



Value of early rest myocardial perfusion imaging with SPECT in patients with chest pain and non-diagnostic ECG in emergency department

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Received: 25 November 2018 / Accepted: 19 December 2018 / Published online: 19 January 2019

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Abstract

Evaluation of atypical presentation of angina chest pain in emergency department is difficult. Hospitalization of this patient may impose additional costs and waste the time, early discharge may lead to miss the patients. The aim of this study was to determine volubility of Single Photon Emission Computed Tomography (SPECT) in management of patients admitted to emergency department with atypical manifestations of angina pain, un-diagnostic Electrocardiogram (ECG) and negative enzyme. Half of 100 patients admitted to emergency department with atypical chest pain and un-diagnostic ECG who were candidate for admission, underwent ECG gated resting SPECT. According to the results of SPECT, low risk patient discharged after negative stress SPECT. All discharged patients were followed up for major cardiac events (cardiac death, nonfatal myocardial infarction and repeat admission for congestive heart failure) for 12 months. According to rest SPECT Myocardial Perfusion Imaging (MPI), about 70% of patients in case group was low risk and 30% of them had moderate or high risk. Case group represented lower hospitalization rate and lower need for Coronary Artery Angiography (CAG) in comparison with control group. Mean cost in case group was significantly lower than control group (175.15\$ vs. 391.33\$, $P < 0.001$). In one year follow-up no cases of mortality or major cardiovascular events as cardiac infraction were found in discharged patients in case group. our study showed that rest SPECT fulfillment in admitted patients in emergency department was validated method for assessing patients' risk which avoids unnecessary hospitalizations and additional costs.

Keywords Chest pains · SPECT scan · Treatment cost

Introduction

It seems that chest pain is the most common cause for refer to emergency department [1]. The risk of cardiovascular disease varies in these patients. New angina pain is associated with changes in the Electrocardiography (ECG) or increase in cardiac enzymes in subjects who were admitted

with coronary heart disease. However, the diagnostic problem remained in some patients with atypical chest pain. The evaluation of atypical chest pain in the emergency setting is difficult, because ECG can be negative in a large number of patients with Ischemic Heart Disease (IHD) who have been referred to the emergency after chest pain relief [2]. Therefore, the diagnostic of patients with atypical chest pain, non-diagnostic ECG and negative enzymes still remains as unsolved issue. In addition, the diagnosis of low-risk individuals for coronary heart disease is still a major problem in an emergency which needs to be admitted and monitored for 48 h after diagnostic process [3].

Unnecessary hospitalization of these patients will waste the time for both patients and clinicians, fill hospital beds and impose excessive costs on society [2] while half of these patients were discharged with final diagnosis of non-cardiac chest pain [4, 5]. Furthermore, early discharge of these patients from the emergency room can increase the risk of

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undiagnosed myocardial infarction without ECG changes and enzymes rising [6, 7]. Therefore, finding methods for diagnosing these patients in an emergency and reducing the amount of unnecessary hospital admissions has been always considered.

Single Photon Emission Computed Tomography (SPECT) perfusion scan is a suitable method to increase the speed and accuracy of Acute Coronary Syndrome (ACS) diagnosis in emergency room with acceptable results [2, 3, 8–12]. Myocardial Perfusion Imaging (MPI) SPECT rest can show evidence of ischemic heart disease at least 3 h after pain relief [13]. Studies have also shown that patients with chest pain with normal SPECT have had no cardiovascular complications during the 6 months follow up. Therefore, in addition to the diagnostic role of SPECT in the emergency department, it can also be used to determine long-term prognosis [14, 15].

Due to the increasing number of patients with IHD and limited hospital beds and high costs of hospitalization, finding a reliable method is necessary for early diagnosis of IHD.

Materials and methods

In a Case- Control Study, 100 patients with chest pain, undiagnostic ECG and negative enzyme test were voluntarily recruited from the emergency department of Tabriz Shahid Madani Hospital from July to December 2015 and they were visited by a cardiologist at emergency room. Sample size was performed using Candell- Rieira et al. research [12]. Average hospitalization time in group A (underwent early rest myocardial perfusion) was 13 ± 6 and in group B (underwent conventional management in the emergency department) was 15.9 ± 8.6 , also with consideration $\alpha = 0.05$ and power 80%, 100 samples were selected. Written informed consent was obtained from all the participants. Inclusion criteria were: chest pain for more than 5 min at last 3 h or lasting until referral time, history and negative examination for active ischemia, echocardiogram without Regional Wall Motion Abnormalities (RWMA) and patients older than 30 years old. Exclusion criteria were: patients with Myocardial Infarction (MI) or diagnosed IHD, typical chest pains that were candidates for diagnostic angiography and low risk patients for Coronary Artery Disease (CAD) with negative enzymatic tests that undergo exercise test. Among hundred patients, fifty underwent nuclear medicine scan for rest SPECT MPI (according to outcomes of ECG and cardiac enzyme tests).

After coordinating with nuclear medicine scanning center and preparing technetium 99 m drug, this drug was intravenously injected to patients with 900 MBq dose (25mCi) in emergency department and patients were sent

to the Nuclear Medicine Center for imaging after 20 min during the next 3 h. Imaging process was performed at ECG- gated SPECT method by Gamma Camera Siemens tomography device with standard protocol. LV images were divided into 17 segments and they were scored from 0 up to 4 (0 = normal, 1 = mild, 2 = moderate, 3 = severe perfusion defect and 4 = without perfusion). If perfusion defects up to grade 2 were detected at least in 2 segments, the rest MPI outcomes were considered to be positive. Patients with positive outcomes were hospitalized and in cases with pain repetition, positive enzymatic tests or ECG changes underwent diagnostic angiography and needed treatments were given. Although patients with negative scan results, negative second enzymatic tests and ECG and without repeated pain were discharged and become candidates for stress MPI for the following day.

All the patients whose test results were negative or with low risk rest SPECT MPI were discharged and the following day exercise test performed based on the Bruce standard protocol with the aim of reaching to at least 85% of optimum modified heart rate by the age-gender. Exercise Tolerance Test (ETT) lasts until reaching 100% of optimum heart rate, emerging angina or dyspnea, ST segment depression more than 2 mm in 0.08 S, hypotension (decreasing pressure more than 20 mmHg) or hypertension. Exercise test was considered positive in the cases of ST segment depression, hypotension or chest pain and technetium 99^m was injected by cutting ETT. Otherwise, technetium was injected after reaching 100% of optimum position, and test was continued for one minute and then ETT was finished.

Intravenous Dipyridamole (Presantin, 5 mg/ml, Boehringer, UK) at the dose of $0.16 \mu\text{g}/\text{kg}/\text{min}$ was injected for patients who were unable to reach at least 80% of optimal HR or unable to complete the test during 4 min and 3 min. Later technetium 99^m at the dose of 740mBq (20mCi) was injected and re-imaging was performed after 30 or 60 min with the same protocol.

All cases of control group that contained 50 patients were hospitalized and according to the hospital, undergone routine trials were accepted guide lines.

All patients were advised to refer to the clinic if any problem was occurred or at re-arising of chest pain, inform their conditions to the research team. One of the health staff was asked to contact everyone after 12 months. According to clinical accidents, patients were considered as CAD cases like sudden death, MI, recurrent angina, Congestive Heart Failure (CHF), need for re-hospitalization and doing diagnostic angiography, Coronary Artery Bypass Graft (CABG) or Percutaneous Coronary Intervention (PCI) in the cases of MI, sudden death or Coronary Angiography (CAG) resulting from any causes with at least one stenosis injury higher than 50%.

The study was approved by the ethics committee of Tabriz University of Medical Sciences. The informed written consent was obtained from all participants.

Statistical analysis

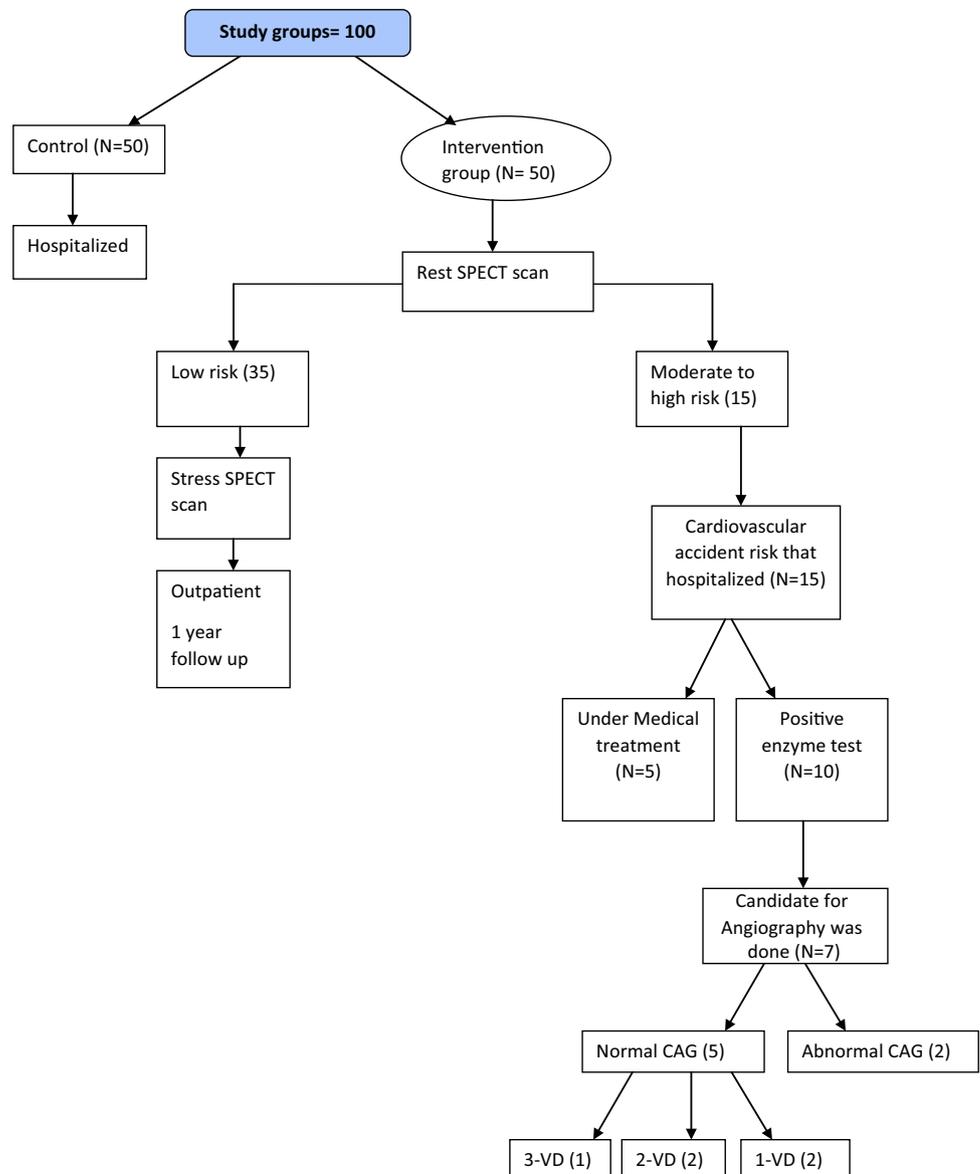
To analyze distribution of the data a Kolmogorov–Smirnov goodness of fit test was done and the results showed that the data had normal distribution. Results are illustrated as mean ± SD and frequency (%). To compare the results, paired t-test was used. The independent sample t-test was done for comparisons between two groups. An analysis of covariance test (ANCOVA) was applied. P value < 0.05 was considered statistically significant. The statistical software SPSS version 21 (SPSS Inc. IL, Chicago, USA) was utilized for data entry and analysis.

Results

Trial flowchart is shown in Fig. 1. This study included a number of 24 males (48%) and 26 females (52%) in each intervention and control group.

According to our results, burning chest pain was seen in 20 subjects (40%), 28 subjects were reported with constrictive chest pain (56%) and 2 subjects (4%) had burning constrictive chest pain. Stable pain was experienced by 4 subjects (8%). Severity of pain was respectively mild, moderate and severe at 26 (52%), 22(44%) and 2(4%) subjects. Average pain lasting time was estimated at 110.7 ± 69.16 min that maximum and minimum pain lasting time was 30 and 360 min. Manifestations like nausea and cold sweating were seen at 3 (6%) and 4 (8%) of patients respectively.

Fig. 1 Flowchart of design and protocol of the study



At ECG evaluation, ST depression was found in 17 subjects (34%). Abnormal T wave was seen in 15 subjects (30%) that included biphasic T wave in 12 (24%), flat T wave in 1 (2%) and Blunt in 2 (4%) subjects. Although, 3 subjects (6%) showed LBBB and one patient was found with RBBB. Cardiac enzymes were evaluated two times and both were negative.

Perfusion scan average score at resting level was estimated 1.60 ± 0.35 that minimum and maximum scores were 0 and 13, respectively. Perfusion scan average score was about 4.48 ± 4.28 at activity stage and for this stage maximum and minimum scores were respectively 0 and 20. Total perfusion scan score was equal to 3.24 ± 3.00 (with median = 3.50). Scores were ranged from 0 to 12 for this index (Table 1).

For better evaluation of clinical outcomes, patients were categorized in low risk ($n = 35$) and moderate to high risk groups ($n = 15$). According to scan results, 15 patients were at moderate to high cardiovascular accidents risk which was hospitalized. According to protocol of study that mentioned before, number of 10 patients as a result of repeated pain or positive enzyme test or ECG abnormalities candidate for coronary artery angiography. Out of 15 patients with mild to moderate risk, 5 of them underwent clinical treatments.

In 7 patients out of 10 patients with mild to moderate risk for cardiovascular accidents that were candidate for

angiography, CAG results showed 5 normal and 2 abnormal subjects including one with 3-VD, 2 with 2-VD and the other 2 with 1-VD. As a result of high creatinine level, co morbidities and dissatisfaction of patients, angiography was not done in 3 patients and patients followed medically.

All of 35 patients who were categorized in low risk group were discharged and were followed for 12 months in terms of cardiac events.

During the follow-up, cardiac events were seen in 12 (24%) patients that caused their re-hospitalization. According to early scan of the study, eight subjects of re-hospitalized ones were from low risk group and 4 of them were in moderate to high risk group. CAG was done for 5 subjects of re-hospitalized ones. (That includes 4 with low risk and one with moderate to high risk patients). (Fig. 2).

Both intervention and control groups followed cardiac events. Data for re-hospitalized patients of both groups were demonstrated in the Table 2.

In case group the average total score of perfusion scan in patients with and without cardiac events were calculated respectively as 3.58 ± 0.75 and 2.97 ± 0.48 Total SPECT score was higher in patients with cardiac events than the other group however this difference was not statistically significant ($p = 0.53$).

Perfusion scan score was also studied in patients with normal CAG and abnormal CAG. Without and results

Table 1 Baseline characteristics of patients

Variables		Frequency (%)
Chest pain	Burning chest pain	20 (40%)
	Constructive chest pain	28 (56%)
	Burning constructive chest pain	2 (4%)
Severity of pain	Mild	26 (52%)
	Moderate	22 (44%)
	Severe	2 (4%)
Abnormal T wave	Total	15 (30%)
	Biphasic T wave	12 (24%)
	Flat T wave	1 (2%)
	Blunt	2 (4%)
Nausea		3 (6%)
Cold sweating		4 (8%)
ST depression		17 (34%)
LBBB		3 (6%)
RBBB		4 (8%)
	Mean \pm SD	Min–Max
Pain lasting time (min)	110.7 ± 69.16	30–360
Perfusion scan score	Total	3.24 ± 3
	Resting level	1.60 ± 0.35
	Activity stage	4.48 ± 4.28

Quantitative and qualitative data are represented as mean \pm SD and frequency (Percent)

LBBB left bundle branch block, RBBB right bundle branch block

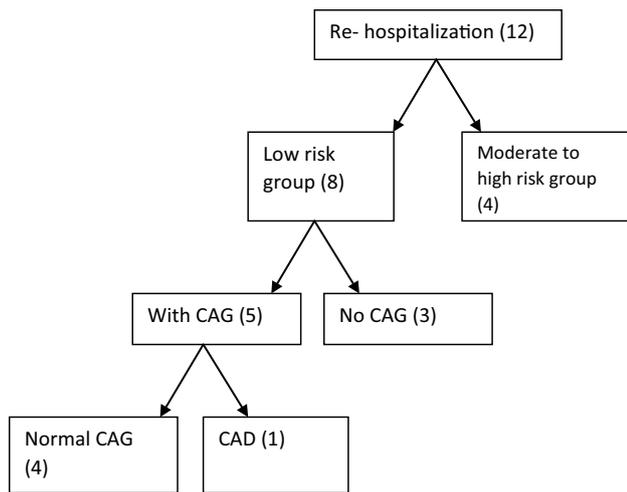


Fig. 2 Re-hospitalization in patients during follow-up

Table 2 Patients characteristics according to groups of the study

Variables	intervention n=50	control n=50	P-value
Gender			0.841**
Male	24 (48%)	26 (52%)	
Female	26 (52%)	24 (48%)	
Age (y)	52.10 ± 8.96	59.40 ± 6.12	0.0001*
Dyslipidemia	25 (50%)	18 (36%)	0.157**
Hypertension	27 (65%)	13 (26%)	0.0001**
Current history of smoking	3 (6%)	4 (8%)	0.695**
Renal failure	1 (2%)	1 (2%)	1.000**

Quantitative and qualitative data are represented as mean ± SD and frequency (Percent)

*P-value was reported based on ANOVA.

**P-value was reported based on Chi-Square test

P < 0.05 statistically significant

illustrated patients with abnormal CAG who had clear score higher than patients with normal CAG (p = 0.02, 4.50 ± 2.13 against to 7.42 ± 2.37).

In addition, in this study costs also were evaluated for patients. The average cost for each patient referring to emergency room, performing perfusion scan and then discharging (n = 35) was estimated about 175.15 dollars for US in 2015. Average cost for patient referring to emergency room, doing perfusion scan and then hospitalizing (n = 15) was calculated as 401.81 dollars. Average cost for each patient in control and intervention group has been shown in Fig. 3.

Regarding the hospitalization costs, the control group has higher costs than the other group and this difference was statistically significant (p < 0.001). The average costs for intervention group was estimated equal to 243.15 dollars

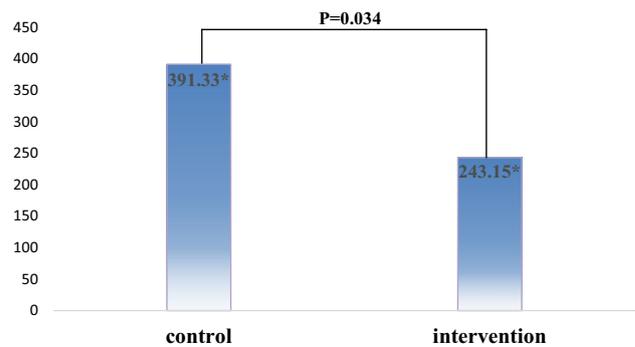


Fig. 3 Average cost for each patient in control and intervention group *US \$

Table 3 Average cost for each patient

	Frequency (Dollar*)	P-value
Intervention group	50 (243.15)	0.034
perfusion scan and then discharging	35 (175.15)	
perfusion scan and then hospitalizing	15 (401.81)	
Control group	50 (391.33)	

*The average cost for each patient was estimated for US\$

and for control group was 391.33 dollars and this difference was statistically meaningful (P value = 0.034) (Table 3).

Discussion

Traditional approach to evaluate and triage of patients with acute chest pain syndrome may lead to unnecessary hospitalizations, unnecessary occupation of hospital beds and also increasing costs of health caring system. Despite significant progress in therapeutic and management strategies of these patients, like diagnostic algorithms, distinct clinical evaluations and developed diagnostic tools, there is a great challenge for clinicians in diagnosis and early management of low risk patients for ischemic cardiac events (like who presented with chest pain, un-diagnostic ECG and negative enzyme tests) [16–18]. Although, low incidence of complications was reported in these patients like death or MI [19], but because of the fact that these complications are seriously dangerous, it won't rational to ignore them. In recent years, lots of efforts were carried out in order to create guide lines and methods for the exact monitoring of low risk patients which was done with the aim of decreasing complications and un-wanted events.

Performing rest SPECT cardiac perfusion scan is one of these proposed methods in order to recognize high risk subjects among these patients. In some emergency centers, perfusion scan was done to diagnose etiology of chest pain and

numerous protocols were used in order to evaluate patients' prognosis [3, 20, 21]. But, this instrument is not available in small centers and affordability of this method was not estimated in our country, so far. Some studies have shown that perfusion scan method is beneficial to decrease unnecessary hospitalizations and false discharging [3, 22, 23].

In this study, we attempted to evaluate the role of ECG-gated SPECT in patients with chest pain, un-diagnostic ECG and negative cardiac troponin, who need for hospitalization and appropriate clinical investigation.

Based on rest SPECT scan, 70% of patients were at low risk of cardiac events, 26% and 4% of patients were disposed of cardiac events with moderate and high risk, respectively and according to these findings, 20% of patients were hospitalized.

This study showed that there was lower rate of hospitalization and need for CAG in rest SPECT group comparison to the control group. Cardiovascular events occurred at low rate during the follow-up of these patients. Furthermore, cases with abnormal CAG showed higher SPECT scan score in comparison to normal CAG cases.

De Azevedo *et al.* showed that evidences of cardiac ischemia in SPECT perfusion scan (high risk group) were followed by higher risk of cardiovascular events [24]. Forberg *et al.* also showed that SPECT scan can be used for decreasing hospitalization rate in patients with atypical chest pain [25]. In a multi-centric clinical trial study, Udelson *et al.* demonstrated that in patients with chest pain and un-diagnostic ECG, SPECT scan can reduce unnecessary hospitalizations about 20% [9].

In recent years, participation of diagnosis and treatment costs in clinical decision making is taken to consideration [26]. Cost-effectiveness analyze can help clinicians and respondents in the appropriate and optimized use of limited recourses and in the use of high-costing and new imaging modalities [27].

Although, this study has revealed that average cost of each subjects who were referred to emergency room in case group (rest SPECT perfusion scan and then discharge of low risk patients), was about 175.15 dollars but in the control group with traditional approach (hospitalization and inpatient follow up), diagnostic and therapeutic costs will rise to over than two times. So, perfusion scan reduced costs for patients' evaluation and decreased the rate of unnecessary hospitalization in our country.

Wong *et al.* showed the same results which confess that SPECT performing reduced hospitalization duration 2.9 days for each patient in comparison with standard strategies and reduced therapeutic cost equal to 781 dollars [2].

Bengal and Zafrir showed that in term of hospitalization costs, cases with normal scan results had lower costs compared to cases with abnormal scan result. In fact, in the patients with chest pain and un-diagnostic ECG this method

is so exact, confident and it has functional effects on differentiation between low and high risk patients [10]. Stowers *et al.* has also explained that patients who underwent SPECT evaluation compared to the other group have clearly reduced costs by 1843 dollars and they have reduced hospitalization duration of 2 days [13, 27].

Also cost reduction can be reached by suitable and appropriate administration of diagnostic tests with lower rate of coronary artery angiography prescription in low risk patients [28].

Conclusion

It seems that performing SPECT can help to diagnose the high risk patients with atypical presentation and avoid unnecessary hospitalizations and reduce costs.

Acknowledgements The authors thank all of the patients who eagerly participated in the current study. The authors also wish to thank the Research Vice Chancellor of Tabriz University of Medical Sciences.

Funding This research did not receive any specific grants from funding agencies in the public, commercial, or not-for-profit sector.

Compliance with ethical standards

Conflict of interest The authors declare no conflict of interest.

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