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Original Article

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The Complexity of Peripheral Arterial Disease and Coronary Artery Disease in Diabetic Patients: An Observational Study

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Abstract

Background: Atherosclerosis is a systemic disease that causes luminal narrowing. Patients with peripheral arterial disease (PAD) also exhibit an increased risk of death from cardiovascular complications. This risk is the same for symptomatic or asymptomatic patients. Over a 5-year period, patients with PAD have a 20% chance of suffering from a stroke or myocardial infarction. Additionally, their mortality rate is 30%. This study aimed to assess the relationship between coronary artery disease (CAD) complexity using SYNTAX score and PAD complexity using Trans-Atlantic Inter-Society Consensus II (TASC II) score.

Methods: The study was designed as single-center cross-sectional observational and included 50 diabetic patients referred for elective coronary angiography and peripheral angiography was done.

Results: Most of the patients were males (80%) and smokers (80%) with mean age of 62 years. The mean SYNTAX score was 19.88. There was a significant negative correlation between SYNTAX score and ankle brachial index (ABI) (r = -0.48, P = 0.001) and a significant positive correlation with glycated hemoglobin (HbA1c) level (R^2 = 26, P = 0.004). Complex PAD was found in nearly half of the patients with 48% having TASC II C or D classes. Those with TASC II classes C and D had higher SYNTAX scores (P = 0.046).

Conclusions: Diabetic patients with more complex CAD had more complex PAD. In diabetic patients with CAD, those with worse glycemic control had higher SYNTAX scores and the higher the SYNTAX score, the lower the ABI.

Keywords: Peripheral arterial disease; Coronary artery disease; TASC II; SYNATX score

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Introduction

Atherosclerosis is a systemic disease of the large and medium-sized arteries causing luminal narrowing (focal or diffuse) [1].

Patients with peripheral arterial disease (PAD) have a 2-3% chance of suffering a myocardial infarction (MI). There is a 2 - 3 times higher chance of developing angina compared to age-matched controls. Patients with PAD also exhibit an increased risk of death from cardiovascular complications [2]. This risk is the same for patients with symptomatic PAD or asymptomatic PAD. Over a 5-year period, patients with PAD have a 20% chance of suffering from a stroke or MI. Additionally, their mortality rate is 30% [3].

The AGATHA study discovered that patients with PAD in only one vascular territory had a 35% chance of having disease in at least one other territory. This information suggests that patients with PAD have a significantly greater risk of contracting cerebrovascular disease or coronary heart disease [2, 3].

By the time a patient presents with PAD, it is already severe. About 20-30% of patients with PAD also have diabetes mellitus. However, it is likely that only a fraction of PAD cases is diagnosed by asymptomatic presentations and lower degrees of PAD. To detect low degrees of PAD, a patient can be tested using an ankle brachial index (ABI) [3].

The SYNTAX score is a validated scoring system used to the assessment of complexity and anatomical severity of coronary artery disease (CAD). It correlates well with major adverse cardiovascular events and cardiovascular mortality [4, 5].

Trans-Atlantic Inter-Society Consensus II (TASC II) classification is an internationally derived definition that is dedicated for the assessment of PAD according to anatomical distribution, number, and nature of lesions [6].

In this study, we tried to find the relationship of complexity of PAD and CAD in a group of diabetic patients. Most of the available data included diabetics as well as non-diabetics.

Materials and Methods

This is a prospective cross-sectional observational study. It included 50 diabetic patients referred for elective coronary angiography with documented CAD and PAD detected by peripheral angiogram. An informed written consent was taken from

Table 1. TASC II Classification of Aortoiliac Lesions [6]

Type A lesions	Unilateral or bilateral stenoses of CIA Unilateral or bilateral single short (≤ 3 cm) stenosis of EIA
Type B lesions	Short (≤ 3 cm) stenosis of infrarenal aorta Unilateral CIA occlusion Single or multiple stenosis totaling 3 - 10 cm involving the EIA not extending into the CFA Unilateral EIA occlusion not involving the origins of internal iliac or CFA
Type C lesions	Bilateral CIA occlusions Bilateral EIA stenoses 3 - 10 cm long not extending into the CFA Unilateral EIA stenosis extending into the CFA Unilateral EIA occlusion that involves the origins of internal iliac and/or CFA Heavily calcified unilateral EIA occlusion with or without involvement of origins of internal iliac and/or CFA
Type D lesions	Infra-renal aortoiliac occlusion Diffuse disease involving the aorta and both iliac arteries requiring treatment Diffuse multiple stenoses involving the unilateral CIA, EIA and CFA Unilateral occlusions of both CIA and EIA Bilateral occlusions of EIA Iliac stenoses in patients with AAA requiring treatment and not amenable to endograft placement or other lesions requiring open aortic or iliac surgery

AAA: abdominal aortic aneurysm; CFA: common femoral artery; CIA: common iliac artery; EIA: external iliac artery; TASC II: Trans-Atlantic Inter-Society Consensus II.

each participant.

The aim of this study was to assess the relationship between CAD complexity using SYNTAX score and PAD complexity using TASC II classification in diabetic patients.

The study was approved by the local Institutional Ethical Committee of Faculty of Medicine, Ain Shams University. This study was conducted in compliance with the ethical standards of the responsible institution on human subjects as well as with the Helsinki Declaration.

Sampling

All 50 patients, in the time period from August 2016 till July 2017, were enrolled using quota sampling from patients referred for elective coronary angiogram with documented PAD by examination and confirmed by duplex ultrasound.

Inclusion criteria

Patients with chronic coronary syndrome undergoing diagnostic coronary angiography with documented CAD and PAD were included.

Exclusion criteria

Exclusion criteria included: 1) patient's refusal, 2) vasculitis, 3) contraindication for coronary angiography (e.g., active bleeding, coagulopathy, active infection, etc.), 4) non-atherosclerotic stenosis, 5) acute limb-threatening ischemia, 6) patients with known or suspected infectious or inflammatory conditions, and 7) patients with serum creatinine more than 1.3 mg/dL.

Procedures

Procedures included: 1) History taking. 2) Complete physical examination. 3) Laboratory investigations. 4) Coronary angiography. It was performed using conventional techniques and was analyzed by experienced interventional cardiologists. 5) SYNTAX scoring. SYNTAX score was calculated using an online calculator [7]. A SYNTAX score of 0 indicates no measurable coronary disease, while a score 1 indicates the presence of CAD, with CAD complexity increasing as the SYNTAX score increases. The SYNTAX score algorithm includes: dominance; number of lesions; segments involved per lesion with lesion characteristics; total occlusions with subtotal occlusions (number of segments, age of total occlusion, blunt stump, bridge collaterals, first segment beyond occlusion visible by anterograde or retrograde filling, and side branch involvement); trifurcation, number of diseased segments; bifurcation type and angulation; aortic osteal lesion; severe tortuosity; lesion length; heavy calcification; thrombus; diffuse disease with numbers of segments. 6) Peripheral angiography and TASC II classification (Tables 1, 2 [6]). Peripheral angiography was done at the same index coronary angiography procedure by experienced interventional cardiologist for both lower limbs. It was performed using conventional techniques and was analyzed by experienced interventional cardiologists.

Statistical analysis

We used the statistical package SPSS 17. Continuous variables were reported as means ± standard deviation (SD) or as me-

Table 2. TASC II Classification of Femoral Popliteal Lesions [6]

Type A lesions	Single stenosis ≤ 10 cm in length Single occlusion ≤ 5 cm in length
Type B lesions	Multiple lesions (stenoses or occlusions), each ≤ 5 cm Single stenosis or occlusion ≤ 15 cm not involving the infra geniculate popliteal artery Single or multiple lesions in the absence of continuous tibial vessels to improve inflow for a distal bypass Heavily calcified occlusion ≤ 5 cm in length Single popliteal stenosis
Type C lesions	Multiple stenoses or occlusions totaling > 15 cm with or without heavy calcification Recurrent stenoses or occlusions that need treatment after two endovascular interventions
Type D lesions	Chronic total occlusions of CFA or SFA (> 20 cm, involving the popliteal artery) Chronic total occlusion of popliteal artery and proximal trifurcation vessels

CFA: common femoral artery; SFA: superficial femoral artery; TASC II: Trans-Atlantic Inter-Society Consensus II.

dian and interquartile range (IQR) when skewed. Categorical variables were reported as percentages and compared using the χ^2 test. Continuous variables were compared by the Mann-Whitney U test. Kruskal-Wallis test was used when more than two groups were compared. A P value of < 0.05 was considered statistically significant. All tests were two-sided. Correlations between continuous homogenous variables were done using Pearson correlation coefficient.

Results

Baseline characteristics

Most of the 50 diabetic patients were males (80%), hypertensives (84%) and smokers (80%). All of them had high low-density lipoprotein (LDL) levels, with mean of 157 mg/dL and the majority had uncontrolled diabetic mellitus (DM) with high levels of glycated hemoglobin (HbA1c) with mean of 8.47±1.47%. Most of the cohort had no symptoms of PAD (94%) (Table 3).

SYNTAX score

The mean SYNTAX score was 19.88 ± 13.34, where 60% had a score < 22 (mild CAD), 24% had a score between 22 and 32 (moderate), and 16% had a score > 33 (severe) (Fig. 1).

TASC II classification

The PAD classification and complexity was nearly evenly distributed with 24% TASC II A, 28% TASC II B, 22% TASC II C and 26% TASC II D (Fig. 2).

Relationship between complexity of CAD and PAD

Complex PAD anatomy represented by TASC II C and D classes showed higher SYNTAX scores (P = 0.046) (Fig. 3, Table 4).

The highest median (IQR) SYNTAX score in patients with TASC II class C was 26.5 (19 - 36) (P < 0.001) (Fig. 4).

Relationship between complexity of PAD and ABI

The mean ABI was 0.8 ± 0.07 which is lower with increased complexity of the PAD as shown in Table 5, where all the patients in TASC II D class had low ABI < 0.9 (P = 0.001).

Relationship between complexity of CAD and ABI

The higher the SYNTAX score, the lower the ABI with a sig-

Table 3. Demographic and Baseline Characteristics

Males	40 (80%)
Age (years)	62.12 ± 5.71
Smoking	40 (80%)
HTN	42 (84%)
Dyslipidemia	50 (100%)
FH	9 (18%)
Creatinine (mg/dL)	1.03 ± 0.07 0.9 - 1.2
HbA1c (%)	8.47 ± 1.47 6.7 - 12
LDL (mg/dL)	157 ± 15 135 - 200
LVEF (%)	53.6 ± 5.2 40 - 64
ABI	0.8 ± 0.1 0.7 - 1.1
Symptoms for PAD	3 (6%)

Continuous variables are represented as mean ± SD, and categorical variables as percentages. ABI: ankle brachial index; FH: family history; HbA1c: hemoglobin A1c; HTN: hypertension; LDL: low-density lipoprotein; LVEF: left ventricular ejection fraction; PAD: peripheral arterial disease; SD: standard deviation.

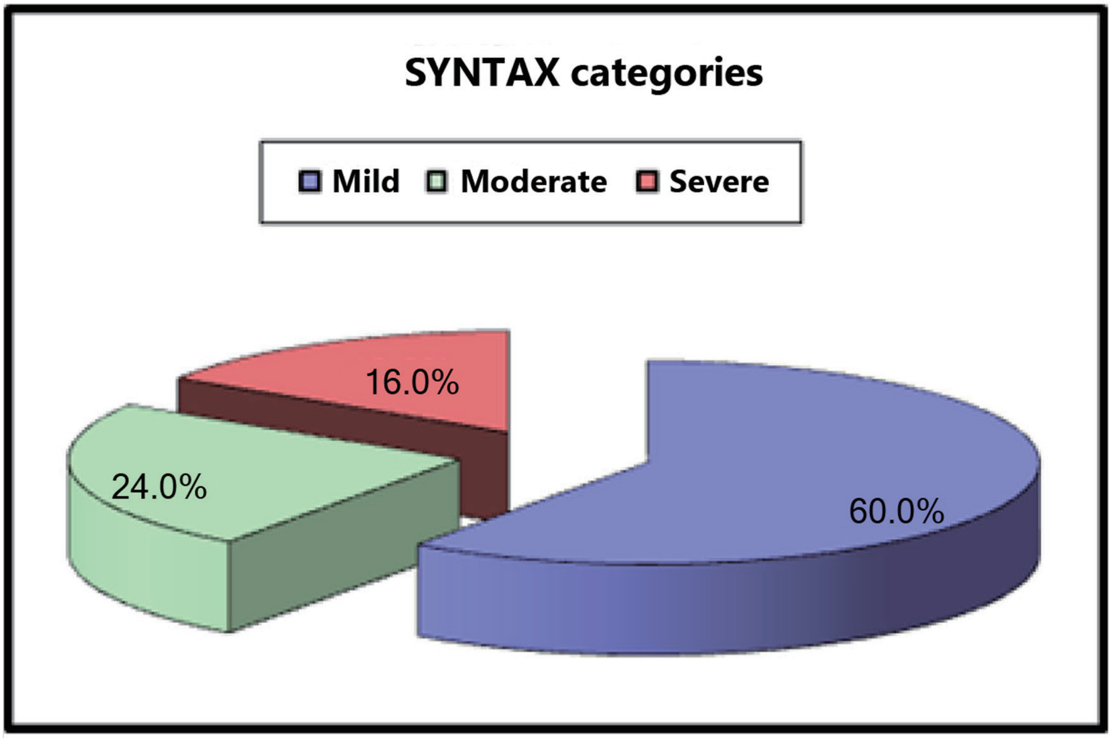

Figure 1. SYNTAX score categories.

nificant negative correlation between SYNTAX score and ABI with correlation coefficient of -0.48 and R^2 of 23 ($P < 0.001$) (Fig. 5).

Relationship between complexity of CAD and HbA1c

The higher the HbA1c, the higher the SYNTAX score with a significant positive correlation between SYNTAX score and HbA1c with correlation coefficient of 0.51 and R^2 of 26 ($P < 0.01$) (Fig. 6).

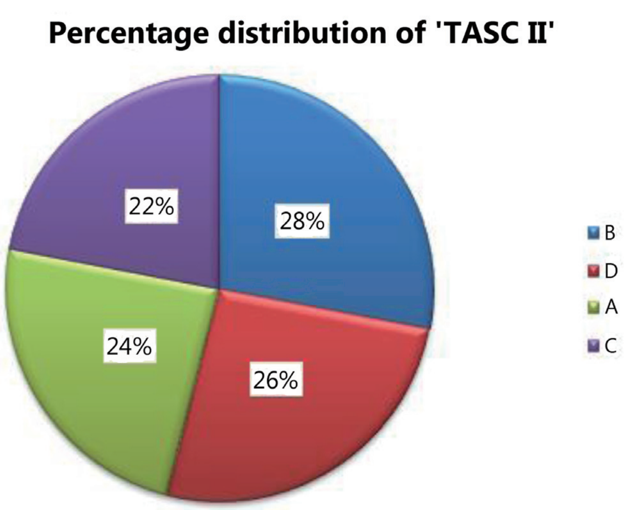

Figure 2. TASC II classification distribution. TASC II: Trans-Atlantic Inter-Society Consensus II.

Discussion

In this prospective cross-sectional observational study, we investigated the relationship between the complexity of CAD assessed by SYNTAX score and the complexity of associated PAD assessed by TASC II class in a group of diabetic patients with normal kidney functions.

Baseline characteristics

Most of the studied Egyptian cohort were males, smokers, hypertensives, with high LDL levels and inadequate glycemic control. Where these represent the traditional risk factors for atherosclerosis with high prevalence among the studied group, they were shown in the registry published by Shaheen et al [8] in the European Society of Cardiology Registry on ST elevation MI; compared to other countries, Egyptian patients had higher prevalence of traditional risk factors.

Relationship between complexity of CAD and PAD

Complex PAD anatomy represented by TASC II C and D classes showed higher SYNTAX scores. The median SYNTAX scores of diabetic patients with TASC II A, TASC II B,

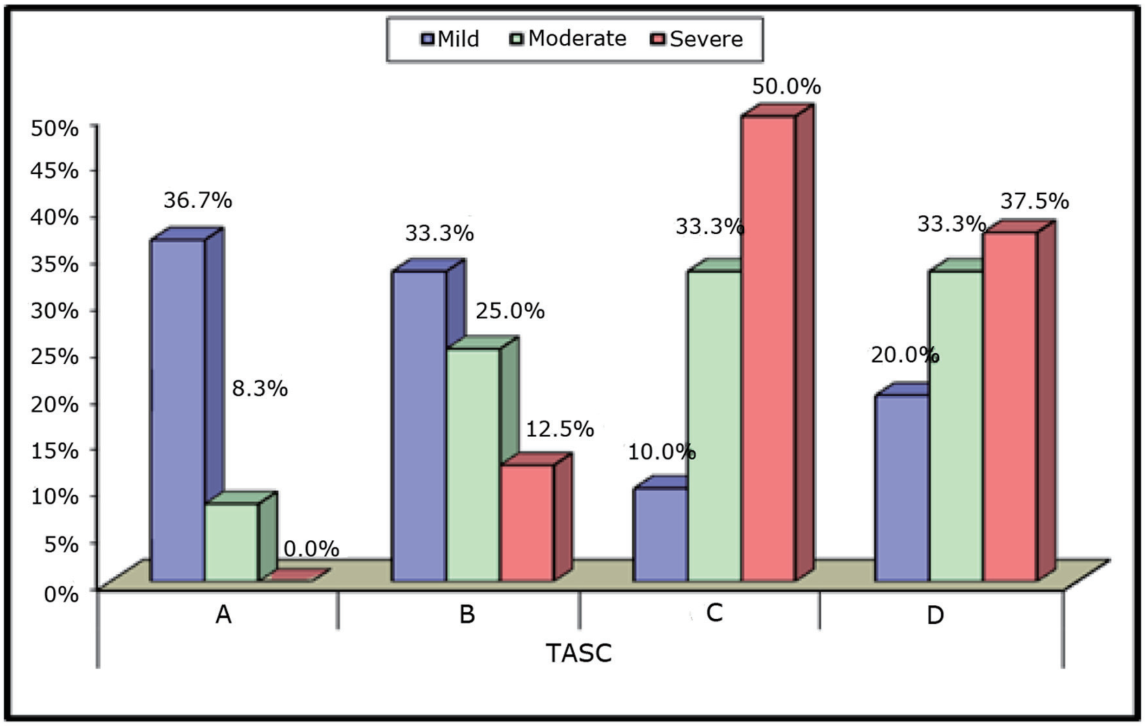

Figure 3. Relation between SYNTAX scores and TASC II classification. TASC II: Trans-Atlantic Inter-Society Consensus II.

TASC II C, and TASC II D were 10, 13.5, 26.5, and 19.5, respectively, compared with the results in the study by Aykan et al [9]. They studied 449 patients, 30% of whom had diabetes. They found that patients with TASC II A, TASC II B, TASC II C, and TASC II D had median SYNTAX scores of 13.25, 14, 19, and 19, respectively. These findings were relatively higher in diabetic patients. Vuruskan et al [10] developed a scoring system (total peripheral score (TPS)) using the TASC II classification and the SYNTAX II score to predict CAD severity in patients with lower extremity arterial disease. They showed a modest positive correlation between TPS and SYNTAX (Pearson correlation = 0.467, P < 0.001).

Relationship between complexity of CAD and glycemic control

In the current study, mean HbA1c was 8.47% (higher than the target value in current guidelines) and was significantly positively correlated with CAD severity as represented by the SYNTAX score. The higher the HbA1c level, the higher the

Table 4. SYNTAX Versus TASC II Class

SYNTAX	TASC II class				P value	
	A (N = 12)	B (N = 14)	C (N = 11)	D (N = 13)		
SYNTAX groups					0.046	
Mild	11(91.7%)	10 (71.4%)	3 (27.3%)	6 (46.2%)		
Moderate	1 (8.3%)	3 (21.4%)	4 (36.4%)	4 (30.8%)		
Severe	0 (0.0%)	1 (7.1%)	4 (36.4%)	3 (23.1%)		
SYNTAX score					0.008	
Median (IQR)	10.00 (2.5 - 16)	13.50 (10 - 22.5)	26.50 (19 - 36)	19.50 (13 - 27)		
Range	1 - 37	5 - 38.5	11 - 54	8 - 67		
Post hoc analysis	A vs. B	A vs. C	A vs. D	B vs. C	B vs. D	C vs. D
SYNTAX groups	0.38	0.006	0.044	0.066	0.348	0.612
SYNTAX score	0.31	0.002	0.02	0.022	0.149	0.343

IQR: interquartile range; TASC II: Trans-Atlantic Inter-Society Consensus II.

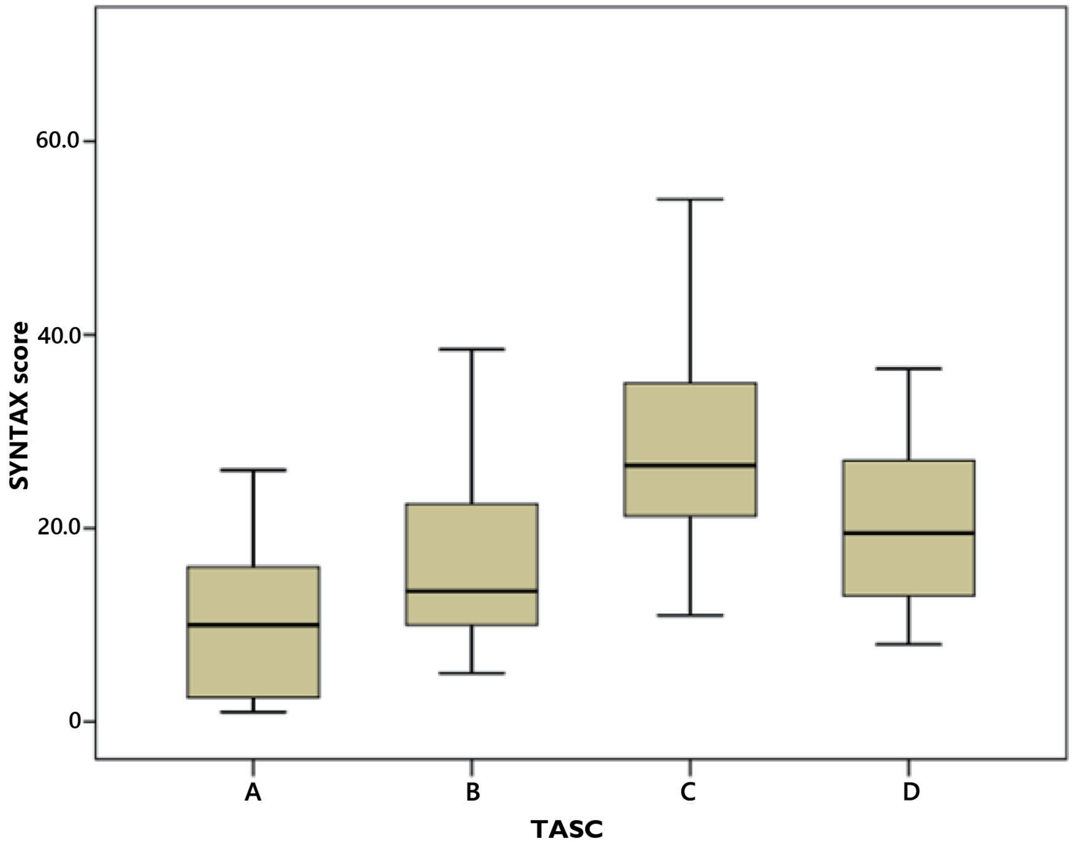

Figure 4. Relation between SYNTAX scores IQR and TASC II classification. IQR: interquartile range; TASC II: Trans-Atlantic Inter-Society Consensus II.

SYNTAX score.

Our results were consistent with similar findings by Dar et al [11]. They studied the prevalence of type 2 DM and association of HbA1c with severity of CAD in patients presenting as non-diabetic acute coronary syndrome and found a significant positive correlation between HbA1c and CAD complexity represented by Gensini score.

Study limitations

The main limitation of this study is being a single-center trial

Table 5. TASC II Class and ABI

ABI	TASC II				P-value	
	A (N = 12)	B (N = 14)	C (N = 11)	D (N = 13)		
ABI score					0.001	
Mean ± SD	1.03 ± 0.05	0.92 ± 0.05	0.83 ± 0.06	0.81 ± 0.07		
Range	1 - 1.1	0.85 - 1.08	0.73 - 0.93	0.7 - 0.87		
ABI groups					0.001	
Normal	12 (100.0%)	1 (7.1%)	0 (0.0%)	0 (0.0%)		
Borderline	0 (0.0%)	7 (50.0%)	1 (9.1%)	0 (0.0%)		
Low	0 (0.0%)	6 (42.9%)	10 (90.9%)	13 (100.0%)		
Post hoc analysis	A vs. B	A vs. C	A vs. D	B vs. C	B vs. D	C vs. D
ABI score	0.001	0.001	0.001	0.001	0.001	0.291
ABI groups	0.001	0.001	0.001	0.044	0.018	0.573

ABI: ankle brachial index; SD: standard deviation; TASC II: Trans-Atlantic Inter-Society Consensus II.

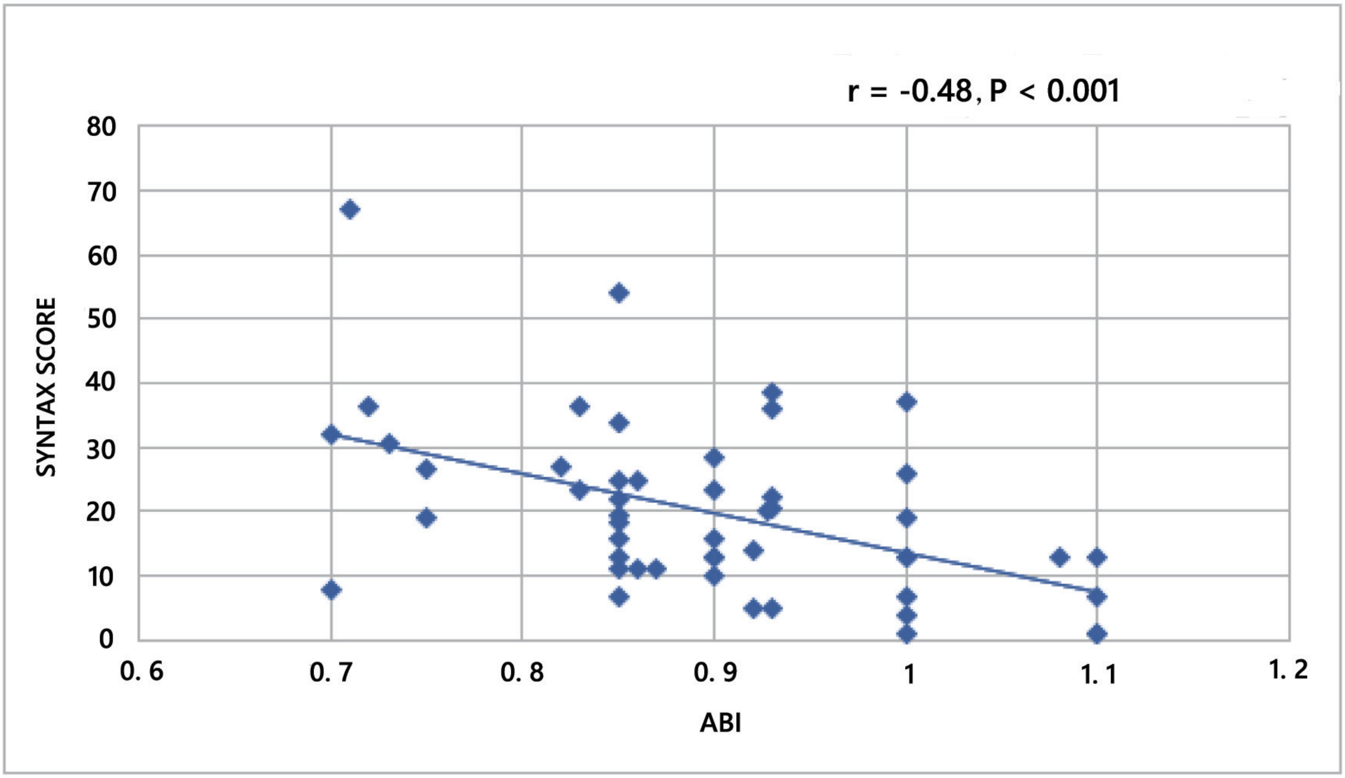

Figure 5. Correlation between SYNTAX score and ABI. ABI: ankle brachial index.

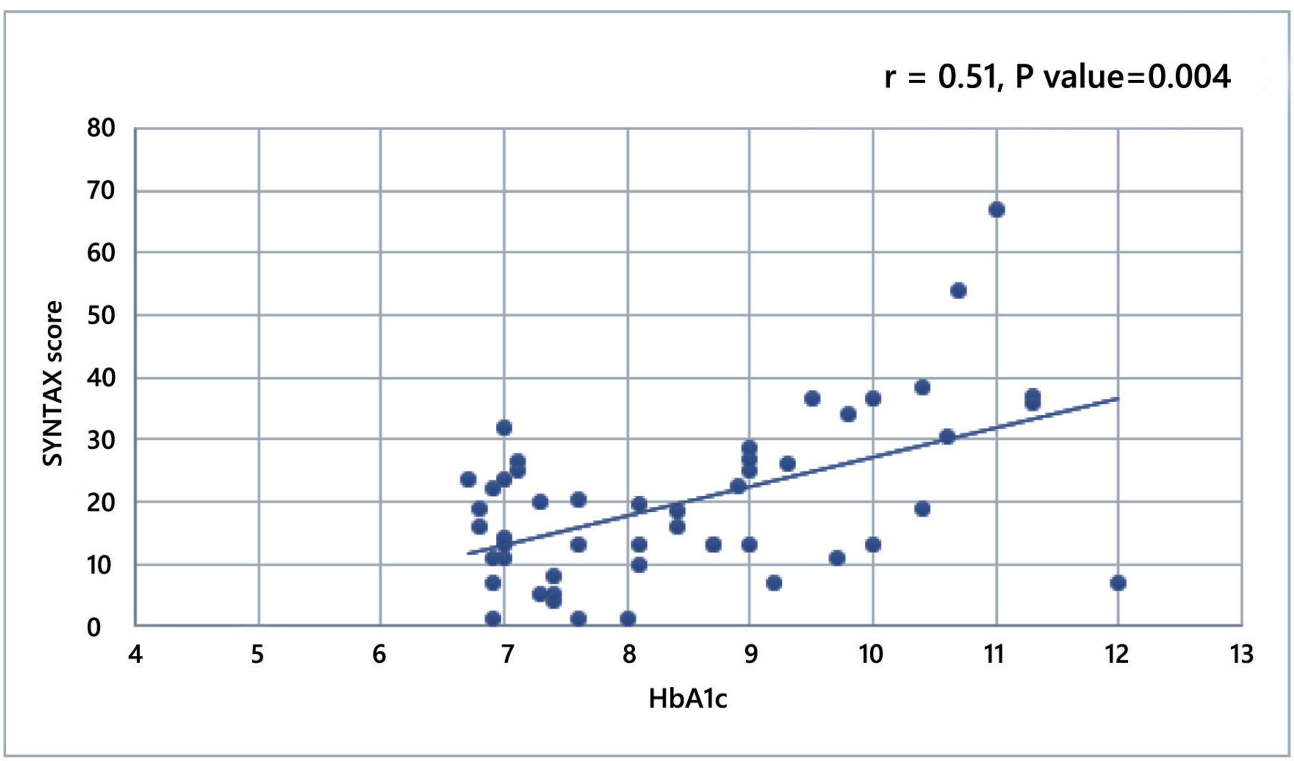

Figure 6. Correlation between SYNTAX score and HbA1c. HbA1c: glycated hemoglobin.

with relatively limited number of participants. A larger number of enrolled patients in the study population can also result in a higher positive correlation to be obtained in future studies.

The exclusion of patients with renal impairment also removed an important risk factor in diabetic patients with atherosclerotic CAD.

Conclusions

Diabetic patients with more complex CAD had more complex PAD. In diabetic patients with CAD, those with worse glycemic control had higher SYNTAX scores and the higher the SYNTAX score, the lower the ABI.

Acknowledgments

None to declare.

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Conflict of Interest

The authors declare that they have no conflict of interest.

Informed Consent

No data were collected before detailed information was given to the patient and a written consent was obtained.

Author Contributions

KA conceptualized the project, reviewed the literature, collected the data, analyzed the data, and wrote the manuscript. HF conceptualized the project and collected the data. AE conceptualized the project, reviewed the literature, collected the data, and analyzed the data. SS conceptualized the project and reviewed the literature. All authors read and approved the final manuscript.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Abbreviations

AAA: abdominal aortic aneurysm; ABI: ankle brachial index; ACS: acute coronary syndrome; CA: coronary angiography; CAD: coronary artery disease; CFA: common femoral artery; CIA: common iliac artery; DM: diabetes mellitus; EIA: external iliac artery; IQR: interquartile range; LDL: low-density lipoprotein; LVEF: left ventricular ejection fraction; MI: myocardial infarction; PAD: peripheral arterial disease; SFA: superficial femoral artery; TASC II: Trans-Atlantic Inter-Society Consensus II

References

1. Writing Committee to Develop Clinical Data Standards for Peripheral Atherosclerotic Vascular Disease, Creager MA, Belkin M, Bluth EI, Casey DE, Jr., Chaturvedi S, Dake MD, et al. 2012 ACCF/AHA/ACR/SCAI/SIR/STS/SVM/SVN/SVS key data elements and definitions for peripheral atherosclerotic vascular disease: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Clinical Data Standards (Writing Committee to Develop Clinical Data Standards for Peripheral Atherosclerotic Vascular Disease). Circulation. 2012;125(2):395-467.
2. Fowkes FG, Low LP, Tuta S, Kozak J, Investigators A. Ankle-brachial index and extent of atherothrombosis in 8891 patients with or at risk of vascular disease: results of the international AGATHA study. Eur Heart J. 2006;27(15):1861-1867.
3. Thiruvoipati T, Kielhorn CE, Armstrong EJ. Peripheral artery disease in patients with diabetes: Epidemiology, mechanisms, and outcomes. World J Diabetes. 2015;6(7):961-969.
4. Sianos G, Morel MA, Kappetein AP, Morice MC, Colombo A, Dawkins K, van den Brand M, et al. The SYNTAX Score: an angiographic tool grading the complexity of coronary artery disease. EuroIntervention. 2005;1(2):219-227.
5. Serruys PW, Onuma Y, Garg S, Sarno G, van den Brand M, Kappetein AP, Van Dyck N, et al. Assessment of the SYNTAX score in the Syntax study. EuroIntervention. 2009;5(1):50-56.
6. Norgren L, Hiatt WR, Dormandy JA, Nehler MR, Harris KA, Fowkes FG, TASC II Working Group. Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II). J Vasc Surg. 2007;45(Suppl S):S5-67.
7. http://www.syntaxscore.com.
8. Shaheen S, Wafa A, Mokarab M, Zareef B, Bendary A, Abdelhameed T, Rashwan A, et al. Presentation, management, and outcomes of STEMI in Egypt: results from the European Society of Cardiology Registry on ST elevation myocardial infarction. Egypt Heart J. 2020;72(1):35.
9. Aykan AC, Hatem E, Karabay CY, Gul I, Gokdeniz T, Kalaycioglu E, Turan T, et al. Complexity of lower extremity peripheral artery disease reflects the complexity of coronary artery disease. Vascular. 2015;23(4):366-373.
10. Vuruskan E, Saracoglu E, Polat M, Duzen IV. Prediction of coronary artery disease severity in lower extrem-

ity artery disease patients: A correlation study of TASC II classification, Syntax and Syntax II scores. Cardiol J. 2017;24(5):495-501.

11. Dar MI, Beig JR, Jan I, Shah TR, Ali M, Rather HA, Tramboo NA. Prevalence of type 2 diabetes mellitus and association of HbA1c with severity of coronary artery disease in patients presenting as non-diabetic acute coronary syndrome. Egypt Heart J. 2020;72(1):66.