The Myocardial Perfusion Scintigraphy in Predicting Risk for Coronary Artery Disease in Patients with Anxiety and Depression Symptoms

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Abstract

Introduction: An association between psychological factors and cardiovascular disease, has long been suspected. However, it is not clear whether chest pain is caused by emotional distress or whether coronary spasms are caused by the onset of coronary artery disease (CAD). We aimed to predict the risk for CAD in patients referred to myocardial perfusion imaging (MPI) with chest pain using depression, stress, and anxiety symptoms.

Methods: The emotional status of all patients was evaluated using the Hospital Anxiety and Depression Scale (HADS-A and HADS-D), the State and Trait Anxiety Inventory (STAI-1 and STAI-2), the Perceived Stress Scale (PSS), and the Anxiety Sensitivity Index-3 (ASI). Myocardial perfusion was measured using a 17-segment model and 5-point scoring system (0: normal perfusion; 4: no perfusion).

Results: MPI revealed reversible perfusion defects in 24 of 141 patients and no perfusion defects in 117 patients. The STAI-2 and HADS-A and HADS-D scores were significantly higher in patients with myocardial ischemia than in those without (STAI-2: 50.8 ± 7.5 vs. 46.3 ± 7.1, respectively; p = 0.008; HADS-A: 9.5 ± 3.9 vs. 7.8 ± 3.4, respectively; p = 0.033; HADS-D: 8.7 ± 3.0 vs. 7.3 ± 3.0, respectively; p = 0.05). Unadjusted correlation analysis showed that there was statistically significant correlation between reversible perfusion defects and anxiety scores (r=0.186, p= 0.029).

Conclusion: The patients with symptoms of depression and high-trait anxiety may be at higher risk of myocardial ischemia than patients without such symptoms. Thus, the emotional status of patients should be taken into consideration during clinical evaluation for CAD.

Key words: Myocardial perfusion imaging, anxiety, depression, perceived stress.

Introduction

As the angina pectoris is the most prominent symptom of coronary artery disease (CAD), patients with chest pain mostly referred to further investigation. Symptoms of chest pain are not always related to ischemic episode. It is sometimes associated with gastro esophageal reflux, hyperventilation syndrome and chest wall syndromes. Some authors suggested that there was a connection between chest pain experience and the emotional distress (1). St-jean et al. showed that angina pain was more severe in people with high levels of distress regardless of their ischemic status (2). On the other hand, Rohani et al. investigated depression and anxiety symptoms in chest pain patients and reported that patients with anxiety disorder were at a lower risk of underlying CAD (3). Prospective studies showed that psychosocial factors like depression, anxiety and stress have been linked to prognosis of CAD (4,5). However, most of these studies included patients with already known CAD. Myocardial perfusion imaging (MPI) is a non-invasive diagnostic modality for the detection of coronary artery disease in patients with chest pain. MPI provides valuable information for the risk stratification in both of patients with suspected or known CAD. It is well known that a normal MPI findings gives a very low risk for cardiac events in patients with stable angina pectoris (6). In the present study, we used a multiparametric psychiatric interview modality to assess depression, trait and state anxiety, perceived stress, and anxiety sensitivity in patients with chest pain who were referred for MPI. We aimed to investigate the relationship between psychological factors and reversible perfusion defects of patients who were suspected of CAD.

Materials and Method

Study Design

The study has been conducted in accordance with the principles of the Helsinki Declaration and
approved by the local Institutional Review Board (No:2012/238, Date:15/11/2012). Written informed consent was obtained from all subjects.

A total of 141 patients suffered from chest pain and referred to the Department of Nuclear Medicine of our university for MPI, between December 2012 and January 2014 constituted the study group. None of the patients had a known CAD, a percutaneous transluminal coronary angioplasty, coronary artery bypass grafting or prior myocardial infarction, and also none of the patients had psychiatric medications, pregnancy and structural abnormalities of the heart.

Screening for Anxiety and Depression

The emotional status of the patients was evaluated prior to MPI using Hospital Anxiety and Depression Scale (HADS-A and HADS-D), State and Trait Anxiety Inventory (STAI-1 and STAI-2), Perceived Stress Scale (PSS) and Anxiety Sensitivity Index (ASI).

Hospital Anxiety and Depression Scale

HADS is a self-administered scale consisting of two subscales, one assessing anxiety (HADS-A) and other one evaluating depression (HADS-D) (7). Each subscale consists of seven items. The items are scored from 0 (no distress) to 3 (maximum distress). Total scores range between 0 and 21 for each subscale. The validity and reliability of HADS in the Turkish language was reported by Aydemir et al. (8).

State and Trait Anxiety Inventory

This is a self-rating scale that was first developed by Spielberger et al. in 1970 in order to measure the level of anxiety (9). The reliability and validity of the data collection tools were tested in Turkish settings in 1985 by Oner and Le Compte (10). STAI is an instrument that quantifies state (STAI-1) and trait (STAI-2) anxiety. Scores range from 20 to 80; higher scores indicate greater anxiety.

Perceived Stress Scale

The 14-item scale was used to assess stress perceptions of participants (11). It is comprised of seven positive and seven negative items. The PSS measures the degree to which situations in one’s life are perceived as stressful. Participants rate items on a five-point Likert scale ranging from 0 to 4. The PSS scores are obtained by reversing the positive items and then summing the 14 items. Thus, the total PSS scores range from a low of 0 to a high of 56 with higher scores indicating greater stress perceptions.

Anxiety Sensitivity Index

Participants completed the 16-item scale to assess second order anxiety, defined as fear of anxiety-related sensations (12). The ASI measures the degree to which participants fear negative consequences stemming from anxiety symptoms. Respondents indicated the degree to which individual items characterized them on a 5-point Likert scale ranging from 0 (very little) to 4 (very much).

Myocardial Perfusion Imaging

Myocardial perfusion SPECT images were obtained in a standard one-day stress-rest protocol. Patients underwent a symptom-limited treadmill test (Bruce protocol). Technetium-99m sestamibi (Tc-99m) was injected intravenously (8-10mCi). Patients unable to exercise or those who failed to achieve their age predicted heart rate underwent a pharmacologic stress test with a 6-minute adenosine infusion protocol. SPECT images were acquired 45-60 minutes after the injection of a radiotracer using a dual headed detector gamma camera (Siemens, e-cam), fitted with low energy, high resolution collimators. Rest images were obtained after the injection of 24-30 mCi Tc-99m sestamibi. Gated SPECT left ventricular ejection fraction was measured using QGS software (Cedars-Sinai Medical Center, Los Angeles, California).

Two experienced physicians interpreted the images. Myocardial perfusion was evaluated using a 17 segment model and a 5-point scoring system (0= normal perfusion, 1= equivocal hypoperfusion, 2= moderate hypoperfusion, 3= severe hypoperfusion, and 4= absent perfusion). Perfusion defects graded 2 and more points below the at-rest imaging results were considered to be ischemic. Nuclear medicine physicians were blinded to the results of the questionnaires.

Statistical Analysis

Data were analyzed using the IBM Statistical Package for Social Sciences v20 (SPSS Inc., Chicago, IL, USA). A normal distribution of the quantitative data was checked using Kolmogorov-Smirnov test. Independent-samples t-test and Mann-Whiney U-test were used to compare independent groups. The correlation among anxiety and depression test’s scores and perfusion scores was evaluated with Spearman’s test. Data are expressed as mean±SD or median (interquartile range), as appropriate. All differences associated with a chance probability of .05 or less were considered statistically significant.
Results

A total of 141 patients met the eligibility criteria for the study. Of the 141 patients (90 females, 51 males) whose charts were reviewed, the mean age was 53±11.95 (range 33 to 80) years. Myocardial perfusion SPECT revealed that 17% (n=24) of patients had myocardial ischemia. The mean age of patients with ischemia was 53.04±8.3 years. The patients with normal myocardial perfusion included 117 patients (73 females, 44 males) with a mean age of 54.0±12.5 years. Both groups did not differ from each other by means of age and gender (p=0.45, and p=0.43, respectively).

With respect to clinical characteristics, diabetes mellitus (p=0.3), hypercholesterolemia (p=0.34), family history of CAD (p=0.07), hypertension (p=0.19), smoking (p=0.08), two groups did not show significant differences and were comparable. Ejection fraction was lower in patients with ischemia than in those without (p=0.04) (Table 1).

Table 1. Clinical characteristics of the patients.

<table>
<thead>
<tr>
<th></th>
<th>Ischemic Group (n=24)</th>
<th>Non-ischemic Group (n=117)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes mellitus</td>
<td>7/24 (29.2%)</td>
<td>23/117 (19.7%)</td>
<td>0.3</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>8/24 (33.3%)</td>
<td>28/117 (23.9%)</td>
<td>0.34</td>
</tr>
<tr>
<td>Family history of</td>
<td>15/24 (62.5%)</td>
<td>50/117 (42.7%)</td>
<td>0.07</td>
</tr>
<tr>
<td>coronary artery disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>14/24 (58.3%)</td>
<td>51/117 (43.6%)</td>
<td>0.19</td>
</tr>
<tr>
<td>Smoking</td>
<td>4/24 (16.6%)</td>
<td>26/117 (22.2%)</td>
<td>0.08</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>65.7±10.5</td>
<td>70±9.2</td>
<td>0.04</td>
</tr>
</tbody>
</table>

The patients with or without ischemia did not differ significantly with respect to STAI-1 (p=0.15), PSS (p=0.33), and ASI (p=0.083), although these scores were tending to be higher in patients with myocardial ischemia. STAI-2 (p=0.008), HADS-A (p=0.033), and HADS-D (p=0.05) scores were significantly higher in patients with ischemia compared to non-ischemia (Table 2, Figure 1).

Unadjusted correlation analysis showed that there was statistically significant correlation between reversible perfusion defects and anxiety scores (r=0.186, p=0.029).

Discussion

In the present study, we attempted to investigate the relation between psychological status and myocardial ischemia in patients with chest pain using MPI. Our study showed that patients with depression and high trait anxiety symptoms may be in higher risk of having myocardial ischemia.

Psychological factors such as depression, anxiety and anger has been hypothesized the being a predisposing risk factor for CAD for a long time (13). Previous studies have showed that patients with CAD had higher depression and anxiety scores. However, pathophysiological mechanisms are undefined. Several explanations about the association between negative emotional factors and CAD have been hypothesized as endothelial dysfunction, increased atherosclerosis and platelet reactivity (14).

Trait anxiety refers to a general level of stress that related to personality. State anxiety reflects how an individual currently feels. Patients with reversible...
perfusion defects on myocardium had higher trait anxiety scores compared to patients without perfusion defects. However, there was no difference in state anxiety levels in both study groups. Previously Hernandez et al. investigated association between multiple psychological factors and subclinical atherosclerosis in older age (15). They showed that only trait anxiety was significantly associated with coronary artery calcification. It has been reported that there was an association between chronic anxiety and endothelial dysfunction for elderly males but not for young ones (16). Ekici et al. reported that patients with anxiety had more severe CAD (17). Compatible with the previous studies, we showed that there was a correlation between myocardial ischemia and patients' chronic anxiety levels.

Previous studies demonstrated that depression was associated with an increased risk of CAD (5,18). Many factors can contribute to develop CAD in patients with depressive symptoms. Patients with depression tend to have an unhealthy lifestyle, like smoking, sedentary lifestyle, drinking, and no adherence with prescribed medications. And also depression can contribute to immune dysregulation. Myocardial perfusion SPECT can be an appropriate method for screening patients with depressive symptoms. Lavoie et al. suggested that patients with CAD who had major depressive disorder, depressive symptoms, and exhibit poor exercise tolerance so exercise ECG as compared with SPECT may not be as reliable in detecting ischemia (19). They showed that poorer exercise performance may be less likely to affect the ability of MPI in detecting ischemia in patients who are depressed compared with ECG based ischemia assessment. In the present study, Ischemic Group demonstrated significantly higher depression scores.

In the present study, we also investigated patients’ perceived levels of stress over the previous month by using PSS. Some studies have found no association between perceived stress and subclinical atherosclerosis; however, recently Richardson et al. published a meta-analysis and they declared that high perceived stress was associated with a risk ratio of 1.27 for incident coronary heart disease (15,20-23). The present study demonstrated no association between perceived stress and myocardial ischemia. This result may be the result of different methodology and small population of the present study.

The main limitation of our study was relatively small size of our series. Secondly, some details of history and factors that may influence the outcome may not be completely documented. We did not confirm the patients’ myocardial ischemia by coronary angiography. It would be better to follow up patients' incident of CAD, but we could not do this because of unavailable hospital database. Finally, this was a single-institution study. Due to these restrictions, associations should be interpreted with caution.

In conclusion, patients with depression and high trait anxiety symptoms might be in higher risk of having myocardial ischemia. Therefore, emotional status of patients could be taken into account during clinical evaluation of CAD.

References


