Computed Tomography Angiography Approach in Low-Intermediate Test Probability with Positive Exercise Electrocardiography Test in Young Women

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ABSTRACT

Introduction: Stress imaging tests are recommended in patients with positive exercise electrocardiography (EECG) and intermediate pretest probability. However the role of coronary computed tomography angiography (CCTA) in young women with intermediate pretest probability and positive EECG is under debate. The aim of this study was to assess the diagnostic value of CCTA in young women patients with low-intermediate pretest probability and positive EECG results.

Patients and Methods: From a retrospective registry of 67 young women with positive EECG between January 2011 and January 2014 were included in this study. Of these 67 patients 32 patients underwent CCTA and 35 patients underwent MPS after EECG.

Results: There were no statistically significant differences between groups in demographic variables, or cardiovascular risk profile. The exercise test was positive in all patients. Both groups were similar for exercise capacity and Duke treadmill score. Blood chemistry of the patients were similar. The median pre-test probability of obstructive coronary artery disease (CAD) was lower in CCTA group 28% (15-45%) than in MPS group (15-50) (p= 0.045). Overall 3 patients in the CCTA and 7 patients in the MPS group had significant lesions. All patients in the CCTA positive group had significant CAD, while 3 out of 7 patients with positive MPS findings had significant CAD in coronary angiography.

Conclusion: CCTA may be a valuable alternative of stress imaging tests in women patients with low-intermediate pretest probability and positive EECG.

Key Words: Exercise electrocardiography; computed tomography; angiography; pretest probability; women, young

Düşük-Orta Test Öncesi Olasılığı Olan ve Efor Testi Pozitif Saptanan Genç Bayanlarda Koroner Bilgisayarlı Tomografik Anjiyografi Yaklaşımı

ÖZET

Giriş: Test öncesi olasılığı orta olan ve egzersiz elektrokardiyografi testi (EEKT) pozitif saptanan hastalarda stres görüntüleme yöntemi önerilmektedir. Ancak koroner bilgisayarlı tomografik anjiyografinin (KBTA) test öncesi olasılığı orta olan ve efor testi pozitif saptanan genç bayan hastalarda kullanımı halen tartışmalıdır. Bu çalışmanın amacı düşük-orta test öncesi olasılığı olan ve EEKT pozitif saptanan genç bayanlarda KBTA tanısal öneminin saptanmasıdır.

Hastalar ve Yöntem: Haziran 2011 ile haziran 2014 tarihleri arasında başvuran EEKT pozitif olan 67 genç bayan çalışmamıza retrospektif olarak dahil edildi. Bu 67 hastanın 32'sine KBTA 35'ine MPS yapıldı.

Bulgular: Hastaların demografik ve kardiyovasküler risk profilleri benzerdi. Bütün hastaların EEKT'si pozitifti. Hastaların efor kapasitesi ve Duke treadmil skorları benzerdi. Kan biyokimyası benzerdi. Tıkayıcı koroner arter hastalığı (KAH) açısından ortanca test öncesi olasılığı KBTA grubunda %28 (15-45%) MPS grubundan (15-50) daha düşüktü (p= 0.045). KBTA yapılan 3 hastada MPS yapılan 7 hastada ciddi lezyon tespit edildi. KBTA'sı ciddi olan 3 hastanın hepsinde ciddi KAH saptandı. Ancak MPS'sinde iskemi saptanan 7 hastanın 3'ünde ciddi KAH saptandı.

Sonuç: Test öncesi olasılığı düşük-orta olan efor testi pozitif genç bayan hastalarda KBTA stres görüntüleme yöntemlerine kullanışlı bir alternatif olabilir.

Anahtar Kelimeler: Egzersiz elektrokardiyografi; bilgisayarlı tomografi; anjiyografi; test öncesi olasılık; kadın; genç

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INTRODUCTION

Coronary artery disease is the leading cause of death and morbidity. Diagnosis of coronary artery disease is important to prevent unwanted major adverse cardiovascular events. Various methods are introduced to diagnose coronary artery disease. However, exercise electrocardiography test (EECG), free from radiation, easy, reproducible and safe, is usually the first-line non-invasive examination in the assessment of suspected coronary artery disease. EECG also provides important data on symptoms, exercise capacity, heart rate response to exercise, blood pressure and the presence of exercise-induced arrhythmias. It sensitivity and specificity is decreased in certain situations thus It is usually complemented by other functional tests including stress echocardiography (SE) and myocardial perfusion scintigraphy (MPS) in patients with low and intermediate test results[1]. Coronary computed tomographic angiography (CCTA) is an anatomical evaluation method and alternative to EECG, MPS and SE in patients with intermediate or low pre-test probability.

Determination pretest probability is important for proper test judgment. According to Bias theory, the sensitivity of EECG is low in young women[1]. Stress imaging tests including MPS and SE are recommended in patients with positive EECG and intermediate pretest probability[1]. However the role of CCTA in young women with intermediate pretest probability and positive EECG is under debate. The aim of this study was to assess the diagnostic value of CCTA in young women patients with low-intermediate pretest probability and positive EECG results.

PATIENTS and METHODS

From a retrospective registry of 67 young women with suspected stable coronary artery disease and positive EECG test results who were admitted to our clinic between January 2011 and January 2014 were included in this study. Of these 67 patients 32 patients underwent CCTA and 35 patients underwent MPS after EECG. Patients over 50 years age, with documented CAD, baseline ECG abnormality, atrial fibrillation, right and left bundle branch block, diabetes mellitus, peripheral artery disease were excluded. Informed consent was obtained from all subjects, and the investigation conforms to the principles outlined in the Declaration of Helsinki. The study protocol was approved by local ethics committee.

Weights of the patients, in light clothes without shoes, were measured in kilograms, and their heights were measured. Body mass index (kg/m^2) (BMI) was calculated by dividing body weight in kilograms by the square of body height in meters. Transthoracic echocardiography assessment (Vivid S5 General Electric, Norway) was performed in patients according to the standards of the American Society of Echocardiography[2].

Hypertension was defined by a previous diagnosis of hypertension or the presence of SBP≥ 140 mmHg or DBP≥ 90 mmHg (mean of two consecutive measurements). Dyslipidemia was defined as total cholesterol> 190mg/dL or previous diagnosis of dyslipidemia. Patients who self-reported as having smoked during the previous six months were classified as smokers. Venous blood samples were drawn after a 12-hour overnight fast. Serum glucose, total cholesterol and triglycerides were determined using standard automatic enzymatic methods. High density lipoprotein cholesterol (HDL) cholesterol was determined after specific precipitation and low density lipoprotein (LDL) cholesterol was determined by the Friedewald formula.

Pre-test probability

The pre-test probability of obstructive CAD was determined for each patient using the predictive model of Genders et al[3]. The variables considered in the model are age, gender and symptoms (classified as typical chest pain, atypical chest pain or non-specific chest pain).

Exercise ECG

All patients underwent CCTA 2-3 days after an EECG test. The EECGs were performed and interpreted by the respective attending physicians. EECG tests were performed per standardized Bruce-protocol, with continuous blood pressure, heart rate and ECG monitoring up to at least 5 min into recovery. Tests were classified as inconclusive in patients who did not reach their predicted exercise tolerance (< 85% of the age and sex predicted heart rate or a heart rate pressure product by 18.000). A test was considered positive in case of ≥ 1.0 mm horizontal or downsloping ST deviation at 80 ms after the J-point compared to baseline ECG (≥ 1.5 mm was used for upsloping ST deviation) and/or typical angina and/or ventricular arrhythmia and/or a decrease in systolic blood pressure >10 mm Hg.

Coronary computed tomographic angiography

All patients underwent CCTA on a 64-slice dual-source scanner (Aquilion 64, Toshiba Medical Systems, Tochigi, Japan). All patients received Beta blocker premedication before the procedure and prospective ECG triggering was used in 100% of patients. Acquisition without contrast was performed immediately prior to CCTA in all cases in order to calculate the calcium score. Total CAC score, three-dimensional reconstruction and analysis of the CCTA images were performed on a workstation was calculated using dedicated software (Vitrea 2 version 3.0.9.1, Vital Images, Minnesota. All lesions were added to calculate the total CAC score.

Statistical Analysis

The groups were compared using the Student's t test or Mann-Whitney U test for continuous variables and chi square test for categorical variables. The results for continuous variables with normal and no normal distribution were presented as mean ± standard deviation and median (range), respectively. The statistical analysis was performed using SPSS version 17.0. A two sided $p< 0.05$ was accepted significant.

Table 1. The characteristics of patients

Variable	CCTA (32)	MPS (35)	p
Age, year	42.2 ± 2.3	42.1 ± 2.1	0.536
Body mass index kg/m^2	27.7 ± 5.8	27.4 ± 4.6	0.257
Hypertension, n (%)	12 (37.5%)	14 (40%)	0.854
Dyslipidemia , n (%)	14 (43.8%)	14 (40%)	0.435
Family history of coronary artery disease, n (%)	15 (43.8%)	18 (51.4%)	0.126
Smoking, n (%)	10 (31.3%)	12 (34.3%)	0.247
METs achieved	8.1 ± 2.9	7.8 ± 3.5	0.126
Duke treadmill score	2(-4-4)	2 (-4 - 4)	0.958
Pretest probability, (%)	28 (15-45)	32 (15-50)	0.045
Positive result, n (%)	3 (9.4%)	7 (20.0%)	0.008
Significant coronary artery disease, n (%)	3 (9.4%)	3 (8.6%)	0.420
Low density lipoprotein cholesterol, mg/dL	137.2 ± 26.8	134.3 ± 25.9	0.402
High density lipoprotein cholesterol, mg/dL	46.3 ± 12.1	44.8 ± 11.5	0.220
Creatinine, mg/dL	0.8 ± 0.1	0.8 ± 0.1	0.980
Glucose, mg/dL	92.1 ± 10.3	90.8 ± 15.4	0.261
Left ventricle ejection fraction, (%)	63.4 ± 10.5	64.8 ± 8.5	0.102

CCTA: Coronary computed tomographic angiography, MPS: Myocardial perfusion scintigraphy, MET: Metabolic equivalent of task

RESULTS

There were no statistically significant differences between groups in demographic variables, or cardiovascular risk profiles (Table 1). The EECG was positive in all patients. Both groups were similar for exercise capacity and Duke treadmill score. Blood chemistry of the patients were similar. The median pre-test probability of obstructive CAD was lower in CCTA group 28% (15-45%) than in MPS group (15-50) (p= 0.045). Overall 3 patients in the CCTA and 7 patients in the MPS group had positive findings. All patients in the CCTA positive group had significant CAD, while 3 out of 7 patients with positive MPS findings had significant CAD in coronary angiography. Two patients had soft plaque and one patient had mixed plaque in CCTA.

DISCUSSION

We found that CCTA approach is effective in the diagnosis of significant CAD and prevent further invasive strategy in patients with low-intermediate pretest probability and positive EECG.

The evaluation of suspected stable coronary artery disease involves qualitative and quantitative measurement and estimation of disease risk. Pretest probability is important in the selection of appropriate diagnostic strategy. Patients at very high risk referred directly to invasive coronary angiography while patients with low pretest probability goes on risk factor modification only without further evaluation[1]. Stepwise evaluation is preferred in patients with intermediated probability. The choice of a first-line exam should be based on its advantages and disadvantages in terms of diagnostic accuracy, accessibility, cost and contraindications. Generally the EECG is the first line test for the diagnosis and risk stratification in stable coronary artery disease patients. However, its limited sensitivity and specificity lead to suboptimal performance in many cases which can raise indirect costs: inconclusive tests generally necessitate additional exams, which increases the overall cost of the diagnostic strategy; false negative results can delay or prevent correct diagnosis, while false positive results frequently require more complex and costly non-invasive exams or result in unnecessary diagnostic catheterization, which entails risks and potentially avoidable cost[4]. Evaluation of epicardial fat thickness, ankle brachial index, carotid intima media thickness, aortic stiffness, coronary calcium score and oxidative stress may confer further risk stratification[5-11] It is recommended to continue further imaging stress test to patients with intermediate results and low-intermediate pretest probability[1]. CCTA is a promising non-invasive anatomical test for the evaluation of stable coronary artery disease. It has a high negative predictive value. It is recommended to perform CCTA to patients with low-intermediate pretest probability. The aim of this study is to evaluate and compare the effectiveness of CCTA with MPS in women patients with low-intermediate pretest probability and positive EECG.

We detected that all patients with severe stenosis in CCTA had significant obstructive coronary artery disease. However in MPS group 3 of 7 patients had significant obstructive coronary artery disease. This finding may be related to the functional evaluation advantages of MPS. Hence CCTA is an anatomical

imaging method. But MPS confers functional imaging. Cardiac syndrome X is common among young women. Microvascular dysfunction could not be evaluated with anatomical imaging further functional methods are required.

When appropriately used CCTA could help to minimize unnecessary invasive procedures[12]. However ionizing radiation and iodinated contrast, limits its use in clinical practice. Its cost-effectiveness has been the subject of investigation. When compared with the standard functional tests (exercise testing, SE and MPS), CCTA has been shown to be cost-effective [13]. Additionally CCTA is performed with lower effective radiation doses than for MPS[14].

Our study has certain limitations. Firstly, Since not all patients underwent invasive coronary angiography, it was not possible to assess the true sensitivity and specificity of each of the tests in this population. Secondly, the sample may not have been representative of all patients with suspected CAD, since we included patients with low-intermediate pretest probability. Additionally all patients did not undergo invasive coronary angiography. Therefore it was not possible to assess the true sensitivity and specificity of each of the tests (CCTA and MPS) in this population.

CONCLUSION

CCTA may be a valuable alternative of stress imaging tests in women patients with low-intermediate pretest probability and positive EECG.

CONFLICTS of INTEREST

The authors have no conflicts of interest to declare.

AUTHORSHIP CONTRIBUTIONS

Concept/Design: AÇA, DA, EK, TG
Analysis/Interpretation: AÇA, DA, EK, ŞÇ, İÇ, AU, AOA, ÖÇ, BY
Data acquisition: AÇA, EK, TG
Writing: AÇA, ŞÇ
Critical revision: EK, TG, DA, İÇ, AU, AOA, ÖÇ, BY
Final approval: All of authors

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