI with BMS groups. The difference was significant in both groups (*p* value=0.045).

Regarding MACE between the three groups, the only significant difference was seen in target lesion revascularization (TLR) at 12 months, with CABG was the best group and BMS was the worst (*p* value=0.031). There was no significant difference between DM and non DM patients in all groups as regards the occurrence of MACE. The only exception was TLR at 12 months, where diabetic patients were significantly worse than non diabetics in all groups (*p* value=0.037). There was no significant difference between DSE positive and negative results in all groups as regards the occurrence of MACE. The only exception was TLR at 12 months, where DSE positive patients were significantly worse in diabetics than non diabetics in all groups (*p* value=0.002) Table 6.

**Table 6. Comparison between the three groups as regards MACE**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| ***MACE*** | ***CABG*** | ***PCI with DES*** | ***PCI with BMS*** | ***P value*** |
| **MACE at baseline** | **Death** | **0** | **0** | **0** | **1** |
| **MI** | **0** | **0** | **0** | **1** |
| **Stroke** | **0** | **0** | **0** | **1** |
| **TLR** | **0** | **0** | **0** | **1** |
| **MACE at 6 months** | **Death** | **0** | **0** | **0** | **1** |
| **MI** | **0** | **4** | **1** | **0.067** |
| **Stroke** | **0** | **0** | **0** | **1** |
| **TLR** | **2** | **2** | **6** | **0.180** |
| **MACE at 12 months** | **Death** | **0** | **0** | **0** | **1** |
| **MI** | **0** | **0** | **0** | **1** |
| **Stroke** | **0** | **0** | **0** | **1** |
| **TLR** | **4** | **7** | **15** | **0.031** |

##

## **Discussion**

The present study aims to compare the short & intermediate term role of dobutamine stress echocardio-graphy in evaluation of coronary ischemia in diabetic and non diabetic patients before and after coronary revascularization either by CABG or PCI (with DES or BMS).

Our patients were cross matched as regard age, sex, CV risk factors, ECG findings and duration of diabetes with no significant difference between groups and this is related to the limited number of patients included in the study and this similar to a study done by ***AbdouElhendy et al*(9))** But there was a significant difference between diabetic and non diabetic groups with a considerable large number of patients as in a study done by ***Cortigiani et al*(10)**

Most of cases did not have complications including in addition overall mortality, and this is fixed in the three groups, with no significant difference. This is similar to that documented by ***Lauren Gray et al*(**[**11**](#_ENREF_20)**)**

EF was improved in the three groups, but the improvement was higher and more rapid among cases of the CABG and DES groups compared to BMS groups. There was significant differences between EF of CABG and BMS groups at 6 and 12 months, and between DES and BMS at 6 and 12 months, which showed a significant difference in favor of CABG and DES; respectively. Also comparing EF between diabetic and non diabetic patients among the three groups both before procedure, and at 6 and 12 months post-procedure showed that diabetic patients had delayed improvement as shown by the less improvement at 6 months, this is similar to a study done by ***Cortigiani et al* (**[**12**](#_ENREF_11)**)**and ***Ferro et al* (**[**13**](#_ENREF_24)**)**to evaluate the interaction between prognostic effect of revascularization and viability in diabetic and non-diabetic patients with ischaemic left ventricular dysfunction.

There was no significant downgrading improvement in MR severity after revascularization by either CABG or PCI due to limited number of positive cases with IMR, this is similar to a study done by [***Roshanali F***](http://www.ncbi.nlm.nih.gov/pubmed/?term=Roshanali%20F%5BAuthor%5D&cauthor=true&cauthor_uid=24518225) ***et al*(**[**14**](#_ENREF_25)**)**

Wall motion abnormality (WMA) and WMSI (Wall Motion Score Index) was similar among the three groups at baseline, improved at 6 months and at 12 months; this improvement was highest among CABG, followed by PCI with DES and lastly among PCI with BMS. With significant improvement at 12 months post-procedure,with high improvement among CABG and PCI with DES versus PCI with BMS. Also regarding the presence or absence of DM showed that significant improve-ment occurred among non diabetic patients in the three groups, and only among CABG diabetic patients, while non significant difference was seen among other diabetic patients, this is similar to those done by ***Chaowalit et al***([15](#_ENREF_26)) who showing significant improvement of WMA and WMSI after coronary revascularization with better results regarding procedure with CABG or PCI with DES.

At 1 year follow up there was no significant difference in incidence of mortality, MI and stroke between both groups. The total MACE was higher in PCI group than CABG group. This was largely attributed to higher rate of repeat revascularization in the PCI patients than in CABG patients. As regard the outcomes in the PCI group according to the type of stent used, our study found that the overall MACE was significantly higher in patients treated with BMS than in patients treated by DES. there was non significant difference between DM and non DM patients in all groups as regards the occurrence of MACE. The only exception was TLR at 12 months, where diabetic patients were significantly worse than non diabetics in all groups, also there was significant difference as regarding In-stent restenosis in diabetic patients treated with DES over those treated with BMS, these are similar to a study done by ***Hoffman et al*(**[**16**](#_ENREF_27)**)**and ***Hlatky et al(17)***who reported in a meta-analysis of various studies that there were no significant differences in one-year or three-year mortality rates between the two procedures but did find that in patients who underwent CABG who had significantly fewer subsequent revascularizations than patients who underwent stenting with BMS which coincides with our results.

There was no significant difference between DSE positive and negative results in all groups as regards the occurrence of MACE. The only exception was TLR at 12 months, where DSE positive patients were significantly worse in diabetics than non diabetics in all groups.This is similar to study done by ***Cortigiani et al* (7)**who  found that stress echocardiography was effective in riskstratifyingdiabeticandnon-diabeticpatients.However, major event rates associated with a non ischemic test result were similar indiabeticandnon diabeticpatients during the first year of follow-up and markedly increased in the former thereafter.

## ***Study limitation***

1. Non randomization in choosing the type of selection of patients revascularization procedure.
2. Relatively small number of patients included in this study.
3. Studying the short and intermediate outcomes only.

## ***Conclusionand Recommendation***

## DSE is essential for the evaluation of coronary ischemia and the impact of different procedures of coronary revascularization in diabetic patients for the assessment of cardiac function and relations of the different parameters of the test to the follow up of improvement of the function and occurrence of MACE.

In diabetic patients successful revascularization either with CABG or PCI with DES improves ejection fraction, ischemic mitral regurgitation, wall motion abnormalities, wall motion score index and occurrence of MACE in symptomatic patients in short and intermediate follow-up comparable to PCI with BMS.

Good selection of patients with favorable angiographic characteristics in diabetic patients treated by PCI or CABG enhance success rate and decrease the complications and overall MACE.

Dobutamine stress echocardio-graphy is an essential test for better cardiac evaluation and assessment of coronary ischemia before and after coronary revascularization.

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