Al-Azhar Med. J. (cardiology). *Vol. 52(3), July, 2023, 883 - 894*
DOI: 10.21608/amj.2023.315125
https://amj.journals.ekb.eg/article_315125.html

DETECTION OF MYOCARDIAL ISCHEMIA IN ASYMPTOMATIC PATIENTS WITH DOCUMENTED TRANSIENT ISCHEMIC ATTACKS

By

Amin Mohamed Hassan Soliman, Sami Hassan Noah and

Ahmed Ali Faheem Abdo

Department of Cardiology, Faculty of Medicine, Al-Azhar University

***Corresponding author:** Amin Mohamed Hassan Soliman,

E-mail: aminsoliman0@gmail.com

ABSTRACT

Background: Myocardial ischemia (IHD) has been shown to be the leading cause of death in patients with transient ischemic attacks (TIAs), causing more deaths than stroke. Coronary artery disease (CAD) is a frequent cause of death among stroke survivors. Recently appeared guidelines encourage healthcare professionals to optimize coronary risk evaluation in patients with transient ischemic attack (TIA) and ischemic stroke to establish appropriate strategies to prevent incident coronary artery disease.

Objective: To detect the silent myocardial ischemia among patients presented with transient ischemic attacks.

Patients and methods: This study was conducted on 50 asymptomatic patients with transient cerebral ischemic attack at Al-Azhar University Cardiology Department, during period from October 2019 to October 2021. All patients underwent thorough history taking, clinical examination, electrocardiogram, 2D echocardiography and SPECT scan Myocardial perfusion imaging (MPI).

Results: Echocardiographic data showed that mean ejection fraction of the studied group was 64.82±6.24, 24% of patients had Resting segmental wall motion abnormalities (RSWMA), 24% had dilated left atrium and 72% had diastolic dysfunction. There were statistically significant differences between positive and negative myocardial perfusion imaging (MPI) patients regarding risk factors including diabetes mellitus, dyslipidemia and smoking. Also, there were statistically significant differences between positive and negative myocardial perfusion imaging patients regarding prominent a wave, neurologic symptoms, echocardiographic data (except left ventricular posterior wall end-diastolic dimension (PWEDd) and Interventricular septum diastolic dimension (IVSDd)). Regression analysis showed that age, diabetes mellitus, dyslipidemia, smoking, fractional shortening, resting wall motion abnormalities (RWMA) score index, left atrial (LA) dilation, diastolic dysfunction and left ventricular end-diastolic diameter (LVEDD) were independent predictors of positive single-photon emission computed tomography (SPECT) scan.

Conclusion: Patients who have TIA with no known coronary artery disease have approximately twice the risk for a subsequent myocardial ischemia compared to the general population. This risk accumulated linearly over time for many years after the transient ischemic attack.

Keywords: Myocardial Ischemia, Coronary artery disease, Transient Ischemic Attack.

INTRODUCTION

Involvement of the coronary arteries is common in patients with non-cardio embolic ischemic stroke (IS) or transient ischemic attack (TIA). In the Reduction of Atherosclerosis for Continued Health (REACH) study, established coronary

heart disease coronary heart disease (CHD) was present in 37.9% of the patients with IS or TIA *(Steg et al., 2011)*.

Coronary heart disease is usually considered a significant cause of morbidity and mortality in patients who have had a stroke or TIA *(Adams et al., 2010)*.

While myocardial infarction is caused by coronary atherosclerosis in almost 100% of cases, IS can have various etiologies: large-artery atherosclerosis, cardiac embolism, small-vessel disease, or less common causes such as arterial dissection and hematological disorders, among others. IS etiology may remain undetermined in up to 30–40% of the cases despite extensive investigation, particularly in young adults *(Yamamoto, 2012)*.

In the Multiple Atherosclerosis Site in Stroke study (MASS), 267 autopsies were performed after fatal strokes. Coronary plaques were observed in 69.7% of patients with IS and no history of CHD. When subgroups were analyzed, coronary plaques were present in 77.1% of the cases with atherothrombotic, 65.5% of the cases with cardio embolic, 79% of cases with lacunar and 63% of undetermined cause IS. These high rates of coronary plaques in IS subjects without history of CHD symptoms contrasted with the 24.7% prevalence of coronary atherosclerosis in 442 patients with other neurologic diseases *(Gongora-Rivera et al., 2011)*.

Despite the evidence of association between CHD and IS or TIA, there are no strong recommendations for CHD screening in asymptomatic patients with cerebrovascular disorders. However, asymptomatic coronary heart disease or elevated coronary heart disease risk are significantly more common in patients with ischemic stroke caused by atherosclerosis than by other etiologies, or in patients with ischemic stroke of undetermined cause, are still controversial issues *(Sander et al., 2011)*.

The aim of the present study was to detect the silent myocardial ischemia among patients presented with transient ischemic attacks.

PATIENTS AND METHODS

This study was conducted on 50 asymptomatic patients with transient cerebral ischemic attack at Al-Azhar University Cardiology Department, during the period from October 2019 to October 2021.

Inclusion criteria: Transient cerebral ischemic attack, and asymptomatic from the cardiac point of view.

Exclusion criteria: Patients with known history of CAD, patients with symptoms related to IHD, documented atrial fibrillation, patients with hemorrhagic stroke, brain tumors, and pregnancy.

All patients were subjected to the following:

1. Complete History Taking including age, gender, duration since TIA diagnosed, drug intake and other co morbidities.
2. Clinical Examination including general examination as dyspnea, lower limb edema, BP, HR, jugular venous pulse, local examination: inspection, palpation and auscultation of the heart to examine apical impulse, and heart sounds.

3. Investigations:

- ECG: Rate, Rhythm interpretation, and ST-T abnormalities.
- Echocardiography: Conventional echocardiographic Doppler study and M-mode were performed using Philips iE33. All subjects were examined in the left lateral decubitus position according to the recommendations of the American Society of Echocardiography.

A. Left Ventricular Assessment:

- Systolic function assessment.
- LV Global Systolic Function.
- LV wall motion assessed to detect RSWMAs as a clue for IHD.

B. Left Atrial Assessment.

- Stress ECG test.

SPECT (single photon emission computed tomography) scan: Resting and stress imaging using treadmill were taken. Normal study was considered negative for ischemia while abnormal perfusion defects whether reversible or fixed were considered positive.

After registering, a nuclear medicine technologist inserted a small IV line into patient's arm.

Statistical analysis:

Data were analyzed using the Statistical Package for the Social Science (SPSS) program for Windows (Standard version 21). The normality of data was first tested with one-sample Kolmogorov-Smirnov test. Qualitative data were described using number and percent. Association between categorical variables was tested using Chi-square test. Continuous variables were presented as mean ± SD (standard deviation) for normally distributed data. The two groups were compared with Student t test. For all above mentioned statistical tests done, the threshold of significance is fixed at 5% level. P value < 0.05 was considered significant.

RESULTS

The mean age of the studied group was 58.24±8.36, ranged from 43-74 years. The risk factors were 32% of patients diabetic, 28% HTN, 54% dyslipidemics and 28% smokers.

Drug intake 44% of patients were on beta-blockers, 40% on antiplatelets, 32% on diuretics and 22% used statins. The mean duration from diagnosis of TIA was 9.56 ±1.91 months, mean systolic blood pressure was 125.60±8.66, and mean diastolic blood pressure was 82.50±4.432 mmHg. The symptoms were 28% of patients dyspneic, and 22% had neurological symptoms **(Table 1)**.

Table (1): Demographic data, risk factors, drug intake, general examination and symptoms among the studied group

Parameters		Patients group (n=50)
Demographic data	**Age (Years)** Mean ± SD Min-Max ≤50 y 50-60 y > 60 y	 58.24±8.36 43.00-74.00 11 (22%) 20 (40%) 19 (38%)
	Sex Male Female	 21 (42.0%) 29 (58.0%)
Risk factors	**DM** Yes No	 16 (32.0%) 34 (68.0%)
	HTN Yes No	 14 (28.0%) 36 (72.0%)
	Dyslipidemia Yes No	 27 (54.0%) 23 (46.0%)
	PVD Yes No	 2 (4.0%) 48 (96.0%)
	Smoking Yes No	 14 (28.0%) 36 (72.0%)
Drug intake	Beta Blockers Antiplatelet CCBs ACE, ARB Diuretics Statin	22 (44.0%) 20 (40.0%) 5 (10.0%) 8 (16.0%) 16 (32.0%) 11 (22.0%)
General examination	**Duration from diagnosis** Mean ± SD	9.56±1.91
	SBP Mean ± SD	125.60±8.66
	SBP Mean ± SD	82.50±4.432
	JVP: Prominent a wave Yes No	 10 (20.0%) 40 (80.0%)
Symptoms	**Dyspnea Grade** No Grade 1 Grade 2	 36 (72.0%) 13 (26.0%) 1 (2.0%)
	Neurologic symptoms Yes No	 11 (22.0%) 39 (78.0%)

The mean random blood sugar of the studied group was 108.72±15.20, serum creatinine 0.86±0.17, mean heart rate 81.12±13.58, and 24% of patients had ECG changes. The mean ejection fraction of the studied group was 64.82±6.24, with 24% of patients had RSWMA, 24% with dilated left atrium, 72% diastolic dysfunction, 34% of patients had LVH and 54% had positive SPECT scan **(Table 2)**.

Table (2): Laboratory investigations, ECG, ECHO and Left ventricular thickness and SPECT scan (MPI) among studied group

Parameters	Patients group (n=50)
Laboratory investigations and ECG:	
RBS Mean ± SD	108.72±15.20
S. Cr Mean ± SD	0.86±0.17
HR Mean ± SD	81.12±13.58
ECG rate Mean ± SD	80.94±13.66
ECG Changes Yes No	 12 (24%) 38 (76%)
ECHO data:	
EF % Mean ± SD	64.82±6.24
FS % Mean ± SD	35.84±4.49
RWMA score index Score 1 Score 2	 38 (76%) 12 (24%)
LA dilated Yes No	 12 (24.0%) 38 (76.0%)
Cardiac mass Yes No	 0 (0%) 50 (100.0%)
Intact IAS Yes No	 50 (100.0%) 0 (0%)
Diastolic dysfunction grade No Grade 1 Grade 2	 14 (28.0%) 33 (66.0%) 3 (6.0%)
LVEDD Mean ± SD	4.91±0.55
PWEDd Mean ± SD	1.08±0.12
IVSDd Mean ± SD	1.09±0.14

Left ventricular thickness and SPECT scan:	
Left ventricular thickness	
Normal	33 (66.0%)
LVH	17 (34.0%)
SPECT SCAN (MPI)	
Positive	27 (54.0%)
Negative	23 (46.0%)

There was no statistically significant association found between myocardial ischemia and demographic data, but mean age was high in myocardial ischemia group. Positive and negative MPI patients regarding the risk factors statistically significant **(Table 3)**.

Table (3): Association between myocardial ischemia and demographic data, and risk factors

SPECT SCAN (MPI) / Parameters	Positive (n=27)	Negative (n=23)	p value
Demographic data:			
Age (Years) Mean ± SD	60.55±8.89	55.52±6.92	0.032
Sex			
Male	12 (44.4%)	9 (39.1%)	0.704
Female	15 (55.6%)	14 (60.9%)	
Risk factors:			
DM			
Yes	13 (48.1%)	3 (13.0%)	0.008
No	14 (51.9%)	20 (87.0%)	
HTN			
Yes	5 (18.5%)	9 (39.1%)	0.106
No	22 (81.5%)	14 (60.9%)	
Dyslipidemia			
Yes	19 (70.4%)	8 (34.8%)	0.012
No	8 (29.6%)	15 (65.2%)	
PVD			
Yes	1 (3.7%)	1 (4.3%)	0.908
No	26 (96.3 %)	22 (95.7%)	
Smoking			
Yes	11 (40.7%)	2 (8.7%)	0.01
No	16 (59.3%)	21 (91.3%)	

DISCUSSION

In our study, mean age of the studied group was 58.24±8.36, ranging from 43 to 74 years and 42% of the patients were males. Also, Tse et al. (2015) determined the incidence of and risk factors for MI after TIA. Mean age at the time of TIA was 71±14 years and 41% of the patients were male.

In our study, 32% of patients were diabetics, 28% were hypertensives, 54% were dyslipidemics and 28% were

smokers. *Tse et al. (2015)* found that 62% had hypertension, 11% had diabetes mellitus, and 55% were current or former smokers.

About 44% of patients were on beta-blockers, 40% on antiplatelets, 32% on diuretics and 22% used statins. *Dagenais et al. (2013)* investigated the prevalence of silent myocardial ischemia in patients with symptomatic intracranial atherosclerosis without known CAD, and 5 (8%) patients were receiving beta-blockers and 8 (12%) calcium antagonists.

In our study, we included patients with median duration from diagnosis of TIA was 9.56 ±1.91 months. *Tse et al. (2015)* MI after TIA, yielding an average annual incidence of MI after TIA was 0.95%. There were 456 incident TIAs. Sixty-eight (15%) of these patients had a history of MI before TIA, of whom 8 (12%) had another MI after TIA.

In our study, mean systolic blood pressure was 125.60±8.66 and mean diastolic blood pressure was 82.50±4.432 mmHg, while *Dagenais et al. (2013)* found that the maximal systolic blood pressure was 182 ± 28 mm Hg.

Echocardiographic data showed that mean ejection fraction of the studied group was 64.82±6.24, 24% of patients had RSWMA, 24% had dilated left atrium and 72% had diastolic dysfunction.

We found that 34% of patients had LVH and 54% had positive SPECT scan. We found no statistically significant association between myocardial ischemia and demographic data, but mean age was high in myocardial ischemia group.

We found that there were statistically significant differences between positive and negative MPI patients regarding risk factors including diabetes mellitus, dyslipidemia and smoking.

We found that there were statistically significant differences between positive and negative MPI patients regarding prominent a wave, neurologic symptoms, echocardiographic data (except PWEDd and IVSDd). *Li et al. (2015)* found that hypertension, diabetes, peripheral arterial disease, a history of heart disease, and carotid territory TIAs were associated with an increased risk of MI after TIA. *Heyman et al. (2010)* identified diabetes mellitus, prior MI, prior angina pectoris, electrocardiographic abnormalities, and the presence of ulcerated plaques or obstruction of more than 50% in at least one carotid artery on conventional angiography as risk factors for MI after TIA.

Regression analysis showed that age, diabetes mellitus, dyslipidemia, smoking, fractional shortening, RWMA score index, LA dilatation, diastolic dysfunction and LVEDD were independent predictors of positive SPECT scan. In a multivariate analysis of data from a prospective hospital cohort, risk factors for a coronary event after TIA were increasing age, male sex, a history of ischemic heart disease, and a combination of carotid and vertebrobasilar TIAs at presentation *(Hankey et al., 2011)*.

Sanchez Valiente et al. (2011) used ergometrics to screen 80 patients with TIA for silent myocardial ischemia (SMI). The patients were compared with a control group of 80 with no signs of heart disease. Neither the patients nor the controls had ever shown clinical signs of coronary ischemia and their baseline

electrocardiograms were normal. Stress test results were positive in 31% of the TIA patients, and in 5% of the controls, showing that the prevalence of SMI is significantly higher in TIA patients than in the general population. Hyperlipidemia and diabetes were the risk factors statistically related with a positive stress test.

Dagenais et al. (2013) concluded that more than 50% of the patients with symptomatic intracranial atherosclerosis and not overt CAD show myocardial perfusion defects on stress-rest SPECT. Stenosed intracranial ICA, symptomatic vertebrobasilar stenosis and presence of high Lp(a) and Hcy levels may characterize the patients at a higher risk for occult CAD.

Tse et al. (2015) found that increasing age and hypertension were associated with an increased risk of incident MI after TIA. They identified increasing age, male sex, and the use of lipid lowering therapy at the time of TIA to be independent risk factors for MI after TIA. The association between hypertension and the risk of MI after TIA was no longer statistically significant. TIA etiology was not a significant predictor of MI after TIA.

Tse et al. (2015) showed that patients who had an MI after TIA were approximately three times more likely to die during follow-up than those who did not have an MI after TIA. When adjusted for other factors found to be associated with mortality in this group, MI remained a significant and substantial independent predictor of death after TIA. They found that average annual incidence of MI after TIA is approximately 1%, about double that of the general population. The relative risk increase is especially high in patients under 60 years old. These data are useful for identifying subgroups of patients with TIA at highest risk for subsequent MI.

CONCLUSION

Patients who have had a TIA, but did not have known CAD, have approximately twice the risk for a subsequent myocardial ischemia compared to the general population. This risk accumulated linearly over time for many years after the TIA. Patients younger than 60 years old at the time of a TIA may have an especially high age-adjusted risk for future myocardial ischemia.

REFERENCES

1. **Adams RJ, Chimowitz MI, Alpert JS, Awad IA, Cerqueria MD and Fayad P. (2010):** Coronary risk evaluation in patients with transient ischemic attack and ischemic stroke: a scientific statement for healthcare professionals from the Stroke Council and the Council on Clinical Cardiology of the American Heart Association/American Stroke Association. Circulation, 108(10):1278-90.
2. **Dagenais, G. R., Lu, J., Faxon, D. P., Bogaty, P., Adler, D., Fuentes, F., ... & BARI 2D Study Group. (2013):** Prognostic impact of the presence and absence of angina on mortality and cardiovascular outcomes in patients with type 2 diabetes and stable coronary artery disease: results from the BARI 2D (Bypass Angioplasty Revascularization Investigation 2 Diabetes) trial. Journal of the American College of Cardiology, 61(7), 702-711.
3. **Gongora-Rivera F, Labreuche J, Jaramillo A, Steg PA, Hauw JJ and Amarenco P. (2011):** Autopsy prevalence of coronary atherosclerosis in patients with fatal stroke. Stroke, 38:1203-1210.
4. **Hankey GJ, Slattery JM and Warlow CP. (2011):** Transient ischemic attacks: which patients are at high (and low) risk of serious

vascular events? J Neurol Neurosurg Psychiatry, 55: 610–52.

5. **Heyman A, Wilkinson WE, Hurwitz BJ, Haynes CS, Utley CM, Rosati RA, Burch JG and Gore TB. (2010):** Risk of ischemic heart disease in patients with TIA. Neurology, 34: 626–30.
6. **Li, L., Yiin, G. S., Geraghty, O. C., Schulz, U. G., Kuker, W., Mehta, Z., ... & Study, O. V. (2015):** Incidence, outcome, risk factors, and long-term prognosis of cryptogenic transient ischaemic attack and ischaemic stroke: a population-based study. The Lancet Neurology, 14(9), 903-913.
7. **Sanchez Valiente S, Mostacero E, del Rio A and Morales F. (2011):** Silent myocardial ischemia in patients with transient ischemic attacks. Neurologia, 9(8): 337-41.
8. **Sander D, Carolei A, Diehm C and Hennerici MG. (2011):** Challenges to the management of high-risk stroke patients with multiple-site occlusive vascular disease. Cerebrovasc Dis., 31:315-321.
9. **Steg PG, Bhatt DL and Wilson PW. (2011):** One-year cardiovascular event rates in outpatients with atherothrombosis. JAMA, 297:1197-1206.
10. **Tse, L., Schwarz, S. K., Bowering, J. B., Moore, R. L., & Barr, A. M. (2015):** Incidence of and risk factors for delirium after cardiac surgery at a quaternary care center: a retrospective cohort study. Journal of cardiothoracic and vascular anesthesia, 29(6), 1472-1479.
11. **Yamamoto FI. (2012):** Ischemic stroke in young adults: an overview of etiological aspects. Arq Neuropsiquiatr, 70:462-466.

التنبوء بقصور الشرايين التاجية في المرضي دون أعراض قلبية يعانون من نوبات إقفارية عابرة

أمين محمد حسن سليمان، سامي حسن نوح، أحمد علي فهيم

قسم القلب و الأوعية الدموية، كلية الطب، جامعة الأزهر

E-mail: aminsoliman0@gmail.com

خلفية البحث: نقص تروية عضلة القلب هو السبب الرئيسي للوفاة في المرضى الذين يعانون من النوبات الإقفارية العابرة، مما يتسبب في وفيات أكثر من السكتة الدماغية. ومرض الشريان التاجي سبب شائع للوفاة بين الناجين من السكتة الدماغية. وتشجع الإرشادات التي ظهرت مؤخرًا المتخصصين في الرعاية الصحية على تحسين تقييم مخاطر الشريان التاجي في المرضى الذين يعانون من نوبة إقفارية عابرة والسكتة الدماغية لوضع إستراتيجيات مناسبة لمنع الإصابة بمرض الشريان التاجي.

الهدف من البحث: اختبار نقص تروية عضلة القلب الصامت بين المرضى الذين يعانون من نوبات إقفارية عابرة.

المرضى وطرق البحث: أجريت هذه الدراسة على 50 مريضاً بدون أعراض قلبية، يعانون من نوبة نقص تروية دماغية عابرة في قسم أمراض القلب بجامعة الأزهر، خلال الفترة من أكتوبر 2019 إلى أكتوبر 2021. خضع جميع المرضى لأخذ تاريخ مرضي شامل وفحص سريري وتخطيط كهربائي للقلب وتخطيط صدى القلب ثنائي الأبعاد وفحص تصوير طبي للقلب بأشعة جاما.

نتائج البحث: أظهرت بيانات تخطيط صدى القلب أن متوسط الكسر القذفي للمجموعة المدروسة كان 64.82 ± 6.24، 24٪ من المرضى لديهم شذوذ الحركة الجدارية للبطين الأيسر أثناء الراحة، 24% كان لديهم توسع في الأذين الأيسر و 72٪ لديهم اختلال وظيفي انبساطي. وكانت هناك فروقاً ذات دلالة إحصائية بين مرضى التصوير التروية لعضلة القلب الإيجابية والسلبية فيما يتعلق بعوامل الخطر بما في ذلك داء السكري، وخلل دهون الدم والتدخين. أيضا، كانت هناك فروقاً ذات دلالة إحصائية بين مرضى تصوير إرواء عضلة القلب الموجبة

والسالبة فيما يتعلق بالموجة الأذينية البارزة والأعراض العصبية وبيانات تخطيط صدى القلب (باستثناء البعد الانبساطي الخلفي للجدار الخلفي البطيني و البعد الانبساطي للحاجز البطيني). وأظهر تحليل الانحدار أن العمر، وداء السكري، وعسر دهون الدم، والتدخين، والتقصير الجزئي، شذوذ الحركة الجدارية للبطين الأيسر أثناء الراحة، وتوسع الأذين الأيسر، والخلل الانبساطي، و قطر البطين الأيسر في نهاية الانبساط كانت مؤشراً مستقلاً لإيجابية مسح التصوير المقطعي المحوسب بإصدار فوتون واحد.

الاستنتاج: المرضى الذين أصيبوا بنوبة نقص التروية العابرة ولكن ليس لديهم مرض الشريان التاجي لديهم ما يقرب من ضعف مخاطر الإصابة بنقص تروية عضلة القلب مقارنةً بالاشخاص الطبيعيين، ويتراكم هذا الخطر خطيًا بمرور الوقت لسنوات عديدة بعد النوبة الإقفارية العابرة.

الكلمات الدالة: إقفار عضلة القلب، مرض الشريان التاجي، النوبة الإقفارية العابرة.