ORIGINAL ARTICLE

The Association between Risk Factors and Prodromal Myocardial Infarction Symptoms: A Cross-Sectional Study in Iran

Lida Soltani[1], Sakine Sabzevari[1*], Ali Ravari[2], Tayebeh Mirzaei[2], Behnaz Bagherian[1]

Affiliation and Correspondence:
    [1]Nursing PhD Student.Nursing Research Center, Razi School of Nursing and Midwifery, Kerman University of Medical Sciences, Kerman, Iran
    [2]Department of Medical Surgical Nursing, School of Nursing and Midwifery, Geriatric Care Research Center, Rafsanjan University of Medical Sciences, Rafsanjan, Iran
    *Email: S_Sabzevari@KMU.ac.ir

ABSTRACT

BACKGROUND: *Prodromal symptoms in individuals with risk factors remain challenging, even though myocardial infarction has been noted in research. This study determined the association of risk factors with patients' baseline myocardial infarction related prodromal symptoms*.
METHODS: *In a cross-sectional study, 154 Iranian men and women, mean age 59.62 ± 12.74 years were assessed in 2016–2017. The frequency besides severity of 33 prodromal symptoms and risk factors was assessed using McSweeney Prodromal Myocardial Infarction Symptom Survey*.
RESULTS: *The main cardiac prodromal symptoms experienced by patients were chest pain/discomfort (n = 99, 64.30%), unusual fatigue (n = 78, 50.60%), and sleep disturbance (n = 33, 20.40%). Women experienced more prodromal symptoms than men (33.26 ± 21.88 vs. 25.48 ± 17.75). Among risk factors, only sex was associated with prodromal symptoms score (P < 0.05)*.
CONCLUSION: *The frequently experienced prodromal symptoms, i.e., before MI were chest pain/discomfort, unusual fatigue, and sleep disturbance. A crucial finding was the significant association between sex and prodromal symptoms. Identifying prodromal symptoms in patients with risk factors can prevent the incidence of myocardial infarction*.
KEYWORDS: *Myocardial Infarction, Prodromal Symptoms, Risk Factors, Coronary Heart Diseases, Sex*

INTRODUCTION

Coronary Heart Disease (CHD) kill more than 80% of the people, in developing countries (1). In Iran, CHD prevalence will increase over 2005–2025 and mortality rate accounts for one-fifth of all deaths (2, 3). More than 90% of the persons in Kerman (city in the southeast of Iran) had at least one CHD risk factor (4). According to the results of some studies in the US, Spain, Canada, and Iran 49-95% of the patients experienced prodromal symptoms (PSs) before the onset of myocardial infarction (MI) (5-8). In a study by McSweeney et al. (2014), the PSs were the predictors of acute MI in women (9). Also, in another study, women, and men who had prodromal chest pain

had greater possible risks of chest pain in the acute stage of MI (10). These symptoms are subjective, variable, and transient which may include cardiac and systemic symptoms. Varying in intensity and frequent repetitions, PS sometimes last for hours, days and even months before MI, and disappear later (10-14). In a study in Iran during 2006-2007, 37% of patients with AMI reported cardiac PS and 26% systemic PS. The most common cardiac PS two weeks before AMI was chest pain (24.2%), and the most common systemic PS was loss of appetite (12.7%) (8). Another study in 2016 reported the most common PS were chest pain (68%) and epigastric pain (40%) (7). A systematic review reported chest discomfort/pain (n = 4, 57%), arm pain/discomfort (n = 6, 86%), jaw pain (n = 3, 43%), back/shoulder blade pain (n = 3, 43%), unusual fatigue (n = 7, 100%), shortness of breath (n = 6, 86%), sleep disturbance(n = 2, 29%), dizziness (n = 3, 43%), headache (n = 3, 43%), anxiety (n = 7, 100%), and gastrointestinal complaints (nausea, vomiting, indigestion; n = 5, 71%)(5) related to PS before MI.

In spite of the progress in treatment for MI and upgraded public awareness of the benefits, many people fail to diagnose the PS prior to cardiac event, subsequently leading to increased prehospital delay and incidence of survival of patients with complications such as heart failure (13,15,16). Therefore, PS attentiveness is a vital precursor to quick interventions that can either prevent or delay the progression of CHD with the establishment of rapid lifesaving reperfusion therapies (17-19).

Different variables may influence the presentation and interpretation of PS among patients. In a study, patients with prodromal chest pain (PCP) had a higher number of risk factors compared with individuals with no PCP (20). Previous studies in Canada, the USA, and Norway reported that sex, hypertension (HTN) (10,21), hyperlipidemia (HLP) (12), diabetes mellitus (DM) (8,10), Body Mass Index (BMI)>29 (8,9), smoking (8), and family history (FH) of CHD (8) were associated with PS. In contrast, some other studies in Canada, the USA, Norway indicated that HTN(10), HLP(21) DM, BMI>29, smoking, FH of CHD were not associated with PS (22).

Therefore, the association between risk factors and PS are unknown yet.

Increasing mortality from CHD in developing countries illustrates the need for identifying at-risk groups and areas for probable improvement (23). Particular attention to PS in people with risk factors is critical for all clinicians and nurses. Understanding individual symptoms according to risk factors provides critical diagnostic data. Also, the precise knowledge of the health providers helps warn people who may be at risk and accurately diagnose the process. Information about PS in high-risk people, such as those with HTN, DM, and HLP, is, however, incomplete. This study aimed to describe the prevalence and frequency of PS and risk factors in a sample of MI patients. In particular, we examined the association of prodromal symptoms with risk factors.

MATERIALS AND METHODS

Design and participants: This study had a cross-sectional design that was conducted in three Cardiac Care Units (CCU) of educational hospitals of KermanUniversity of Medical Sciences, in Kerman, the Mainmedical Center in Southern Iran. All patients with MI who were hospitalized in the study settings from 2016 to 2017 were assessed for being eligible to participate in the study. Patients were eligible if they were able to communicate verbally, had PS during the recent three months, and had at least one risk factor. There were no age restrictions. If patients had a non-cardiovascular comorbid condition like cancer, were unable to give verbal and written informed consent, they were excluded from the study. Therefore, 539 hospitalized patients with the MI diagnosis were screened for their eligibility to participate in study using a convenience method. Two hundred and forty-three of them were Non-ST Elevation MI (NSTEMI), 57 of them were without the cardiac risk factor, 74 patients did not had any PS during the recent three months, and 11 were not interested in participating in the study. Finally, 154 patients with ST-Elevation MI (STEMI) eligibled the study. The response rate was 93.33%.

McSweeney Prodromal Myocardial Infarction Symptom Survey (MPMISS): We used the MPMISS includes 33 categorized PS. Discomfort/pain throughout chest, centered high in the chest, left breast, neck/throat, jaw/teeth, back, between/under shoulder blades, top of shoulders, and arm(s)/ leg(s). We combined chest locations (center or high in the chest, and left breast). General symptoms were very tired/unusual fatigue, sleep disturbance, and anxiety. Heart and lung symptoms were cough, heart racing, shortness of breath, and difficulty breathing during the night. Gastrointestinal symptoms were loss of appetite, and frequent indigestion. Sensation in arms symptoms was weak/heavy, ache, tingling, numbness or burning hands/fingers. Neurological symptoms were new onset of vision problem, increased intensity of headaches, increase in the frequency of headaches, and change in thinking or remembering (24). For the PS score, each of the 33 symptoms was weighted according to its reported severity (on a scale of 1 to 3) and frequency (on a scale of 1 to 6, less than monthly = 1 to daily = 6), and was summed across symptoms (range: 1-594). The MPMISS also contains risk factors BMI>29, DM, HTN, HLP, smoking, F.H of CHD, BMI and demographics. The presence of DM, HTN, and HLP were based on self-report and medical records, or the use of medications for these disorders. Nicotine addiction was defined as being a smoker at the time of the MI based on self-report.

Content validity of the MAPMISS was evaluated during the development process of the instrument by seven content experts. The reliability of the MAPMISS as a screening tool was established in Caucasian and African American women (test-retest reliability r = 0.92, P < .001)(24-26). This questionnaire has not been used in Iran. Written permission was attained from Mc Sweeney for the MAPMISS translation. The MAPMISS was translated into Persian by using standard protocols (33). Two bilingual health professionals translated the MAPMISS into Persian and then back into English, with a high percentage of agreement on the back-translation. The Persian versions were pilot-tested in Kerman with 20 members of the target population who had experienced PS. They did not add any additional PS. Fifteen faculty members of Kerman University of Medical Sciences assessed the qualitative and quantitative content validity of the MAPMISS. The Content Validity Index (CVI) was 0.91. The test-retest Pearson Correlation coefficient for 20 patients with two-week interval was 0.76 (P-value <0.001). Therefore, the validity and reliability of the translated questionnaire were acceptable.

Data Collection: On the third day of admission, we conducted bed-side interviews with MI patients in the CCU, when they had a stable conditions. The baseline interview included questions about PS, CHD risk factors, and socio-demographics. The researcher asked about the occurrence of each of the 33 PS in the preceding 90 days. For every one of the symptoms reported, we then asked about the intensity and frequency with which it occurred. Baseline interviews took approximately 30 minutes to complete.

Data analyses: The SPSS-22 statistical software was used to analyze the data. The level of significance was considered 0.05. The frequency, percentage, 95% confidence interval, meanand standard deviation, independent sample t-test or one-way Analyses of Variance (ANOVA), and Pearson Correlation were used. Variables that had P-value<0.25(sex and DM) were entered into multivariate linear regression. All probability values were 2-tailed. As the only predictor of PS score was sex, the frequency of different PSs and risk factors were compared between men and women using thechi-square test or Fisher's Exact Test.

Ethical considerations: The Ethical Committee of Kerman University of Medical Sciences approved the protocol of the study (IR.kmu.REC.13950924). The inquiry follows the principles outlined in the Statement of Helsinki. The project was explained to the patients, and when the patients agreed to participate, they were asked to sign an informed consent form.

RESULTS

The mean age of the participants was 59.62 ± 12.74 years (men: M = 57.35, SD = 12.02; women: M = 66.55, SD = 12.53). On the other hand, 75.3% of the participants were men, and 85.70% were married. Then, 32.50% of the samples were illiterate. The monthly income of 63.60% of the participants was (75-225 U.S Dollar). The majority of the participants were self-employed (33.10%) and resident of the city (90.77%)(Table 1).

Table 1: Socio-demographic characteristics of patient sample (n=154) and their associations with the PS score.

Variable		Frequency(%)	PS score (Mean/SD)	r/t/F	P-value
Age (yr.) **Mean (SD)**		59.62 (12.74)	27.40(19.07)	r= 0.18	0.83
Marital status	Married	132 (85.70)	26.26 (18.17)	t=-1.99	0.08
	Living alone*	22 (14.30)	35.10 (23.90)		
Education	Illiterate	50 (32.50)	28.84 (19.20)	F=1.66	0.18
	Primary	55 (35.70)	30.32 (22.09)		
	Secondary	30 (19.50)	23.83 (15.88)		
	Academic	19 (12.30)	20.79 (10.89)		
Monthly income (U.S Dollar)	<75	20 (13.00)	27.20 (19.45)	F =0.93	0.40
	75 – 225	98 (63.60)	26.07 (20.53)		
	> 225	36 (23.40)	31.14 (14.06)		
Job	Self-employed	51 (33.10)	26.65 (19.31)	F =0.22	0.88
	Employee	28 (18.20)	26.79 (19.70)		
	Retired	42 (27.30)	26.83 (20.88)		
	Housewife	33 (21.40)	29.82 (16.24)		
Location	city	120 (90.77)	27.47 (19.87)	F=0.08	0.94
	Village	34 (10.22)	27.18(16.24)		

*Unmarried/divorced/widowed, r = Pearson correlation coefficient, t= Independent t-test, F = ANOVA

Most participants experienced pain or discomfort (94.2%; CI: 90.2-97.5%), and the most pain or discomfort reported by them was any chest pain/discomfort (n=99, 64.30%) (Table 2). Also, very tired/unusual fatigue (n=78, 50.60%), and sleep disturbance (n=33, 20.40) were the frequently experienced symptoms among general symptoms. The range of PS score was 4-114 (mean±SD 27.40±19.07), and the participants experienced between 1 to 10 symptoms. The of PS score in men and women was (mean ±SD) 3.56 ± 2.11vs. 2.95 ± 1.81.

The most common risk factors were HTN (44.2%), HLP (31.2%) and DM (31.2%), respectively. All participants had at least two and at most six risk factors. Among all risk factors, women reported significantly higher levels of PS score than men (P < 0.05) (Table 3). However, among all symptoms, women had more pain/discomfort than men, but it was not statistically significant (Table 2).

Table 2: The prevalence of Prodromal symptoms and their differences between men and women.

Prodromal symptoms	Frequency	Overall Percent (CI)	Men (Frequency/%)	Women (Frequency/%)	P-value
Pain or discomfort	145	94.2 (90.2-97.5)	107 (92.2)	38 (100)	0.11
General symptoms	96	62.3 (55.7-73.4)	71 (62.9)	25 (60)	0.80
Heart and lung	47	27.8 (24-39)	40 (34.5)	7(18.4)	0.06
Gastrointestinal	33	22.6 (14.3-27.9)	27 (23.3)	6 (15.8)	0.33
Sensation in arms	37	24 (16.9-31.2)	28 (24.1)	9 (23.7)	0.95
Neurological symptoms	27	15.7 (11.6-24)	21 (18.1)	6 (15.8)	0.74
Number of PS					
1	26	16.9 (11 – 22.2)	20 (17.2)	6 (15.8)	0.41
2	42	27.3 (20.1 – 33.8)	29 (25)	13 (34.2)	
3	31	20.1 (13.6 – 26.6)	21 (18.1)	10 (26.3)	
4	17	11 (7.1 – 16.9)	13 (11.2)	4 (10.5)	
5	16	10.4 (5.8 – 15.7)	13 (11.2)	3 (7.9)	
≥6	22	14.3 (9.1 – 20.9)	20 (17.2)	2 (5.3)	

CI = Confidence Interval, PS = Prodromal symptoms, *Fisher's Exact Test

Table 3: The prevalence of risk factors and their associations with the PS score

Risk factors		Frequency (%)	PS Score (Mean/SD)	t-test	P-value
Sex	Male	116 (75.3)	25.48 (17.75)	- 2.21	0.03
	Female	38 (24.7)	33.26 (21.88)		
BMI	>29	19 (12.3)	26.80 (24.35)	- 0.14	0.88
	<29	135 (87.7)	27.50 (18.33)		
Smoke	Yes	45 (29.2)	26.15 (15.15)	- 0.52	0.60
	No	109 (70.8)	27.91 (20.52)		
DM	Yes	48 (31.2)	30.06 (21.28)	1.16	0.25
	No	106 (68.8)	26.19 (17.97)		
F.H of CHD	Yes	45 (29.2)	29.56 (20.15)	0.84	0.40
	No	109 (70.8)	26.62 (18.70)		
HTN	Yes	68 (44.2)	28.59 (20.61)	0.68	0.51
	No	86 (55.8)	26.47 (17.84)		
HLP	Yes	48 (31.2)	29.98 (22.00)	1.12	0.26
	No	106 (68.8)	26.24 (17.56)		

BMI =Body Mass Index, DM = Diabetes Mellitus, F.H of CHD = Family History of Coronary Heart Disease, HTN = Hypertension, HLP = Hyperlipidemia

All risk factors that had a P-value of less than 0.25 in bivariate analysis, i.e., sex and DM, were entered into multivariate linear regression with the backward method. The results indicated that only sex was a significant predictor of the PS score; it explained 2.5% of the variance (B = 7.78, CI = 0.82 – 14.74, P = 0.03; R^2=.026, P = .046).

The prevalence of being a smoker was significantly higher in men than women ($P < 0.05$). Also, positive history of HTN was significantly higher in women than in men ($P < 0.05$). No differences regarding other risk factors were observed between women and men (Table 4). The range of risk factors was 2-6 and men (mean ± SD, 3.41±0.94) vs. women (mean ± SD, 3.61±0.94).

Table 4: The comparisons of risk factors between men and women

Risk factors	Men Frequency (%)	Women Frequency (%)	Chi-square test	P-value*
BMI>29	14 (12.2)	5 (12.8)	0.01	0.91
Smoke	40 (34.8)	5 (12.8)	6.80	0.009
DM	32 (27.8)	16 (41)	2.36	0.12
F.H of CHD	29 (25.2)	12 (30.8)	0.46	0.50
HTN	40 (34.8)	28 (71.8)	16.18	<0.001
HLP	35 (30.4)	13 (33.3)	0.11	0.74
Number of riskfactors				
2	16 (13.8)	3 (7.9)	1.61	0.81
3	54 (46.6)	17 (44.7)		
4	31 (26.7)	11 (28.9)		
5	12 (10.3)	6 (15.8)		
6	3 (2.6)	1 (2.6)		

BMI =Body Mass Index, DM = Diabetes Mellitus, F.H of CHD = Family History of Coronary Heart Disease, HTN = Hypertension, HLP = Hyperlipidemia

DISCUSSION
Our result showed that the majority of the participants experienced pain or discomfort (94%), especially chest pain/discomfort (64.30%). Also, among general symptoms, the participants experienced very tired/unusual fatigue (50.60%) and sleep disturbance

(20.40%) more than other symptoms. The mean score of PS was 27.40 (range = 4-114). Only sex was a predictor of the PS score, i.e. women reported higher levels of PS score than men. Also, the prevalence of being a smoker was higher in men than inwomen while a positive history of HTN was higher in women than men.

In this investigation, the most frequently reported PSs were chest pain (64.30%), unusual fatigue (50.60%), and sleep disturbance (20.40%). In line with our results, O'Keefe-McCarthy et al. in a study on 121 patients diagnosed with ACS in one emergency department in Canada, reported that the most frequent PSs were chest pain (70%), and unusual fatigue (53%)(15). The most frequent PS, in patients with first AMI reported by Hwang et al. in Korea was pain-related symptoms such as chest, epigastria, or back pain (38.6%)(13). Khan et al. stated that the most common PSs in men and womenin Canada, USA, and Switzerland were unusual fatigue (47.2%), and sleep disturbances (41%), but chest painw as approximately 24% (22). In the United States, McSweeney et al., found in a multi-center, retrospective telephone survey of an ethnically diverse group of women who had experienced an AMI (n=1270) that unusual fatigue (73%), and sleep disturbance (50%) were the most frequent PS,; nevertheless, chest discomfort or pain prevalence was 36% (27). Another research in the US on 515 women diagnosed with AMI was done by McSweeney et al. The most frequent PSs during the recent month to AMI were unusual fatigue (70.7%), sleep disturbance (47.8%), and shortness of breath (42.1%). However, chest discomfort incidence was 29.7% (6). The ethnic dissimilarities of symptom presentation are known; however, chest pain is a crucial symptom regularly experienced by patients with heart disease (11,28,29). People with prodromal pain or discomfort, shortness of breath, fatigue, sleep disturbance, and anxiety were more likely to have similar symptoms through the acute phase of an ACS (6,9,10,30-32). Also, in a study, women, and men who had prodromal chest pain had more than five and three times greater possible risks of chest pain in the acute stage of MI than those who did not have PS, respectively (10). In another study by McSweeney et al. (2014), discomfort in jaws/teeth, unusual fatigue, arm discomfort, shortness of breath, and generalized chest discomfort were the predictors of acute cardiac events in women (9). Therefore, according to the previous studies and this study, pain/discomfort, unusual fatigue, sleep disturbance, shortness of breath, are the frequently experienced PSs before AMI.

This study showed that the mean score of PS was 27.40 (Minimum = 4, and Maximum = 114). In contrast with our result, in two studies on women, the PS score was 55 to 80 (6,11). The majority of our participants were men while in McSweeney et al.'s studies, only women were assessed. Therefore, the lower level of PS score in this study, in comparison with the previous studies (9), may be due to the characteristics of the studied sample.

In this study, only sex was a predictor of PS score,i.e. women reported higher levels of PS score than men. In line with our results, in a study by Lovlienet al., 84% of the women and 76% of the men had PS, and these symptoms were found to predict symptoms that occurred in the acute phase of MI(10). Holfgren et al., stated in a sample of Swedish ACS patients (n=914) that women experienced more PS than men (70% vs. 58%) (32). In a cross-sectional study of 1145 ACS patients ≤55 years, who experienced at least one PS, women compared to men, were more likely PS (85% vs. 72%) (22). Graham et al., in a study on patients with ACS in Canada, revealed a significant interaction between sex and PS (12). Contrastingly, the results of a descriptive study in Korea by Hwang et al. demonstrated that 53% of male patients and 54% of female patients had PS; no significant sex-based differences were discerned (13). Also, Løvlien et al., in their study on Norwegian patients with first time AMI (n=533) and O'Keefe-McCarthy et al. in a survey on 121 Canadian patients diagnosed with ACS reported that there were not differences between men and women regarding PS (10,15). The conflict in the consequences might be due to each study's participants' characteristics, the cultural background, personal and families' or friends' disease experiences. However, the reasons for sex variances in PS presentation are not well-known. The anatomical, physiological, biological and psychosocial diversity between men and women may influence the PS presentation(33). The history of different risk factors such as obesity, DM, HTN, HLP, and smoking may affect the presentation of the symptoms. In this study, the higher prevalence of being smoker in men than in women and positive history of HTN in women than men can be reasons for these differences.

However, the prevalence of HTN and smoking in a study in the United States and Spain were not different between women and men (34). In a review research in 2015, it was confirmed that the global prevalence of smoking in men was 48%, nearly five times as high as it was in women (10%), while the prevalence of HTN was parallel in men and women (35). Also, in contrast with our results, in some other studies, women with PS had a higher probability of having a FH of CHD(22, 36). Therefore, the essential causes for gender differences in experiencing PS are

uncertain. Note, we could not find any other similar studies in Iran about the association between PS and gender. More investigation is therefore necessary on this issue in the Iranian context.

In this study, none of the six measured risk factors, i.e., HTN, HLP, DM,BMI>29, smoking, and FH of CHD were a significant predictor of PS score. Our results supported results of some previous studies in Canada, USA, and Norway which indicated that HTN, HLP (10), DM, BMI>29, smoking, and FH of CHD were not associated with PS (22). However, our results are in contrast with results of some previous studies. On the other hand, some of theresults of previous studies showed that HTN (10,14), HLP, DM (8,10), BMI>29 (8,9), smoking (8), FH of CHD (8) were associated with PS. The differences among the studies confirm that the associations between PS and risk factors are controversial and need more investigation.

In conclusion, developed recognition and emergent treatment of PS would benefit all patients who have risk factors. Prodromal chest pain, unusual fatigue, and sleep disturbance were the most dominant symptoms idenified in this sample. The results further suggested that there is an association between sex and PS symptoms. These results may be important for the development of educational and treatment interventions. Additional research is required to confirm if PSs with regard to sex, age, and socio-economic status are a stronger predictor of risk factors-related PS presentation. Initial recognition of PS may help identification of persons at risk for the progress of CHD, early CHD detection through PS screening tools in clinical practice, and individualized risk factor index modification and management. Eventually, information of risk factors-related PS may confirm the decline in CHD morbidity and mortality.

ACKNOWLEDGMENTS

REFERENCES

1. Organization WH. Cardiovascular disease CVD prevention and control: missed opportunities *World Health Organization*; 2016.
2. Ebrahimi K, Salarilak S, Khadem Vatan K. Determine the burden of myocardial infarction. Tehran *University Medical Journal TUMS Publications*. 2017;75(3):208-18.
3. Sadeghi M, Haghdoost AA, Bahrampour A, Dehghani M. Modeling the burden of cardiovascular diseases in Iran from 2005 to 2025: The impact of demographic changes. *Iran J Public Health*. 2017;46(4):506.
4. Najafipour H, Afshari M, Rostamzadeh F. Prevalence of multiple coronary artery disease risk factors in kerman: A population-based study in Southeast Iran. *Iran J Med Sci*. 2018;43(2):140.
5. O'Keefe-McCarthy S, Ready L. Impact of prodromal symptoms on future adverse cardiac-related events: a systematic review. *J Cardiovasc Nurs*. 2016;31(1):E1-E10.
6. McSweeney JC, Cody M, O'Sullivan P, Elberson K, Moser DK, Garvin BJ. Women's early warning symptoms of acute myocardial infarction. *Circulation*. 2003;108(21):2619-23.
7. Soltani l, Ravari a, Sabzevari s. Relationship between prodromal (warning) symptoms and referring time in patients with myocardial infarction. *Iranian Journal of Cardiovascular Nursing*. 2016;4(4):22-31.
8. Mashreghimoghadam H, Kazemi T, Besharatimoghadam F. Prodromal Symptoms in Acute Myocardial Infarction in City of Birjand. *Iranian Journal of Epidemiology (IJE)* 2008;4(2):1-5.
9. McSweeney J, Cleves MA, Fischer EP, Moser DK, Wei J, Pettey C, et al. Predicting Coronary Heart Disease Events in Women A Longitudinal Cohort Study. *J Cardiovasc Nurs*. 2014 Nov-Dec;29(6):482-92. PubMed PMID: WOS:000343772100005.
10. Lovlien M, Johansson I, Hole T, Schei B. Early Warning Signs of an Acute Myocardial Infarction and Their Influence on Symptoms During the Acute Phase, With Comparisons by Gender. *Gend Med*. 2009;6(3):444-53.
11. McSweeney JC, O'Sullivan P, Cleves MA, Lefler LL, Cody M, Moser DK, et al. Racial differences in women's prodromal and acute symptoms of myocardial infarction. *Am J Crit Care*. 2010;19(1):63-73.
12. Graham MM, Westerhout CM, Kaul P, Norris CM, Armstrong PW. Sex differences in patients seeking medical attention for prodromal symptoms before an acute coronary event. *Am Heart J*. 2008;156(6):1210-6.
13. Hwang S, Zerwic JJ, Jeong M. Impact of Prodromal Symptoms on Prehospital Delay in Patients With First-Time Acute Myocardial Infarction in Korea. *J Cardiovasc Nurs*. 2010.
14. O'Keefe-McCarthy S, Ready L, Francis S-L. Cardiac-related prodromal symptoms: A complicated clinical challenge. *The Nurse Practitioner*. 2017;42(1):1-3.

15. O'Keefe-McCarthy S, McGillion MH, Victor JC, Jones J, McFetridge-Durdle J. Prodromal symptoms associated with acute coronary syndrome acute symptom presentation. *Eur J Cardiovasc Nurs*. 2016;15(3):e52-e9.

16. Khoshab H, Nouhi E, Tirgari B, Ahmadi F. A survey on teamwork status in caring for patients with heart failure: A cross-sectional study. *J Interprof Care*. 2018:1-7.

17. Ready L, O'Keefe-McCarthy S. Early cardiac prodromal symptoms: an elusive clinical challenge. *Canadian Journal of Cardiology CJC*. 2013;29(10):S393.

18. Gallagher R, Marshall AP, Fisher MJ. Symptoms and treatment-seeking responses in women experiencing acute coronary syndrome for the first time. *Heart Lung*. 2010;39(6):477-84.

19. Canto JG, Canto EA, Goldberg RJ. Time to standardize and broaden the criteria of acute coronary syndrome symptom presentations in women. *Can J Cardiol*. 2014;30(7):721-8.

20. von Eisenhart Rothe A, Albarqouni L, Gärtner C, Walz L, Smenes K, Ladwig K-H. Sex specific impact of prodromal chest pain on pre-hospital delay time during an acute myocardial infarction: findings from the multicenter MEDEA Study with 619 STEMI patients. *Int J Cardiol*. 2015;201:581.

21. O'Keefe-McCarthy S, McGillion MH, Victor JC, Jones J, McFetridge-Durdle J. Prodromal symptoms associated with acute coronary syndrome acute symptom presentation. *Eur J Cardiovasc Nurs*. 2016 Apr;15(3):E52-E9. PubMed PMID: WOS:000374016400008.

22. Khan NA, Daskalopoulou SS, Karp I, Eisenberg MJ, Pelletier R, Tsadok MA, et al. Sex differences in prodromal symptoms in acute coronary syndrome in patients aged 55 years or younger. *Heart*. 2017;103(11):863-9.

23. Sanchis-Gomar F, Perez-Quilis C, Leischik R, Lucia A. Epidemiology of coronary heart disease and acute coronary syndrome. *Ann Transl Med*. 2016;4(13): 256-12.

24. 24. McSweeney JC, O'sullivan P, Cody M, Crane PB. Development of the McSweeney acute and prodromal myocardial infarction symptom survey. *J Cardiovasc Nurs*. 2004;19(1):58-67.

25. McSweeney JC, Cleves MA, Fischer EP, Pettey CM, Beasley B. Using the McSweeney Acute and Prodromal Myocardial Infarction Symptom Survey to Predict the Occurrence of Short-Term Coronary Heart Disease Events in Women. *Womens Health Issues (WHI)*. 2017;27(6):660-5.

26. McSweeney JC, Cleves MA, Fischer EP, Rojo MO, Armbya N, Moser DK. Reliability of the McSweeney Acute and Prodromal Myocardial Infarction Symptom Survey among black and white women. *Eur J Cardiovasc Nurs*. 2013;12(4):360-7.

27. McSweeney CJ, etal. Racial Differences in Women's Prodromal and Acute Myocardial Infarction Symptoms. *Am J Crit Care*. 2010;19(1):63–73.

28. Hravnak M, Whittle J, Kelley ME, Sereika S, Good CB, Ibrahim SA, et al. Symptom expression in coronary heart disease and revascularization recommendations for black and white patients. *J Public Health*. 2007;97(9):1701-8.

29. Canto JG, Shlipak MG, Rogers WJ, Malmgren JA, Frederick PD, Lambrew CT, et al. Prevalence, clinical characteristics, and mortality among patients with myocardial infarction presenting without chest pain. *JAMA*. 2000;283(24):3223-9.

30. Cole CS, McSweeney JC, Cleves MA, Armbya N, Bliwise DL, Pettey CM. Sleep disturbance in women before myocardial infarction. *Heart Lung*. 2012;41(5):438-45.

31. O'Keefe-McCarthy S, McGillion M, Victor J, McFetridge-Durdle J. The influence of prodromal symptoms on acute coronary syndrome pain severity. *Pain Res Manage*. 2013;18.

32. Hofgren C, Karlson BW, Herlitz J. Prodromal symptoms in subsets of patients hospitalized for suspected acute myocardial infarction. *Heart Lung*. 1995;24(1):3-10.

33. McSweeney JC, Allan JD, Mayo K. Exploring the use of explanatory models in nursing research and practice. *J Nurs Scholarsh*. 1997;29(3):243-8.

34. Leifheit-Limson EC, D'Onofrio G, Daneshvar M, Geda M, Bueno H, Spertus JA, et al. Sex differences in cardiac risk factors, perceived risk, and health care provider discussion of risk and risk modification among young patients with acute myocardial infarction: the VIRGO study. *J Am Coll Cardiol*. 2015;66(18):1949-57.

35. Appelman Y, van Rijn BB, Monique E, Boersma E, Peters SA. Sex differences in cardiovascular risk factors and disease prevention. *Atherosclerosis*. 2015;241(1):211.

36. Barsky AJ, Peekna HM, Borus JF. Somatic symptom reporting in women and men. *J Gen Intern Med*. 2001;16(4):266-75.