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The prevalence of panic disorder and its related factor in hospitalized patients with chest pain and normal angiography

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Abstract:

BACKGROUND: Chest pain is one of the common causes for referrals to cardiologists, 50% of which have no-cardiac origin. The occurrence of chest pains is among the most important factors responsible for psychological disorders. This study aimed to determine the prevalence of panic disorder and its related factor in hospitalized patients with chest pain and normal angiography.

MATERIALS AND METHODS: In a cross-sectional study, 144 patients who referred to Emam Ali Cardiac Hospital of Kermanshah because of chest pain in 2013 and had a normal angiography during admission were selected using census sampling method. The statistical indicators of Chi-square and logistic regression were applied.

RESULTS: From 144 patients with atypical chest pain, 95 were male (66%) and 49 were female (34%). Overall, 41 patients met the criteria for panic diagnosis and thus, the prevalence of panic attacks among patients with atypical chest pain was calculated as 28.5%. The results of multiple logistic regression analysis showed that female gender, early age, and the being single were among the predictive factors for the existence of panic disorder in patients with atypical chest pain and normal angiography ($P < 0.001$).

CONCLUSIONS: Given the high prevalence of panic disorder in patients hospitalized for chest pain with normal angiography, it is recommended to consider the importance of paying attention to this disorder and identifying patients and referring them to professional psychiatrists.

Keywords:

Chest pain, panic disorder, patient

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Introduction

For many years, disease specialists and clinical sciences have always faced the problem of evaluating the management of patients with chest pain. This problem is more complicated for patients without symptoms of coronary heart disease. As a consequence, many of these patients consume heart medicines for long terms without having any evidence of cardiac involvement.^[1] Chest pain is one of the common causes

for referring to cardiologists.^[2,3] The origin of chest pain could be cardiac (coronary and no coronary) and non-cardiac.^[4] The studies show that the chest pain of 50% of patients referring to cardiologists had a no-cardiac origin.^[5] Variety of reasons such as pulmonary disorders, gastrointestinal disorders, neck osteoarthritis, and psychological factors can cause no-cardiac chest pain (NCCP).^[6] NCCP is common in the general population. However, patient history and pain characteristics are not reliable for distinguishing between cardiac

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or esophageal causes of chest pain.^[7,8] When a patient comes with chest pain, the priority is to rule out any cardiovascular disease that is life-threatening.^[9] Concerns about the potentially devastating effects of chest pain may lead patients to seek more medical attention despite normal cardiovascular workup.^[10] Compared to patients with cardiac angina, those with NCCP are usually younger and are more likely to have unusual symptoms and a normal resting electrocardiogram.^[11] In addition, anxiety levels of NCCP patients were significantly higher in patients with angina and at least 2 months after heart clinic visit remained higher than social norms.^[12] Cardiac patients find their status more manageable and understandable than NCCP patients.^[13]

Among these factors, psychological disorders are one of the most important factors responsible for the occurrence of chest pains.^[14] The result of the previous studies shows 44%,^[15] 34%,^[16] and 42%.^[17] Prevalence of panic disorder in patients with chest pain. Panic disorder is defined by the sudden emergence of anxiety attacks following physical and emotional symptoms, fear of having a new attack, and avoiding events and conditions with panic attacks.^[18] In most patients, panic period tends to become chronic.^[19,20] Association of other psychological disorders with panic disorder in patients with NCCP is reported up to 75%–85%.^[21,22] Problems such as major depression, anxiety, neuroticism, hypochondriasis behaviours, obsessive-compulsive disorder, phobic disorders, and somatization disorder are repeatedly reported in these patients, among which depression disorder is in the second rank for psychological disorders in these patients with an approximate prevalence of 21%–38%.^[23-25] Panic disorder is associated with reduced quality of life, psychosocial dysfunction,^[26-28] increased risk of suicide,^[29] and high prevalence of strokes.^[30] Increased risk of death in patients with cardiovascular problems^[31] and the additional burden of health-care costs.^[32] Since the prevalence of panic disorder and the other associated disorders are high in patients with chest pain and normal angiography and that this disorder has an inevitable impact on the life quality of patients, this research and its obtained results could lead to the correct diagnosis and appropriate treatment measures for these patients which in turn, could be an effective step for improving life quality of these patients.

In addition, chest pain results in substantial use of resources; nearly 83% of primary care patients with chest pain receive diagnostic testing, at a mean cost of \$272 per evaluation. Only 6% of these evaluations lead to an organic diagnosis, and hence, the average testing cost per organic diagnosis made is \$4354.^[33]

In this study, with a relatively large sample of patients and logistic regression method, we assessed the

prevalence of panic disorder and its related factors among patients with chest pain. Therefore, the objective of the present study was to determine the prevalence of panic disorder and its correlative diagnosis in patients hospitalized with chest pain and normal angiography.

Materials and Methods

The present study is a cross-sectional study that was done to determine the prevalence and risk factors of panic disorder in people who referred to cardiologist due to chest pain and had normal angiography during admission.

The study population included all patients who were referred to a cardiologist at Emam Ali Hospital, Kermanshah, Iran between July 15 and January 15, 2013, undergoing necessary examinations, and no clinical diagnosis was given for them.

These patients were introduced by a cardiologist to a collaborator psychiatrist. After explaining the goals of the research by the researcher and if the patient was willing, they entered the study according to inclusion and exclusion criteria. A patient was included in the study if the following criteria were met: chest pain and normal coronary angiography. The exclusion criteria were: Non-cardiac organic causes Chest pain, including endocrine disorders, Taking medical drugs, digestive diseases and lack of willingness to participate in the study. Also, people with a history of substances use were excluded from the study.

At the beginning of the study, the researcher first introduced himself/herself, and after providing complete information about the study, its objectives, and the method of completing the questionnaires, he/she emphasized the fact that the information provided by the participants would remain confidential and the results of the study would be published without mentioning the name and personal information of the participants.

144 patients were selected using census sampling method. At first, demographic information including age, gender, marital status, education, and history of medical were collected by asking the patient and the list was registered that was previously designed by the researcher.

So, patients were evaluated according to the Diagnostic and Statistical Manual of Mental Disorders structured interview by a psychiatrist to check for panic disorder and its symptoms.

This study approved by the Medical Research and Ethical Committee of Kermanshah University of Medical Sciences, Kermanshah, Iran with registration number Kums.REC.1394.516 at the date of June 29, 2015.

Data were analysed using SPSS statistical software version 19.0 (IBM Corp., Armonk, NY, USA). For descriptive data analysis Chi-square test, to investigate the predictive factors in the presence or absence of panic disorder were used logistic regression. $P < 0.05$ was considered statistically significant.

Results

The sample for the present study included 144 patients with atypical chest pain, from which 41 patients met the diagnostic criteria for panic attacks. Therefore, the prevalence of panic disorder was calculated as 28.5%. When comparing two groups of patients with and without panic disorders, the results showed that there were 18 males (43.9%) and 23 females (56.1%) in the group with panic disorder. In the group without panic disorder, there were 77 males (74.8%) and 26 females (25.2%) and therefore. The median age for the patients in the group with panic disorder was 32.80 ± 8 and was 45.13 ± 7.14 for the group without panic disorder. In terms of marital status, 12 patients were celibate (29.3%) and 29 patients were married (70.7%) in the group with panic disorder, and 12 patients (11.7%) were single and 91 patients were married (88.3%) in the group without panic disorder. In terms of educational level, 3 patients (7.3%) had primary education or were uneducated, 26 patients (63.4%) had high school diploma or below, and 12 patients (29.3%) had academic education in the group with panic disorder. In the group without panic disorder these statistics were 12 patients (11.7%), 61 patients (59.2%), and 30 patients (29.1%), respectively ($P > 0.05$). In terms of family history of heart disease, 8 patients (19.5%) and 25 patients (24.3%) had a positive family history of heart disease in the group with and without panic disorder, respectively. In patients with atypical chest pain diagnosed with panic disorder, the outbreak of symptoms included increased heart rate in 22 patients (53.7%), dyspnea in 18 patients (43.9%), perspiration in 33 patients (80.5%), nausea and vomiting in 20 patients (48.8%), stomach pain in 28 patients (68.3%), and numbness in 17 patients (41.5%). Difficulty in concentration was reported in 35 patients (85.4%). In addition, the feeling of impending death and destruction was reported in 12 patients (29.3%) [Table 1].

Results of Table 2 show that the first and most important variables that affect the risk of panic disorder are age. This means that at younger age in comparison with older age panic disorder is 1.5 more likely ($B = 0.289$ odds ratio [OR] = 1.33, $P < 0.001$). The second variable that affects the risk of panic disorder was gender. Female patient increases the likelihood of developing panic disorder as much as 0.264% ($B = -1.331$ OR = 0.264, $P < 0.01$). Among the variables age, gender, marital status, marital status had the lowest impact on the panic

Table 1: Demographic characteristics in the studied sample

Variable	Panic disorder	
	Yes (%)	No (%)
Prevalence	41 (28.47)	103 (71.52)
Gender		
Female	23 (56.1)	26 (25.2)
Male	18 (43.9)	77 (74.8)
Age (years)	32.80 (8)	45.13 (14.7)
Marital status		
Married	12 (29.3)	12 (11.7)
Single	48 (24.6)	91 (88.3)
Education		
Uneducated/primary	3 (7.3)	12 (11.7)
high school diploma or higher degree	26 (63.4)	61 (59.2)
Academic degree	12 (29.13)	30 (29.1)
Family history of heart disease	8 (19.5)	25 (24.3)
Symptoms of panic disorder		
Increased heart rate		22 (53.5)
Dyspnea		18 (43.9)
Perspiration		33 (80.5)
Nausea and vomiting		20 (48.8)
Stomach pain		28 (68.3)
Numbness		17 (41.5)
Difficulty in concentration		35 (85.4)
Feeling of impending death		12 (29.3)

disorder. Being single increased the likelihood of panic disorder about 0.069% ($B = -2.671$, OR = 0.069, $P < 0.001$). In summarized, panic disorder is more likely in younger age, female gender, being single [Table 2].

Finally, the logistic regression model was shown as below:

Regression model = $3.715 + 0.289$ (age) – 1.331 (gender) – 2.671 (being single).

Discussion

The present study was carried out to determine the prevalence of panic disorder and its correlative diagnosis in patients hospitalized with chest pain and normal angiography on 144 patients that referred to Emam Ali Cardiac Hospital of Kermanshah because of chest pain in 2013. Chest pain is one of the common causes for referrals to cardiologists.^[2,3,8,9] Many patients with atypical chest pain struggle with psychological disorders such as panic disorder. Chest pain is a common symptom in primary care settings, associated with considerable morbidity and health-care utilization. Failure to recognize panic disorder as the source of chest pain leads to increased health-care costs and inappropriate management.

The prevalence of panic disorder in patients with chest pain was calculated as 28.5% in this study. The result

Table 2: Predictive factors in the presence or absence of panic disorder in our sample

Variable	B	SE	Wald	df	Significant	Exp (B)	95.0% CI for Exp (B)	
							Upper	Lower
Sex	-1.331	0.548	5.909	1	0.015	0.264	0.090	0.773
Age	0.289	0.051	31.746	1	0.001	1.335	1.207	1.475
Marital	-2.671	0.813	10.785	1	0.001	0.069	0.014	0.341
Constant	-3.715	1.687	4.850	1	0.028	0.024		

SE=Standard error, CI=Confidence interval

for this prevalence was reported as 34% in research by Beitman^[16] in a study by Mukerji *et al.*, 42% of these patients had panic symptoms.^[17] Foldes-Busque *et al.* determined the prevalence of panic anxiety disorder as 44%.^[15] Furthermore, the mean annual prevalence of NCCP in six population-based studies was approximately 25%.^[34]

In evaluating the predictive factors for the occurrence of the panic disorder in patients with chest pain, the results of the present study are also consistent with previous studies such that in our study women, younger and single people were more likely to suffer from panic disorder.

Evidence showed a higher prevalence of panic disorder in women than men that may be due to the limited role of women in social activities, environmental stress, biological factors, family, and marital problems.^[35-37] To explain why the prevalence of panic disorder in the age of 32.80 years was higher than that of the other age groups, it can be argued that in this age group the occupational, social, and economic stressors are more common and such stressors can lead to higher prevalence of panic disorder in this age group.^[38] The reason for the higher prevalence of panic disorder in single people can be due to the boring lifestyle, optimism to the future, economic and social problems, feeling loneliness, and concerns about family formation.^[39]

These results could also be found in some other previous studies. In a study by Dammen *et al.* associated factors with the occurrence of panic were reported as female gender, early age, undesirable employment status, low educational level, and low income.^[22] In a study by Huffman and Pollack predictive factors for panic included female gender, early age, and a high level of depressive disorder.^[40]

Eslick *et al.* evaluated the prevalence of NCCP in Australia by using a mailing of a validated Chest Pain Questionnaire to 1000 randomly selected individuals. The study demonstrated a prevalence rate of 33% with almost equal gender distribution (32% in males versus 33% in females). This study also showed that the population prevalence of NCCP decreases with increasing age.^[23,41] A nationwide population-based study from South America

found that the annual prevalence of NCCP was 23.5% and that NCCP has been equally reported by both sexes.^[42] Another epidemiologic study revealed that the annual prevalence of NCCP in the Chinese population was 19%.^[43] Epidemiologic studies report a decrease in the prevalence of NCCP with increasing age. Women under 25 years of age and those between 45 and 55 years of age have the highest prevalence rates.^[23] Patients with NCCP are younger, consume greater amounts of alcohol and tobacco, and are more likely to suffer from anxiety than their counterparts with ischemic heart disease. Patients with NCCP continue to seek treatment on a regular basis after the diagnosis was established for both chest pain and other unrelated symptoms, but few are in contact with hospital services.^[44]

Considering the higher prevalence of panic disorder for atypical chest pain in women, people with lower ages, and single people, it seems that a more accurate assessment for the probability of panic disorder in the field of atypical chest pain should be done with more careful examination for this group of patients.

By reporting the results and prevalence of this disorder and informing cardiologists in this regard, the importance of paying attention to this disorder and identification of the patients and referring them to psychiatrists will be demonstrated.

The limitations of this study like other epidemiological studies are sampling methods, screening techniques, classification, and diagnosis. Given the existing limitations and cultural differences, to more accurate assessment of the prevalence of panic disorder, more extensive studies are recommended, and also comprehensive studies are needed in the field of etiology and phobia.

Conclusions

Finally, it can be concluded that screening of panic disorder and other anxiety disorders is necessary for patients with chest pain before undergoing invasive diagnostic procedures.

Since psychological disorders are one of the important factors for the occurrence of chest pains, it is recommend

for the health care system to employ psychiatric services of cardiac hospitals more than before. The present study was carried out among patients hospitalized in Emam Ali Cardiac Hospital of Kermanshah with chest pain and normal angiography. Therefore, generalization of results should be done with caution.

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Conflicts of interest

There are no conflicts of interest.

References

- Lantinga LJ, Sprafkin RP, McCroskery JH, Baker MT, Warner RA, Hill NE, et al. One-year psychosocial follow-up of patients with chest pain and angiographically normal coronary arteries. *Am J Cardiol* 1988;62:209-13.
- Haug TT, Mykletun A, Dahl AA. The association between anxiety, depression, and somatic symptoms in a large population: The HUNT-II study. *Psychosom Med* 2004;66:845-51.
- Sheps DS, Creed F, Clouse RE. Chest pain in patients with cardiac and noncardiac disease. *Psychosom Med* 2004;66:861-7.
- Bass C, Mayou R. Chest pain and palpitations. In: Mayou RA, Bass C, Sharpe M, editors. *Treatment of Functional Somatic Symptoms*. Oxford: Oxford University Press; 1995.
- Kroenke K, Arrington ME, Mangelsdorff AD. The prevalence of symptoms in medical outpatients and the adequacy of therapy. *Arch Intern Med* 1990;150:1685-9.
- Kasper D, Braunwald E, Fauci A, Hauser S, Longo D, Jameson J, et al. *Harrison's Principles of Internal Medicine*. 17th ed. New York: McGraw-Hill Medical Publishing Division; 2008.
- Jerlock M, Welin C, Rosengren A, Gaston-Johansson F. Pain characteristics in patients with unexplained chest pain and patients with ischemic heart disease. *Eur J Cardiovasc Nurs* 2007;6:130-6.
- Fass R, Navarro-Rodriguez T. Noncardiac chest pain. *J Clin Gastroenterol* 2008;42:636-46.
- Fenster PE. Evaluation of chest pain: A cardiology perspective for gastroenterologists. *Gastroenterol Clin North Am* 2004;33:35-40.
- Ockene IS, Shay MJ, Alpert JS, Weiner BH, Dalen JE. Unexplained chest pain in patients with normal coronary arteriograms: A follow-up study of functional status. *N Engl J Med* 1980;303:1249-52.
- Dumville JC, MacPherson H, Griffith K, Miles JN, Lewin RJ. Non-cardiac chest pain: A retrospective cohort study of patients who attended a rapid access chest pain clinic. *Fam Pract* 2007;24:152-7.
- Sekhri N, Feder GS, Junghans C, Hemingway H, Timmis AD. How effective are rapid access chest pain clinics? Prognosis of incident angina and non-cardiac chest pain in 8762 consecutive patients. *Heart* 2007;93:458-63.
- Robertson N, Javed N, Samani NJ, Khunti K. Psychological morbidity and illness appraisals of patients with cardiac and non-cardiac chest pain attending a rapid access chest pain clinic: A longitudinal cohort study. *Heart* 2008;94:e12.
- Miller L. Psychotherapeutic approaches to chronic pain. *Psychotherapy* 1993;30:115.
- Foldes-Busque G, Fleet R, Poitras J, Chauny JM, Belleville G, Denis I, et al. Preliminary investigation of the panic screening score for emergency department patients with unexplained chest pain. *Acad Emerg Med* 2011;18:322-5.
- Beitman BD. Panic disorder in patients with angiographically normal coronary arteries. *Am J Med* 1992;92:335-40S.
- Mukerji V, Beitman BD, Alpert MA. Chest pain and angiographically normal coronary arteries. Implications for treatment. *Tex Heart Inst J* 1993;20:170-9.
- Bruce SE, Yonkers KA, Otto MW, Eisen JL, Weisberg RB, Pagano M, et al. Influence of psychiatric comorbidity on recovery and recurrence in generalized anxiety disorder, social phobia, and panic disorder: A 12-year prospective study. *Am J Psychiatry* 2005;162:1179-87.
- Kessler RC, Chiu WT, Demler O, Merikangas KR, Walters EE. Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the national comorbidity survey replication. *Arch Gen Psychiatry* 2005;62:617-27.
- Eaton WW, Kessler RC, Wittchen HU, Magee WJ. Panic and panic disorder in the United States. *Am J Psychiatry* 1994;151:413-20.
- Husser D, Bollmann A, Kühne C, Molling J, Klein HU. Evaluation of noncardiac chest pain: Diagnostic approach, coping strategies and quality of life. *Eur J Pain* 2006;10:51-5.
- Dammen T, Ekeberg O, Arnesen H, Friis S. Personality profiles in patients referred for chest pain. Investigation with emphasis on panic disorder patients. *Psychosomatics* 2000;41:269-76.
- Eslick GD, Jones MP, Talley NJ. Non-cardiac chest pain: Prevalence, risk factors, impact and consulting – A population-based study. *Aliment Pharmacol Ther* 2003;17:1115-24.
- Fass R, Achem SR. Noncardiac chest pain: Epidemiology, natural course and pathogenesis. *J Neurogastroenterol Motil* 2011;17:110-23.
- Hocaoglu C, Gulec MY, Durmus I. Psychiatric comorbidity in patients with chest pain without a cardiac etiology. *Isr J Psychiatry Relat Sci* 2008;45:49-54.
- Sherbourne C, Wells K, Judd L. Functioning and well-being of patients with panic disorder. *Yearb Psychiatry Appl Ment Health* 1997;1997:359-60.
- Mendlowicz MV, Stein MB. Quality of life in individuals with anxiety disorders. *Am J Psychiatry* 2000;157:669-82.
- Heldt E, Blaya C, Isolan L, Kipper L, Teruchkin B, Otto MW, et al. Quality of life and treatment outcome in panic disorder: Cognitive behavior group therapy effects in patients refractory to medication treatment. *Psychother Psychosom* 2006;75:183-6.
- Weissman MM, Markowitz JS, Ouellette R, Greenwald S, Kahn JP. Panic disorder and cardiovascular/cerebrovascular problems: Results from a community survey. *Am J Psychiatry* 1990;147:1504-8.
- Coryell W, Noyes R, Clancy J. Excess mortality in panic disorder. A comparison with primary unipolar depression. *Arch Gen Psychiatry* 1982;39:701-3.
- Edlund MJ, Swann AC. The economic and social costs of panic disorder. *Hosp Community Psychiatry* 1987;38:1277-9, 1288.
- Papanicolaou MN, Califf RM, Hlatky MA, McKinnis RA, Harrell FE Jr., Mark DB, et al. Prognostic implications of angiographically normal and insignificantly narrowed coronary arteries. *Am J Cardiol* 1986;58:1181-7.
- Kroenke K, Mangelsdorff AD. Common symptoms in ambulatory care: Incidence, evaluation, therapy, and outcome. *Am J Med* 1989;86:262-6.

34. Katerndahl DA, Trammell C. Prevalence and recognition of panic states in STARNET patients presenting with chest pain. *J Fam Pract* 1997;45:54-63.
35. Sheikh JI, Leskin GA, Klein DF. Gender differences in panic disorder: Findings from the national comorbidity survey. *Am J Psychiatry* 2002;159:55-8.
36. Weissman MM, Bland RC, Canino GJ, Faravelli C, Greenwald S, Hwu HG, et al. The cross-national epidemiology of panic disorder. *Arch Gen Psychiatry* 1997;54:305-9.
37. Joyce PR, Bushnell JA, Oakley-Browne MA, Wells JE, Hornblow AR. The epidemiology of panic symptomatology and agoraphobic avoidance. *Compr Psychiatry* 1989;30:303-12.
38. Kessler RC, Chiu WT, Jin R, Ruscio AM, Shear K, Walters EE. The epidemiology of panic attacks, panic disorder, and agoraphobia in the national comorbidity survey replication. *Arch Gen Psychiatry* 2006;63:415-24.
39. Stansfeld SA, Marmot MG. Social class and minor psychiatric disorder in British civil servants: A validated screening survey using the general health questionnaire. *Psychol Med* 1992;22:739-49.
40. Huffman JC, Pollack MH. Predicting panic disorder among patients with chest pain: An analysis of the literature. *Psychosomatics* 2003;44:222-36.
41. Eslick GD. Noncardiac chest pain: Epidemiology, natural history, health care seeking, and quality of life. *Gastroenterol Clin North Am* 2004;33:1-23.
42. Chiocca JC, Olmos JA, Salis GB, Soifer LO, Higa R, Marcolongo M, et al. Prevalence, clinical spectrum and atypical symptoms of gastro-oesophageal reflux in argentina: A nationwide population-based study. *Aliment Pharmacol Ther* 2005;22:331-42.
43. Wong WM, Lai KC, Lam KF, Hui WM, Hu WH, Lam CL, et al. Prevalence, clinical spectrum and health care utilization of gastro-oesophageal reflux disease in a Chinese population: A population-based study. *Aliment Pharmacol Ther* 2003;18:595-604.
44. Tew R, Guthrie EA, Creed FH, Cotter L, Kisely S, Tomenson B. A long-term follow-up study of patients with ischaemic heart disease versus patients with nonspecific chest pain. *J Psychosom Res* 1995;39:977-85.