

Coronary Artery Disease Patterns in Diabetic Patients

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Abstract

Background: Cardiac involvement in diabetes usually manifest as coronary artery disease which is the main cause of mortality in diabetes. Definitive diagnosis, accurate assessment and anatomic severity of coronary artery disease requires invasive diagnostic tool like coronary angiography. **Aim of study:** We aimed to compare angiographic extents, type, number of vessels and SYNTAX score between acute coronary syndrome patients with and without diabetes. **Patients and Methods:** Prospective comparative study on 100 patients with acute coronary syndrome (50 patients with diabetes, and 50 patients without diabetes) were recruited to evaluate detailed angiographic coronary findings. **Results and conclusion:** A significant correlation was found between the degree of lesion complexity with both the number of vessels affected and the duration of diabetes mellitus. The higher the number of vessels affected and the longer the diabetes mellitus duration, the more complex is the lesion. Diabetes has a deleterious effect on the anatomy of coronary arteries, causing more multi-vessel and extensive coronary artery disease as well as higher SYNTAX score than in patients without diabetes.

Keywords: Coronary artery disease, diabetes mellitus, acute coronary syndrome, SYNTAX score

Background

A high incidence of cardiovascular diseases including coronary artery diseases (CAD) and an increased risk of cardiovascular death was found in diabetic patients(1) and is considered the main cause of mortality in such patients(2).

Diabetes mellitus (DM) can affect the heart in 3 ways: 1- Accelerated atherosclerosis leading to CAD; 2- cardiac autonomic neuropathy; and 3- diabetic cardiomyopathy(3).

Invasive coronary angiography is considered the gold standard modality for diagnosis, detecting the location, and severity of CAD (4 & 5).

The SYNTAX score (SX score) is a full-scale angiographic scoring system derived entirely from the anatomy of coronary arteries and their characteristic lesions(6, 7). It was initially designed to quantify lesion complexity; however, it was found to predict major cardiac adverse events following percutaneous revascularization in patients with left main disease (8) and/or multi-vessel CAD (9-11).

Methods

Participants

100 patients were recruited between August 2018 and August 2019 presented with acute coronary syndrome (ACS). 50 patients of them have type 2 diabetes (group D) and 50 patients are non-diabetic (control group) (group C). All patients underwent coronary angiography.

Study design

The study was a single-center prospective study that was carried out to evaluate detailed angiographic coronary findings by studying angiographic extents, type of vessels, number of vessels and complexity of CAD by using the SX score in patients with ACS and compare those findings between patients with and without diabetes.

All patients presented to the cardiology department in Mansoura university hospital with chest pain, diagnosed as ACS and underwent elective coronary angiography were recruited in our study, either diabetic or non-diabetic. Patients who refused to sign consent to share in the study, with non-interpretable coronary angiography or

inadequate imaging of the coronary artery were excluded.

All patients were subjected to history taking with emphasis on age, gender, occupation, analysis of chest pain including timing, risk factors of CAD (hypertension, DM, dyslipidemia, cigarette smoking) and history of any medication. Any patient with ≥ 140 mmHg systolic and/or ≥ 90 mmHg diastolic blood pressure was considered hypertensive (12) or current treatment with blood pressure-lowering medications. Diabetes was defined by prior diagnosis with current antidiabetic medications, Hemoglobin A1C $\geq 6.5\%$, Fasting plasma glucose ≥ 126 mg/dL, 2-hour plasma glucose or random plasma glucose ≥ 200 mg/dl in a patient with classic symptoms of hyperglycemia (i.e. polydipsia, polyphagia, polyuria, weight loss) or hyperglycemic crisis. Dyslipidemia was defined by prior diagnosis with current cholesterol-lowering medications, or fasting serum cholesterol >175 mg/dl, low density lipoprotein (LDL) $> 160-189$ mg/dl and high-density lipoprotein (HDL) cholesterol <40 mg/dl, triglycerides levels >150 mg/dl(13). Smokers were defined as current smokers. All patients underwent clinical examination with emphasis on pulse, blood pressure and local cardiac examination,

biochemical assessment with venous blood samples taken from each patient at the time of admission (Blood glucose, serum creatinine, complete blood count and troponin I values of each patient were recorded), electrocardiogram (ECG) and coronary angiography that was performed in a single session at our center using Philips Allura FD 20 Machine (Germany) via femoral artery approach or radial access approach by experienced interventional cardiologists with subsequent analysis including the angiographic extents, number of vessels, type of vessels, severity of lesion involving coronary artery and its branches and Assessment of Coronary Artery Stenosis by SX Score. The decision-making for percutaneous coronary intervention (PCI) strategy, coronary artery bypass graft (CABG), or medical treatment was left taken by the interventional cardiologist who is a consultant at the cardiology department.

Statistical analysis of the data

Statistical analysis was carried out by the use of SPSS 21. Numerical data are presented as mean \pm SD for parametric data, median (interquartile range) for continuous variables with non-parametric distributions and as percentages for

categorical variables. Comparison between the two groups was tested using Student t test for parametric data and Mann Whitney test for non-parametric data. Qualitative data were described using number and percent. Association between categorical variables were checked using Chi-square test and when the expected cell count is less than 5, Fischer exact test was used.

Ethics approval and consent to participate

The study was approved by the Local Ethical Committee of Faculty of Medicine, Mansoura University. The committee reference number is not applicable. A written informed consent was obtained from all patients. The study was carried out in accordance with the Declaration of Helsinki and the principles of good clinical practice. There were adequate provisions to maintain privacy of participants and confidentiality of the data, and the names of participants were hidden and replaced by code numbers. We used the results of the research only for scientific purposes and not any other aim.

Results

Epidemiology

Patients with diabetes and ACS are 31 males (62%) and 19 females (38%), with

mean age ranges 48 ± 8 , 60% (30 cases) were treated with insulin, 34% (17 cases) were treated with oral anti-hyperglycemic medications and only 6% (3 cases) were on combined therapy.

Peak incidence of ACS in the diabetic group (group D) was in the third and fourth decade compared to fifth and sixth decade in group C. The incidence of ACS in group D was 62% in males versus 38% in females and in group C was 80% in males versus 20% in females, so, the risk of developing ACS in females was more in those with diabetes compared to those without.

Hypertension was the most prevalent risk factor, affecting 41 diabetic patients (82%) and 29 non-diabetic patients (58%), smoking was the second most prevalent risk factor affecting 9 diabetic patients (18%) and 17 non-diabetic patients (34%), while dyslipidemia was presented in 4 diabetic patients (8%) and 2 non-diabetic patients (4%). **Table.1**

Disease pattern

ECG Interpretation: Most of our study population presented with normal ECG 32 patients (64%) in group D, 34 patients (68%) in group C, ST-Elevation Myocardial Infarction (STEMI) was seen in [10 patients in group D (20%) and 7

patients in group C (14%)], Non-ST-Elevation Myocardial Infarction (NSTEMI) was seen in [5 patients in group D (10%) and 3 patients in group C (6%)], while other ECG interpretations such as Left Bundle Branch Block (LBBB), Atrial Fibrillation were recorded in only [3 patients in Group D (6%) and 6 patients in group C (12%)].

Character of chest pain: Typical chest pain was noticed in group C (37 patients, 74%) more than Group D (32 patient, 64%), while Atypical chest pain was noticed in Group D (18 patient, 36%) more than group C (13 patient, 26%).

Laboratory findings

In Group D minimum level of Random blood sugar (RBS) was 130 mg/dl, and the maximum was 503 mg/dl (mean= 259.72 ± 81.96 mg/dl), while in group C the minimum level of RBS was 73 mg/dl and the maximum was 161 mg/dl (mean= 103.58 ± 17.46 mg/dl).

Regarding the low density lipoprotein (LDL) the minimum level in Group D was 80u/l and the maximum was 305u/l (mean= 147.36 ± 48.61 u/l), while in group C The minimum level was 66 u/l and the maximum was 270u/l (mean= 125.06 ± 29.64 u/l).

Angiographic findings

Site of culprit lesion among studied patients: Normal left main coronary artery (LMCA) was found in 43 patients (86%) in Group D versus 30 in group C (60%), while <50% lesion was found in 4 patients in Group D (8%) versus 17 in group C (34%) , 50-70% lesion was found in 3 patients in Group D (6%) versus 2 patients in group C (4%) , Ectatic LMCA was found only in 1 patient in group C (2%),

Table.2.

Normal left anterior descending (LAD) was found in 14 patients in Group D (28%) versus 15 in group C (30%), while <50% lesion was found in 6 patients in Group D (12%) versus 13 in group C (26%) , 50-70% lesion was found in 7 patients in Group D (14%) versus 8 in group C (16%) , >70% lesion was found in 22 patients in Group D (44%) versus 13 in group C (26%), ectatic LAD was found in only 1 case in both groups (2%), **Fig.1.**

Normal left circumflex (LCX) was found in 29 patients in Group D (58%) versus 18 in group C (36%), while <50% lesion was found in 5 patients in Group D (10%) versus 19 in group C (38%) , 50-70% lesion was found in 6 patients in Group D (12%) versus 5 in group C (10%) , >70%

lesion was found in 9 patients in group D (18%) versus 7 in group C (14%), Ectatic LCX was found in only 1 case in both groups (2%), **Table.3**

Normal right coronary artery (RCA) was found in 25 patients in Group D (50%) versus 18 in group C (36%), while <50% lesion was found in 4 patients in Group D (8%) versus 20 in group C (40%), 50-70% lesion was found in 2 patients in Group D (4%) versus 5 in group C (10%), >70% lesion was found in 17 patients in Group D (34%) versus 6 in group C (12%), Ectatic RCA was found in only 1 patient in both groups (2%), and **posterior descending artery** occlusion was found in 1 patient in Group D (2%), **Table.4.**

Management

By comparing the results, PCI was done in 31 cases of Group D (62%) and in 22 cases of group C (44%), while CABG was done in 9 cases of Group D (18%) and 5 cases of group C (10%), normal coronary angiography was found in 11 cases of group C (22%) and 1 case of Group D (2%), finally, 9 cases of Group D (18%) and 12 case of group C (24%) were managed medically **Fig.2.**

Syntax Score

The median value of syntax score in Group D was 11 (0.0-29), versus 4.50 (0.027) in group C. **Fig.3** with higher intermediate syntax score (22-33) in diabetic patients (5 cases (10%) in Group D vs 2 cases (4%) in group C) and higher low syntax score (<22) in group C (48 cases (96%) in group C vs 45 cases (90%) in group D).

Correlation between Numbers, Severity of vessels affected and duration of diabetes

There are three major classifications of lesion severity; type A (low risk) lesions which are discrete, concentric with no calcification or thrombus, type C (high risk) lesions which are diffuse with excessive tortuosity and chronic total occlusion and type B (medium risk) lesions with characteristics in between type A and C. (14). In this study, the majority of the cases had one vessel disease who are subcategorized into Type A Lesion (6 cases, 54.5%), Type B Lesion (16 cases, 57.1%), and Type C Lesion (15 cases, 48.4%). Twenty-one cases had two vessel disease subcategorized into Type A Lesion (5 cases, 45.5%), Type B Lesion (10 cases, 35.7%), and Type C Lesion (6 cases, 19.4%). Twelve cases had three vessel disease subcategorized into Type B Lesion

(2 case, 7.1%), and Type C Lesion (10 cases, 32.3%). **Table.5, Fig.4**

There is a statistically significant correlation between duration of DM and type of Lesion with p value = 0.043

Table 1. Risk Factors among the studied groups

Factors	DM group Risk (n=50)		Control group (n=50)		P-value
	No.	%	No.	%	
HTN	41	82.0	29	58.0	0.009*
Smoking	9	18.0	17	34.0	0.087
Dyslipidemia	4	8.0	2	4.0	0.678

* :significant p <0.05 DM; diabetes mellitus

Table 2. LMCA as the site of culprit lesion among the studied groups

LMCA as the Site of lesion	DM group (n=50)		Control group (n=50)		P-value
	No.	%	No.	%	
Normal	43	86.0	30	60.0	0.009*
<50%	4	8.0	17	34.0	
50-70%	3	6.0	2	4.0	
Ectatic	0	0	1	2.0	

LMCA: left main coronary artery; *: significant p <0.05 DM; diabetes mellitus

Table 3. LCX as the site of lesion among the studied groups

Degree of LCX stenosis	DM group (n=50)		Control group (n=50)		P-value
	No.	%	No.	%	
Normal	29	58.0	18	36.0	0.026*
<50%	5	10.0	19	38.0	
50-70%	6	12.0	5	10.0	
>70%	9	18.0	7	14.0	
Ectatic	1	2.0	1	2.0	

LCX; left circumflex; *: significant p <0.05 DM; diabetes mellitus

Table 4. RCA as the site of lesion among the studied groups

Degree of RCA stenosis	DM group (n=50)		Control group(n=50)		P-value
	No.	%	No.	%	
Normal	25	50.0	18	36.0	0.002*
<50%	4	8.0	20	40.0	
50-70%	2	4.0	5	10.0	
>70%	17	34.0	6	12.0	
Ectatic	1	2.0	1	2.0	
PDA occluded	1	2.0	0	0	

RCA: right coronary artery; PDA: posterior descending artery; *: significant p <0.05 DM; diabetes mellitus

Table 5. Type of lesion in relation to number of vessels affected and duration of DM among all study population.

P-value	Type of lesion			
	A	B	C	
No. of vessels				
single	6 (54.5%)	16 (57.1%)	15 (48.4%)	0.037*
2 vessels	5 (45.5%)	10 (35.7%)	6 (19.4%)	
3 vessels	0 (0.0%)	2 (7.1%)	10 (32.3%)	
Duration of DM	9.5 (5-26)	10 (4-26)	19 (6-30)	0.043*

*: significant p <0.05 DM; diabetes mellitus; type A: discrete (<10 mm) concentric non-angulated segment <45° smooth contour little or no calcification less than totally occlusive not ostial in location no major branch involvement absence of thrombus; type B: tubular (10-20 mm) eccentric moderate tortuosity of proximal segment moderately angulated, 45-90° irregular contour moderate to heavy calcification ostial in location bifurcation lesions requiring double guidewires some thrombus present; type C: diffuse excessive tortuosity of proximal segment extremely angulated, >90° inability to protect major side branch degenerated vein graft with friable lesions

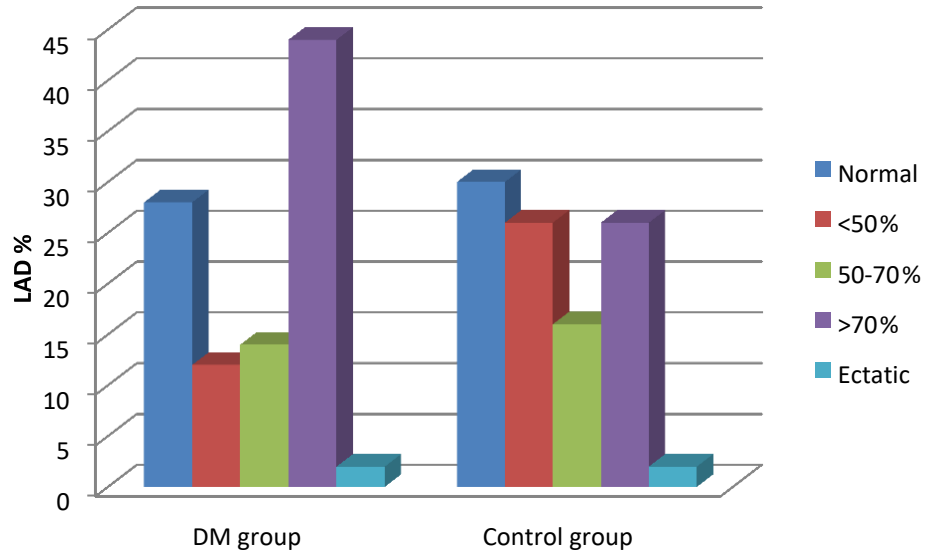


Figure 1. LAD affection among studied groups.

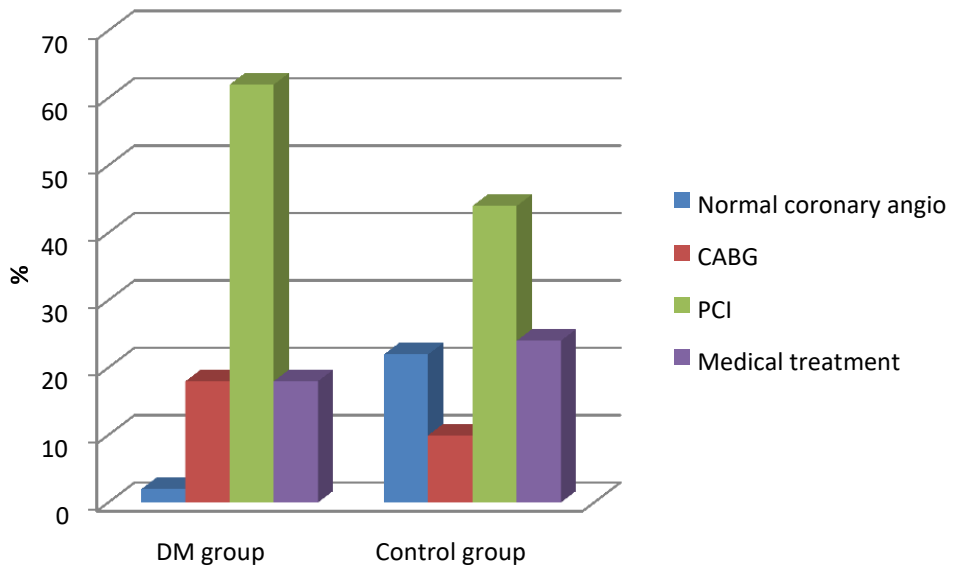


Figure 2. Management among the studied groups

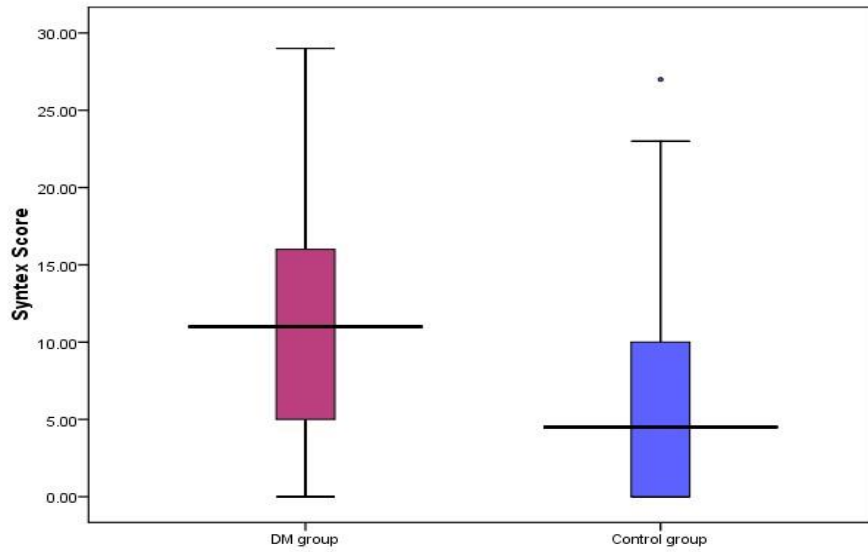


Figure 3. Box plot for median SYNTAX Score among diabetics and control.

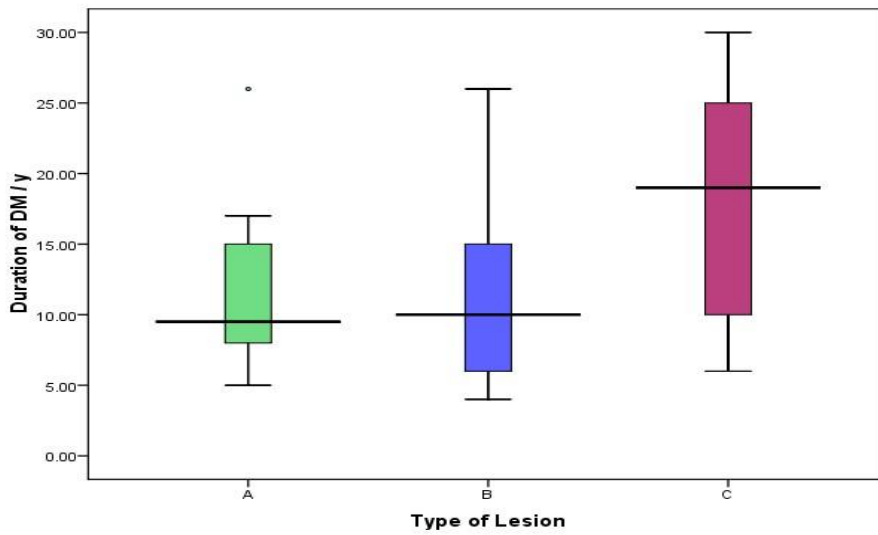


Figure 4. Box plot for median DM duration among diabetics and control.

Discussion

This is an observational case-control study that enrolled 100 patients with ACS who were subjected to coronary angiography to compare detailed angiographic coronary findings between patients with and without diabetes.

Diabetes and hypertension are known risk factors leading to atherosclerosis and its comorbidity, including strokes and heart attacks. There is a true overlap between diabetes and hypertension, reflecting overlap in their etiology and disease mechanisms. In the Hong Kong Cardiovascular Risk Factor Prevalence Study, only 42% of people with diabetes were normotensive and only 56% of people with hypertension were not diabetic(15). In the United States population, hypertension occurs in nearly 30% in patients with type 1 diabetes and in 65 % in patients with type 2 diabetes(16). Another study in the United States reported that hypertensive patients were almost 2.5

times as likely to develop type 2 diabetes as in normotensive subjects(17).

In reality, the occurrence of both hypertension and diabetes together in the same patient are found more often than would occur by chance(18).

This is very concordant with our study findings, in which age, gender and all conventional risk factors except for prevalence of hypertension weren't statistically significantly differ between the study groups. Hypertension was significantly prevalent among diabetic than non-diabetic patients.

In diabetes, dyslipidemia is an important risk factor leading to cardiovascular morbidity and is dominated by hypertriglyceridemia, and low levels of HDL. Although average levels of LDL may not be increased, higher levels of small dense LDL found in diabetic patients are

contributing to atherogenesis with subsequent progression of atherosclerosis(19).

This is somehow concordant to our study findings, in which LDL levels were significantly higher in patients with diabetes than those without diabetes.

In our study, the type of ACS wasn't a variable of statistical difference between diabetics and non-diabetics, in which STEMI was present in 20% and NSTEMI in 10% of the diabetic population.

In a previous large-scale retrospective study including 3242 patients admitted with ACS, to investigate the prevalence of DM among ACS patients and the effect of DM on patient's outcome. Type 2 DM was found among 31.5% of the overall population, and a higher prevalence (37%) was found among patients with STEMI(20).

In another study, conducted on 514 Iranian patients with acute coronary events to assess

the presence of DM and other conventional risk factors for coronary heart disease. Twenty four percent had myocardial infarction and 76% had unstable angina. Myocardial infarction was more prevalent among patients with diabetes (36.4% vs. 19.2%, $P < 0.001$)(21).

Diabetic patients have a wide range of atypical presentations and more frequently asymptomatic due to diminished awareness of ischemic chest pain which makes CAD diagnosis to be challenging (22).

Although not reaching the level of statistical significance, in our study, atypical presentation was more prevalent in people with diabetes than in those without diabetes (36% vs 26%).

In a previous large scale study, reviewing the angiography registry of 18137 patients with ACS or stable angina aiming to investigate the prevalence of significant stenosis of LMCA among patients with ACS or stable angina and assess the influence of

demographic and clinical profiles on these findings. They found that DM was an independent risk factor of LMCA stenosis (23).

However, in our study, normal LMCA was significantly more prevalent in people with diabetes than in those without. Such discordance may be attributed to small sample size of our study as well as slightly different inclusion criteria, in which patient with stable angina were included in the previously mention study but not in ours.

In a recent study, conducted on 322 patients with ACS who underwent pre-intervention optical coherence tomography imaging of the culprit lesion, the characteristics of culprit plaque were compared between patients with diabetes (n=95) and those without diabetes (n=227). The prevalence of affection of each coronary artery (LAD, LCX and RCA) wasn't significantly different between both groups (24).

In our study, this was also the case with LAD. However, LCX and RCA affection were significantly higher in people without diabetes.

In a recent study, that was conducted on 559 consecutive ACS patients with 'known DM' or 'hyperglycemia', to assess management of diabetic patients hospitalized for ACS. Eighty seven percent were managed by PCI and 8.3% managed by CABG. While mean SX score with its corresponding SD were 18.2 ± 13 (25).

Duarte and colleagues conducted a study on 521 patients suffering from ACS, consecutively hospitalized in the Cardiology Intensive Care Unit in order to define the risk factors, clinical and angiographic characteristics, and evolution of ACS in a population of diabetic patients. The found that there was a greater need for CABG and less PCI in people with diabetes than in non-diabetic patients (26).

In our study, the need for PCI or CABG was more in people with diabetes but not to the level of statistical significance. While more non-diabetic patients were treated medically. Also, SX score results were significantly higher in patients with diabetes than non-diabetic patients.

Study Limitations

Despite the relatively small sample size of our study, the results are quite comparable to larger studies.

This study was single-institutional observational in nature, which possibly made some restrictions on identifying and analyzing all potential confounding factors.

The choice between PCI and CABG as a treatment is dependent on the treating physician leading to some sort of selection bias.

Lastly, we didn't demonstrate the effect of treating different modifiable risk factors on CAD lesion complexity.

Conclusion:

Type 2 diabetes has a significant adverse effect on the anatomy of coronary arteries, causing more extensive and multi-vessel coronary artery disease as well as higher SYNTAX score than in patients without diabetes. So, diabetic patients with ACS benefit more from new oral antiplatelet agents and aggressive revascularization strategies.

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