Original Article

Intravascular evaluation of coronary atherosclerotic lesions among Egyptian diabetic patients with acute coronary syndromes

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Abstract

Background: Coronary artery disease is one of the main causes of death in diabetes mellitus (DM). Egypt was listed among the world top 10 countries regarding the number of diabetic patients by the International Diabetes Federation (IDF).

Aim of work: Assessment of the extent of coronary atherosclerotic disease and lesion tissue characterization among diabetic compared to non-diabetic Egyptian patients.

Methodology: IVUS studies of 272 coronary lesions in 116 patients presented with unstable angina were examined. The patients were divided into two groups: diabetic group (50 patients with 117 lesions) and non-diabetic group (66 patients with 155 lesions).

Results: As compared to the non-diabetic group, the diabetic patients were more dyslipidemic (84% vs 39.4%, p = 0.001) with higher total cholesterol level (194.6 ± 35.3 vs 174.4 ± 28.5 mg/dl, p = 0.001) and higher LDL-C (145.3 ± 27.1 vs 123.2 ± 31.4, p = 0.001). Regarding lesions characteristics, the diabetic group had longer lesions (19.4 ± 7.4 vs 16.3 ± 7.9 mm, p = 0.002) with higher plaque burden (60.8 ± 15.3 vs 54.8 ± 14.0, p = 0.002) and more area stenosis percentage (60.8 ± 15.6 vs 55.6 ± 14.1, p = 0.008). Structurally, the diabetic group lesions had more lipid content (19.8 ± 8.8 vs 16.8 ± 8.7, p = 0.008) and more necrotic core (17.6 ± 7.4 vs 14.7 ± 4.8, p = 0.008) but less calcification (6.9 ± 3.6 vs 11.8 ± 6.3, p = 0.001). The RI was negative in both groups, 0.95 ± 0.13 in the diabetic group vs 0.98 ± 0.19 in non-diabetic group (p = 0.5). Within the diabetic group lesions, the dyslipidemic subgroup had more lipid content (23. ± 5.2 vs 14.6 ± 8.6 , p = 0.01) but less fibrotic component (48.6 ± 4.7 vs 59.1 ± 13.6%, p = 0.01) and less calcification (10.9 ± 6.8% vs 14.07 ± 3.8%, p = 0.02) as compared to the nondyslipidemic subgroup.

Conclusions: Diabetic patients with coronary atherosclerosis in Egypt have longer lesions with higher plaque burden and more percent area stenosis with negative remodeling index. The diabetic lesions had more lipid content and more necrotic core but less calcification.

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1. Introduction

Coronary artery disease (CAD) is the principal cause of mortality in Diabetes mellitus (DM). The prevalence of DM is rising worldwide and associated with a 2 to 4-fold increased mortality risk from heart disease. In addition, DM is associated with other risk factors for cardiovascular disease (CVD) such as hypertension, dyslipidemia and obesity.

The term diabetic dyslipidemia describes increased LDL-C and triglycerides with reduced HDL-C. The lipid abnormalities are prevalent in diabetes mellitus because insulin resistance or deficiency affects key enzymes involved in lipid metabolism. Also, it has been proposed that the lipid particles in diabetic dyslipidemia is more atherogenic than other types of dyslipidemia. This means that even normal lipid concentrations might be more atherogenic in diabetic patients than in nondiabetic people.

In Egypt, the prevalence of diabetes is around 15.5% and has increased rapidly from 4.4 million in 2007 to 7.5 million in 2013. It is expected this number will jump up to 13.1 million by 2035.

2. Aim of work

Our aim was to study the extent of coronary atherosclerotic disease and lesion tissue characterization among diabetic
compared to non-diabetic Egyptian patients with acute coronary syndromes.

3. Patients and methods

This is a cross-sectional study conducted at Critical Care Department, Cairo University on 116 patients presented with unstable angina subjected to cardiac catheterization.

Patients with renal impairment, previous coronary artery bypass grafting (CABG), coagulopathy and severe thrombocytopenia were excluded.

Informed consents were obtained from all individual participants included in this study.

The patients were divided into two groups: diabetic group (50 patients) and non-diabetic group (66 patients).

Coronary catheterizations were done using Philips CV20, 2011-Netherlands, with imaging speed 15 frame per second (fps).

Two hundreds seventy-two coronary lesions were assessed by IVUS before intervention (117 lesions in diabetic group and 155 lesions in non-diabetic group).

Assessment of lipid profile was done after overnight fasting of 10–12 h. serum concentrations of cholesterols, triglycerides, and calculated LDL-C were measured. A total cholesterol of >190 mg/dl has been classified as high while >200 mg/dl has been classified as high while 150–199 mg/dl as borderline high level.

A LDL-C of >160 mg/dl has been classified as high while 130–159 mg/dl as borderline high level. A serum triglycerides of >200 mg/dl has been classified as high while 150–199 mg/dl as borderline high level.

3.1. Intravascular ultrasound imaging protocol and analysis

IVUS runs with (iLab TM, Boston Scientific Inc., USA) were performed using a 40 MHz, 6F compatible catheter (Atlantis SR Pro; Boston Scientific) after administration of 200 mcg intracoronary nitroglycerin.

Image acquisition using automated retrograde transducer pull back at 0.5 mm/second was performed from at least 10 mm distal to the studied lesions.

The measurements were performed according to the guidelines of the American College of Cardiology for the acquisition, measurement and reporting of IVUS studies by two experienced IVUS readers.

For each 1 mm of axial length, lumen and external elastic membrane (EEM) cross-sectional areas (CSAs) were measured.

Plaque plus media (P&M) CSA = EEM CSA minus lumen CSA.

Plaque burden = P&M CSA divided by EEM CSA.

The proximal and distal reference segments were the most apparently normal segments within 5 mm proximal and distal to the lesion.

Remodelling index (RI) =EEM CSA divided by mean reference EEM CSA.

Characterization of coronary plaques structure was done using colored-coded iMap-IVUS.

3.2. Statistical analysis

Data was summarized using mean, standard deviation, median and inter quartile range for quantitative variables and frequency and percentage for qualitative ones using the Statistical Package of Social Science Software program, version 21 (SPSS). Pearson correlation coefficients were calculated to get the association between different quantitative variables. P values less than 0.05 were considered statistically significant, and Graphs were used to illustrate some information.

4. Results

4.1. Demographic and clinical data

We evaluated 272 coronary lesions in 116 patients with a mean age of 52.2 ± 9.2 years and divided them into two groups: diabetic group (50 patients with 117 lesions) and non-diabetic group (66 patients with 155 lesions).

As compared to the non-diabetic group, the diabetic group was more dyslipidemic (84% vs 39.4%, p = 0.001) with higher total cholesterol level (194.64 ± 35.28 vs 174.42 ± 28.51, p = 0.001) and higher LDL-C (145.32 ± 27.14 vs 123.18 ± 31.36, p = 0.001) as shown in Table 1.

No statistically significant difference between both groups regarding smoking, hypertension, body mass index (BMI) or ejection fraction (EF).

4.2. Angiographic data

Interestingly, left main lesions were significantly more in the diabetic group with higher syntax score denoting much more complexity of coronary disease. Stenting of 134 lesions were done without complications apart from non-flow limiting edge dissections of 2 cases of the nondiabetic group. The dissections were managed by stenting. Only 2 patients of the diabetic group died during ICU stay due to extensive bronchopneumonia and septic shock (Table 2).

4.3. Intravascular ultrasound (IVUS) data

As compared to the non-diabetic group, the diabetic group had longer lesions (19.37 ± 7.44 vs 16.27 ± 7.91, p = 0.002) with higher...
plaque burden (60.78 ± 15.25 vs 54.79 ± 14.0, p = 0.002) and more percent area stenosis (60.75 ± 15.6 vs 55.6 ± 14.07, p = 0.008) (Table 2).

Also, the diabetic group lesions had more lipid content (19.83 ± 8.75 vs 16.81 ± 8.7, p = 0.008) and more necrotic core (17.59 ± 7.38 vs 14.72 ± 4.8, p = 0.008) with less calcification (6.9 ± 3.61 vs 11.77 ± 6.3, p = 0.001) (Figs. 1 and 2).

The RI was negative in both groups (0.95 ± 0.13 vs 0.98 ± 0.19) in the diabetic and non-diabetic groups respectively with p = 0.5 (Table 3).

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**Fig. 1.** Coronary lesions component. A: diagram of diabetic patients. B: diagram of non-diabetic patients. Blue = fibrotic component. Green = lipidic component. Violet = calcium component. Red = necrotic component.

**Fig. 2.** IVUS runs of LAD lesions. A: grey scale run of non-diabetic patient. B: iMAP study of lesion A. C: grey scale run of diabetic patient. D: iMAP study of lesion C. Green = fibrous component. Yellow = Lipid component. Red = necrotic component. Blue = dense calcium.
4.4. Effect of dyslipidaemia

We subdivided each group into 2 subgroups to study the effect of hypercholesterolaemia and hypertriglyceridaemia on coronary lesion characteristics.

Interestingly, within the diabetic group lesions, the dyslipidaemic subgroup had more lipid content (23. ± 5.2 vs 14.6 ± 8.6, p = 0.01) but less fibrotic component (48.6 ± 4.7 vs 59.1 ± 13.6%, p = 0.01) and less calcification (10.9 ± 6.8% vs 14.07 ± 3.8%, p = 0.02) as compared to the nondyslipidaemic subgroup (Table 4).

For the non-diabetic group, the dyslipidaemic subgroup had more lipid content (21.7 ± 8.1 vs 18.1 ± 9.02, p = 0.014) but less necrotic core (16.3 ± 4.6 vs 18.7 ± 9.1, p = 0.04) as compared to the nondyslipidaemic subgroup (Table 4).

The TGL was positively correlated with lipidic content of diabetic (p = 0.001, r = 0.43) and nondiabetic (p = 0.001, r = 0.48) groups.

The TGL was not correlated with necrotic core of diabetic (p = 0.03, r = 0.18) but positively correlated in the nondiabetic (p = 0.86, r = 0.17) but positively correlated in the nondiabetic groups.

The LDL-C was positively correlated with lipidic content of diabetic (p = 0.001, r = 0.43) and nondiabetic (p = 0.002, r = 0.26) groups.

The TGL was positively correlated with lipidic content of diabetic (p = 0.001, r = 0.43) and nondiabetic (p = 0.001, r = 0.48) groups.

The LDL-C was not correlated with necrotic core of diabetic (p = 0.036, r = 0.17) but positively correlated in the nondiabetic (p = 0.03, r = 0.18) groups.

5. Discussion

Diabetes mellitus (DM) is one of the major causes of coronary artery diseases. In Egypt, the prevalence of diabetes has increased rapidly over last decade and it is expected to jump up to 13.1 million by 2035.

DM poses stresses regarding the choice of the appropriate interventions during coronary interventions and post catheterization management. Proudly, this is the first study that assesses the coronary atherosclerosis among the Egyptian diabetic patients with unstable angina using IVUS.

Confirming the close relation between DM and lipid metabolism, we found that the diabetic patients had more dyslipidemia than the non-diabetics but there was no significant difference between both groups regarding obesity, hypertension or smoking. Our results were similar to other studies that showed the close association between diabetes mellitus and dyslipidaemia.

The lipid changes associated with diabetes mellitus are attributed to increased free fatty acid flux secondary to insulin resistance.

We found that the diabetic patients with coronary atherosclerosis had longer lesions with higher plaque burden and more percent area stenosis.

Our results were similar to the IVUS meta-analysis by Nicholls et al. that showed extensive atheroma volumes and progression in diabetic patients.

Also, our results were similar to the results of Niccoli et al. that showed extensive coronary atherosclerosis among diabetic patients with acute coronary syndromes using optical coherence tomography (OCT).

Lawand et al. demonstrated longer lesions and increased plaque volumes in diabetic patients admitted with acute coronary syndrome as compared to non-diabetic patients.

Our study showed negative remodeling in both groups but without statistical significance. Jensen et al. concluded that the majority of coronary lesions in patients with type II diabetes mellitus had negative remodeling and that explain the appearance of coronary arteries as small sized in diabetic patients.

However, Lawand et al. showed positive remodeling index in both groups.

We found the diabetic group lesions had more lipidic content and more necrotic core with less calcification than the non-diabetic lesions. Tadashi Araki et al. demonstrated the increased lipid content and necrotic plaque volume in diabetic patients with stable angina. Amano et al. showed the association between lipid-rich coronary plaques and abnormal glucose regulation.

Diabetes mellitus was associated with more dyslipidaemia in the form of hypercholesterolaemia mainly increased LDL-C and increased TGL. The diabetic dyslipidaemia was associated with more vulnerable atherosclerotic plaques (more lipid component and necrotic core with less fibrosis) which may result in recurrent acute coronary syndromes. This finding may explain the importance of intense lipid profile control for patient with diabetes mellitus.

Moreover, patients with ischaemic heart disease admitted with acute coronary syndromes, presence of dyslipidaemia was associated with vulnerable plaques (more lipid component and necrotic core).

Finally our results may support the importance of control of dyslipidaemia especially diabetic dyslipidaemia for patients with ischaemic heart disease.

### Table 3

| IVUS criteria | Diabetic group | Non-diabetic group | P value |
|---------------|----------------|--------------------|---------|
| Vessel area (EEM CSA) (mm²) | 10.38 ± 3.7 | 10.05 ± 3.6 | 0.47 |
| Max.vessel diameter (mm) | 3.72 ± 0.70 | 3.86 ± 0.63 | 0.2 |
| Min.vessel diameter (mm) | 3.26 ± 0.60 | 3.39 ± 0.64 | 0.21 |
| Lesion MLA (mm²) | 4.39 ± 2.82 | 4.47 ± 1.9 | 0.79 |
| Lesion max.diameter (mm) | 2.30 ± 0.58 | 2.60 ± 0.35 | 0.001 |
| Lesion min.diameter (mm) | 1.85 ± 0.47 | 2.08 ± 0.47 | 0.002 |
| Area stenosis (%) | 60.75 ± 15.6 | 55.6 ± 14.07 | 0.008 |
| Plaque burden | 60.78 ± 15.25 | 54.79 ± 14.06 | 0.002 |
| Lesion length (mm) | 19.37 ± 7.44 | 16.27 ± 7.91 | 0.002 |
| Lesions structure
  Fibrosis (%) | 55.64 ± 7.91 | 56.3 ± 12.82 | 0.6 |
  Lipids (%) | 19.83 ± 8.75 | 16.81 ± 8.7 | 0.008 |
  Necrosis (%) | 17.59 ± 7.38 | 14.72 ± 4.8 | 0.008 |
| Calculication (%) | 6.9 ± 3.61 | 11.77 ± 6.3 | 0.001 |
| Proximal reference area (mm²) | 11.45 ± 3.7 | 11.72 ± 3.8 | 0.58 |
| Proximal max. RVD (mm) | 4.15 ± 0.58 | 4.27 ± 0.47 | 0.28 |
| Proximal min.RVD (mm) | 3.75 ± 0.59 | 3.74 ± 0.58 | 0.97 |
| Distal reference area (mm²) | 8.92 ± 3.3 | 9.02 ± 3.4 | 0.27 |
| Distal max.RVD (mm) | 3.6 ± 0.68 | 3.54 ± 0.51 | 0.62 |
| Distal min.RVD (mm) | 3.24 ± 0.66 | 3.2 ± 0.48 | 0.71 |
| Remodeling index | 0.95 ± 0.13 | 0.98 ± 0.19 | 0.5 |

### Table 4

Dyslipidaemia and coronary lesions characteristics.

| IVUS criteria | Dyslipidaemic group | Non-dyslipidaemic | P value |
|---------------|---------------------|------------------|---------|
| The diabetic group
  Plaque burden | 60.34 ± 15.2% | 62.08 ± 15.7% | 0.61 |
  Lesions structure
    Fibrosis (%) | 48.6 ± 4.7 | 59.1 ± 13.6% | 0.01 |
    Lipids (%) | 23. ± 5.2 | 14.6 ± 8.6 | 0.01 |
    Necrosis (%) | 15.06 ± 4.9 | 13.78 ± 4.4 | 0.23 |
    Calculication (%) | 10.9 ± 6.8% | 14.07 ± 3.8% | 0.02 |
| The nondiabetic group
  Plaque burden | 52.4 ± 14.4 | 56.9 ± 13.5 | 0.056 |
  Fibrosis (%) | 54.48 ± 10.3 | 56.68 ± 10.28 | 0.21 |
  Lipids (%) | 21.7 ± 8.1 | 18.1 ± 5.02 | 0.014 |
  Necrosis (%) | 16.3 ± 4.6 | 18.7 ± 9.1 | 0.04 |
  Calculication (%) | 7.48 ± 3.8 | 6.38 ± 3.4 | 0.07 |
6. Study limitations

The current study was single center study.

7. Conclusion

Diabetic patients with coronary atherosclerosis in Egypt have longer lesions with higher plaque burden and more area stenosis percentage with negative remodeling index. This explains the diffuse disease and small caliber vessels of diabetic patients. Also, the diabetic lesions had more lipid content and necrotic core indicating high vulnerability with recurrent acute coronary syndromes. The optimal management of diabetic patients with anti-diabetic drugs for blood glucose control should include intense lipid lowering measures.

8. Conflict of interest and funding

No conflict of interest and no funds had received for this study.

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