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ROLE OF CORONARY COMPUTED TOMOGRAPHY ANGIOGRAPHY AND STRESS SINGLE PHOTON EMISSION COMPUTED TOMOGRAPHY IN EVALUATION OF CHEST PAIN IN DIABETIC AND NON-DIABETIC PATIENTS

By

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ABSTRACT

Background: In the evaluation of patients with suspected coronary artery disease (CAD), the role of non-invasive imaging has increased exponentially over the past decades.

Objective: To assess the diagnostic value of coronary computed tomography angiography (CTA) and stress single photon emission computed tomography (SPECT) in evaluation of chest pain in diabetic and non-diabetic patients.

Patients and Methods: This study included 150 patients with chest pain suggestive of coronary artery disease seen in outpatient cardiology clinic at Al-Hussein and Bab-Elshareia University Hospitals. The study was carried during the period from April 2019 till January 2021. Patients underwent coronary angiography (CA). Patients randomly included 100 diabetic patients and 50 nondiabetic patients. All patients were examined with ECG, echocardiography, 64-slice computed tomography (CT) scanner and ECG gated SPECT.

Results: Positive CTA and CA significantly increased in diabetic group than non-diabetic group (P = 0.005 and 0.014). There was an insignificant difference (good agreement) between CA and CTA (P = 0.001). There was a significant difference (bad agreement) between SPECT and CA (P = 0.001).

Conclusions: In both patients with diabetes mellitus (DM) and without DM, CTA had a good agreement with the results of CA unlike SPECT. Positive CA and CTA were more common with DM.

Keywords: Coronary Computed Tomography Angiography, Stress Single Photon Emission Computed Tomography, Diabetes.

INTRODUCTION

In the evaluation of patients with suspected CAD, the role of non-invasive imaging has increased exponentially over the past decades. Particularly in patients with an intermediate before-test likelihood of CAD, non-invasive imaging plays an important role in risk stratification and selection of further treatment strategies. Traditionally, the detection of CAD by non-invasive imaging was based on assessment of the hemodynamic significance of the stenoses through visualization of inducible ischemia *(Taqueti et al., 2017).*

Several noninvasive techniques are available for this purpose, including stress ECG and single-photon emission computed tomography (SPECT) and coronary computed tomography angiography (CTA) *(Danad et al., 2017).*

Previously published results have proved the high values of sensitivity and specificity, and negative predictive value almost 100% of CTA for the assessment of coronary disease, even in patients treated with stent or bypass. However, in patients with coronary calcification, the CT examination presents several limitations in residual vessel lumen evaluation. Otherwise, multidetector CTA sometimes shows some limitations in the grading of coronary stenosis due to motion artefacts or severe vessel calcification *(Collet et al., 2018).*

Diabetes mellitus (DM) is associated with an increased risk of coronary atherosclerosis and excess cardiovascular morbidity and mortality. Atherosclerosis in patients with diabetes manifests in a more accelerated and progressive manner. Overall, a twofold risk for developing CAD has been observed in this patient population. Patients with diabetes may have a similar risk for new-onset myocardial infarction as patients without diabetes with prior myocardial infarction. Cardiac stress testing is considered appropriate for the identification of CAD in symptomatic patients with an intermediate or high risk. However, the role of stress imaging in asymptomatic patients remains controversial *(Sarwar et al., 2010).*

Diabetes causes severe vessel calcifications resulting in lower diagnostic accuracy of CTA in detection of coronary stenosis in diabetic patients. In this case, it could be useful to work with hybrid imaging of SPECT, overcoming the limits of the two techniques *(Hsiao et al., 2010).*

The aim of this study was to assess the diagnostic value of CTA and stress SPECT in evaluation of chest pain in diabetic and non-diabetic patients.

PATIENTS AND METHODS

This study population included 150 patients with chest pain suggestive of CAD seen at outpatient cardiology clinic and underwent coronary angiography (CA) at Al-Hussein and Bab-Elshareia University Hospitals, The study was carried during the period from April 2019 till January 2021. Patients randomly included 100 diabetic patients and 50 nondiabetic patients. After approval from the Ethical Committee, informed written consents were taken from all patients for the study participation.

Exclusion criteria: Poor echo window, known history of CAD, frequent extrasystole, hemodynamic instability, severe valvular heart disease, and cardiomyopathy.

All patients were subjected to:

1. Careful history.
2. General and local cardiac examination were done for all patients including vital signs, head and neck examination, upper and lower limb examination, abdominal examination and local examination.
3. Resting surface 12 lead ECG was done for all patients.

4. Echocardiography.
5. Computed tomography angiography: Examination was done using 64-slice CT scanner and patients with heart rate higher than 65 pbm were treated with beta blocker with or without Ivabradine to control heart rate.
6. ECG gated SPECT examination: Stress-rest study using technetium with exercise ECG protocol was performed. The left ventricular myocardium was divided into 17 segments. Each of 17 segments scored according to the guidelines for semi quantitative analysis, the five point model: 0=normal, 1=mildly reduced – not definitely abnormal, 2=moderate reduced – definitely abnormal, 3=severe reduced, 4=absent radiotracer distribution.

Statistical analysis:

Statistical analysis was done by SPSS v25 (IBM©, Chicago, IL, USA). Shapiro-Wilks test and histograms were used to evaluate the normality of the distribution of data. Quantitative parametric data were presented as mean and standard deviation (SD) and range and were analysed by unpaired student t-test. Quantitative non-parametric data were presented as median and interquartile range (IQR) and were analysed by Mann Whitney-test. Qualitative data were presented as number and percent and were compared by chi-square (X2), Fisher's Exact or McNemr test when appropriate. A two tailed P value <0.05 was considered statistically significant.

RESULTS

The age of the patients ranged from 30-79 years with a mean value of 50.05 ± 9.72 years. There were 70 (46.7%) male patients, and 80 (53.3%) female patients. There were 100 (66.7%) diabetic patients, 45 (30%) smokers, and 79 (53%) obese patients **(Table 1)**.

Table (1): Demographic data of the studied patients

Parameters		Patients (n = 150)
Age (years)	**Mean ± SD**	50.05 ± 9.72
	Range	30-79
Sex	**Male**	70 (46.7%)
	Female	80 (53.3%)
DM	**Diabetic**	100 (66.7%)
	Not diabetic	50 (33.3%)
Smoking	**Smoker**	45 (30%)
	Not smoker	105 (70%)
Obesity	**Yes**	79 (53%)
	No	71 (47%)

DM: diabetes mellitus

As regard to CT, 87 (58%) patients were –ve, and 63 (42%) patients were +ve, 3 (4.8%) patients were +ve 1, 7 (11.1%) patients were +ve 2, 19 (30.2%) patients were +ve 3 and 34 (54%) patients were +ve 4. As regard to SPECT, 66 (44%) patients were –ve and 84 (56%) patients were +ve; 60 (71.4%) patients were mild, 16 (19 %) patients were moderate and 8 (9.5%) patients were severe. As regard to CA, 60 (40%) patients were +ve and 90 (60%) patients were –ve, Ca score ranged from 0-432 with a median value 3 **(Table 2)**.

Table (2): CTA, SPECT, Coronary angiography and Ca score of the studied patients

Parameters		Patients (n = 150)
CTA	-ve	87 (58%)
	+ve	63 (42%)
	+ve 1	3 (4.8%)
	+ve 2	7 (11.1%)
	+ve 3	19 (30.2%)
	+ve 4	34 (54%)
SPECT	-ve	66 (44%)
	+ve	84 (56%)
	Mild	60 (71.4%)
	Moderate	16 (19%)
	Severe	8 (9.5%)
Coronary angiography	+ve	60 (40%)
	-ve	90 (60%)
Ca score	Median	3
	Range	0-432

There was an insignificant difference (good agreement) between CA and CTA (P = 0.001). There was a significant difference (bad agreement) between SPECT and CA (P = 0.001) **(Table 3)**.

Table (3): Comparison between CTA and Coronary angiography

Parameters \ Coronary angiography		Positive	Negative	P value
CTA	Positive	87	3	<0.001
	Negative	3	57	
SPECT	Positive	54	12	<0.001
	Negative	36	48	

Demographic data were insignificantly different between diabetic and non-diabetic groups **(Table 4)**.

Table (4): Demographic data in both studied groups

Parameters \ Groups		Diabetic group (n = 100)	Non diabetic group (n = 50)	P value
Age (years)	Mean ± SD	49.92 ± 9.81	50.32 ± 9.65	0.813
	Range	30-79	30-79	
Sex	Male	49 (49%)	21 (42%)	0.418
	Female	51 (51%)	29 (51%)	
Smoking		33 (33%)	12 (24%)	0.345
Obesity		58 (58%)	21 (42%)	0.093

Positive CTA significantly increased in diabetic group than non-diabetic group (P = 0.005) SPECT was insignificantly different between both groups, positive Ca significantly increased in diabetic group than non-diabetic group (P = 0.014), and Ca score significantly increased in diabetic group than non-diabetic group (P = 0.001) **(Table 5)**.

Table (5): CTA, SPECT, Coronary angiography and Ca score in both studied groups

Parameters \ Groups		Diabetic group (n = 100)	Non-diabetic group (n = 50)	P value
CTA	-ve	50 (50%)	37 (74%)	**0.005**
	+ve	50 (50%)	13 (26%)	
SPECT	-ve	42 (42%)	24 (48%)	0.485
	+ve	58 (58%)	26 (52%)	
Coronary angiography	+ve	47 (47%)	13 (26%)	**0.014**
	-ve	53 (53%)	37 (74%)	
Ca score	Median	24.5	0	**0.001**
	Range	0-432	0-126	

DISCUSSION

Myocardial perfusion by CCTA (coronary computed tomography angiography) is still little explored. Stress computed tomography (CT) myocardial perfusion imaging is a technique which has shown consistent results in the diagnosis of obstructive CAD. In its turn, myocardial perfusion scintigraphy is a well-established method for detection of CAD. The possibility of integrating anatomy and function in a single exam can enhance stratification of obstructive CAD and ensure better patient management *(Oliveira et al., 2015)*.

The present study showed that as regard to CT, 58% patients were –ve and 42% patients were + ve, 4.8% patients were +ve 1, 11.1% patients were +ve 2, 30.2% patients were +ve 3 and 54% patients were +ve 4. Positive CT significantly increased in diabetic group than non-diabetic group.

A higher incidence of positive results using SPECT (58%) than using CT (42%) which was partially in agreement with the study done by *Ker et al. (2019)*, 57.1% of the patients presented perfusion defects at myocardial scintigraphy, with 28.5% also presenting defects at CT.

DM has reached epidemic proportions, creating a large population of people at increased risk for cardiac events. Single-photon emission computed tomography myocardial perfusion imaging (SPECT MPI) provides an effective tool to accurately diagnose and risk stratify patients with diabetes, similar to patients without diabetes. Diabetics, however, are at increased risk for coronary events. Diabetics with normal MPI have increased late cardiac events, and even those with mild perfusion defects have increased event rates compared with nondiabetics with similar perfusion abnormalities. Stress MPI can provide valuable risk stratification data for both sexes, with or without diabetes. However, diabetes appears to exert a greater relative impact in women than in men. Despite the absence of symptoms, the incidence and prevalence of CAD is increased in patients with diabetes *(Noble and Heller, 2010)*.

Approximately 75% of diabetic patients die of CAD. CAD is more likely to be silent in diabetic patients. American Diabetes Association guidelines recommend screening for CAD in asymptomatic diabetic patients who have an abnormal resting electrocardiogram (ECG) indicative of myocardial infarction (MI) or ischemia, peripheral arterial disease (PAD), or two or more additional CAD risk factors. These recommendations are the result of expert opinion and are not evidence-based. Stress single-photon emission computed tomography (SPECT) imaging is accurate for diagnostic and prognostic purposes in general and in diabetic populations *(Berman et al., 2010)*.

The current study showed that, as regard to SPECT –ve, SPECT and +ve SPECT were insignificantly different between diabetic and non-diabetic.

Our results were in contrary with the study of *Miller et al. (2010)* as they reported that a higher SPECT percentage of diabetic than nondiabetic patients had abnormal scans (59.2% vs 44.9%). However, the difference between significant which CTA used as a diagnostic tool in the present study.

Owing to the high prevalence of CAD, the role of coronary imaging in diabetic patients may be not to document the presence of coronary atherosclerosis but rather to identify those patients with more extensive disease versus those without any atherosclerosis. In patients with extensive CAD, further testing may be warranted to identify patients with substantial inducible myocardial ischemia who may be candidates for CA and subsequent revascularization. The prognostic utility of stress imaging studies, including myocardial perfusion scintigraphy and dobutamine stress echocardiography, has been validated in numerous studies, and, in general, patients with a normal imaging study result have an annual cardiac ischemic event rate of less than 1%. However, this risk is increased more than twofold in diabetic patients. Therefore, assessing prognosis in patients with DM remains challenging, and further refinement of risk stratification is necessary in this high-risk population *(Kamalesh et al., 2011)*.

Multidetector computed tomographic (CT) CA has emerged as a noninvasive tool for the diagnosis of CAD that enables assessment of the vascular lumen together with the arterial wall. As a result, the technique allows accurate assessment of the presence or absence of CAD with sensitivity and negative predictive values that are near 100% *(Pugliese et al., 2010)*.

In the study in our hands, as regard to CA, 40% patients were +ve and 60% patients were –ve. There was insignificant difference between CA and CT. There was a significant difference between SPECT and CA. Positive CA was significantly increased in diabetic group than non-diabetic group.

Our results were in line with study of *Van Werkhoven et al. (2010)* as they reported that significant differences were observed between diabetic and nondiabetic patients concerning the prevalence of normal coronary arteries (19% vs 26%, respectively) and the prevalence of obstructive disease (51% vs 37%, respectively). Furthermore, diabetic patients showed a higher average number of diseased coronary segments (5.6 vs 4.4), with either obstructive (1.7 vs 1.2) or nonobstructive (3.9 vs 3.1) CAD.

Coronary artery calcium score (CACS) is widely considered a marker of subclinical atherosclerosis, validated in asymptomatic patients. Extent of CACS, in fact, well correlates with the vascular atherosclerotic involvement and the probability of adverse cardiac events in the general population. Although the latest European guidelines on cardiovascular prevention suggested evaluation of the CACS only in diabetic patients with high or very high cardiovascular risk (score > 5% and score > 10%), the latest American guidelines for risk stratification in patients with CAD recommended an “appropriate” use of CACS and CCTA in asymptomatic patients with high global risk *(Wolk et al., 2014)*.

The present study showed that Ca score ranged from 0-432 with a median value 3. Ca score was significantly increased in Diabetic group than Non diabetic group.

Our results were in agreement with study of *Wong et al. (2010)*, as they reported that Type 2 DM patients have higher values of CACS when compared with the general population. The mechanisms responsible for the extensive intracoronary calcium accumulation in diabetic patients are multifactorial and not completely understood. Previous studies revealed that the increased production of advanced glycation end-products induces the overexpression of genes and enzymes involved in active calcification of the coronary plaque. Coronary artery calcium scoring (CACS) has been proposed as a first-line test for CAD in patients with diabetes since it was widely demonstrated that it has higher capability with respect to conventional cardiovascular risk factors for predicting silent myocardial ischemia and short-term outcome. Numerous studies showed that higher values of CACS in diabetic patients with metabolic syndrome are closely associated with increased prevalence of ischemia, adverse cardiac events, AMI, and mortality *(Budoff et al., 2010)*.

Notwithstanding, a significant percentage of patients with DM have very low or zero CACS, with a better long-term prognosis, revealing that DM is not an equivalent of coronary risk. *Raggi et al. (2010)* documented a high proportion of asymptomatic patients with DM (39%) with CACS < 10. In this study, the authors confirmed a significant correlation between CACS and DM, indicating that each increase of CACS correlates with an increase in mortality in diabetic and nondiabetic patients. However, diabetic patients without known CAD showed similar survival to patients without DM and intracoronary calcium (98.8% and 99.4%, respectively). The results of other studies show the same trend *(Lehmann et al., 2014)*.

Furthermore, *Van Werkhoven et al. (2010)* demonstrated that the total Agatston calcium score, which reflects plaque burden, was higher in diabetic patients than in nondiabetic patients .

CONCLUSION

In both patients with diabetes mellitus and without diabetes mellitus, CTA had a good agreement with the results of CA unlike SPECT. Positive CA and CTA were more common with diabetes mellitus.

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دور الأشعة المقطعية للشرايين التاجية والمسح الذري للقلب في تقييم آلام الصدر في مرضى السكري وغير السكري

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خلفية البحث: إزداد دور التصوير غير التدخلي بشكل كبير خلال العقود الماضية في تقييم المرضى المشتبه في إصابتهم بأمراض القلب التاجية.

الهدف من البحث: تقييم القيمة التشخيصية للأشعة المقطعية للشرايين التاجية والتصوير والمسح الذري للقلب في تقييم آلام الصدر لدى مرضى السكري وغير المصابين بالسكري.

المرضي وطرق البحث: شملت الدراسة 150 مريضًا يعانون من آلام في الصدر تشير إلى الإصابة بأمراض القلب التاجية في العيادات الخارجية لأمراض القلب بمستشفى الحسين و مستشفى باب الشعرية الجامعي. تراوحت الدراسه بين شهر أبريل 2019 وشهر يناير2021، وخضعوا لقسطرة الأوعية التاجية. وقد شمل المرضى 100 مريضا بالسكري و50 مريضا غير مصاب بمرض السكري.وقد تم فحص جميع المرضى باستخدام رسم القلب والإيكو والأشعة المقطعية للشرايين التاجية والتصوير والمسح الذري للقلب.

نتائج البحث: هناك زيادة معنوية في التصوير المقطعي المحوسب للأوعية وتصوير الأوعية التاجية في مجموعة مرضى السكر

مقارنـــة بالمجموعـــة غيـــر المصـــابة بالســـكري P = 0.005 (و 0.014). وكـــان هنـــاك فـــرق ضـــئيل بـــين تصـــوير الأوعيـــة التاجيـــة وتصـــوير الأوعيـــة المقطعـــي المحوســـب (P = 0.001). كمـــا كـــان هنـــاك فـــرق كبيـــر بـــين التصـــوير المقطعـــي المحوســـب بانبعـــاث فوتـــون واحد وتصوير الأوعية التاجية (P = 0.001).

الاســـتنتاج: هنـــاك توافـــق جيـــد بـــين الأشـــعة المقطعيـــة للشـــرايين التاجيـــة ونتـــائج قســـطرة الأوعيـــة التاجيـــة. علـــى عكـــس المســـح الـــذري للقلـــب. وتعـــد قســـطرة الأوعيـــة التاجيـــة الإيجابيـــة والأشـــعة المقطعيـــة للشـــرايين التاجية أكثر شيوعًا مع مرضى السكري.

الكلمـــات الدالـــة: تصـــوير الأوعيـــة الدمويـــة بالتصـــوير المقطعـــي للشـــريان التـــاجي، تصـــوير مقطعـــي محوســـب بانبعـــاث فوتـــون واحـــد، مرض السكري.