

Circulation

JOURNAL OF THE AMERICAN HEART ASSOCIATION



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Circulation published online Nov 3, 2003;

DOI: 10.1161/01.CIR.0000097116.29625.7C

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 72514

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Women's Early Warning Symptoms of Acute Myocardial Infarction

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Background—Data remain sparse on women's prodromal symptoms before acute myocardial infarction (AMI). This study describes prodromal and AMI symptoms in women.

Methods and Results—Participants were 515 women diagnosed with AMI from 5 sites. Using the McSweeney Acute and Prodromal Myocardial Infarction Symptom Survey, we surveyed them 4 to 6 months after discharge, asking about symptoms, comorbidities, and demographic characteristics. Women were predominantly white (93%), high school educated (54.8%), and older (mean age, 66 ± 12), with 95% ($n=489$) reporting prodromal symptoms. The most frequent prodromal symptoms experienced more than 1 month before AMI were unusual fatigue (70.7%), sleep disturbance (47.8%), and shortness of breath (42.1%). Only 29.7% reported chest discomfort, a hallmark symptom in men. The most frequent acute symptoms were shortness of breath (57.9%), weakness (54.8%), and fatigue (42.9%). Acute chest pain was absent in 43%. Women had more acute (mean, 7.3 ± 4.8 ; range, 0 to 29) than prodromal (mean, 5.71 ± 4.36 ; range, 0 to 25) symptoms. The average prodromal score, symptom weighted by frequency and intensity, was 58.5 ± 52.7 , whereas the average acute score, symptom weighted by intensity, was 16.5 ± 12.1 . These 2 scores were correlated ($r=0.61$, $P<0.001$). Women with more prodromal symptoms experienced more acute symptoms. After controlling for risk factors, prodromal scores accounted for 33.2% of acute symptomatology.

Conclusions—Most women have prodromal symptoms before AMI. It remains unknown whether prodromal symptoms are predictive of future events. (*Circulation*. 2003;108:●●●-●●●.)

Key Words: angina ■ myocardial infarction ■ women

Diagnosing coronary heart disease (CHD) in women is challenging,^{1,2} yet few studies have focused on the scope of women's prodromal and acute CHD symptoms. Although syntheses of research on women and CHD are increasing,^{1,3-7} findings regarding women's typical CHD presentation lack consistency because some studies did not differentiate between ischemic and acute myocardial infarction (AMI) symptoms^{8,9} or did not separate symptoms by gender.¹⁰ Chest pain, a hallmark symptom of ischemia in men, is often not of significant prognostic value in women.^{1,2,9,11,12} Thus, no clear picture has emerged on women's typical CHD symptoms and how or whether they relate to AMI symptoms.

Little is known about early warning or prodromal CHD symptoms in women. In our earlier work,^{7,13,14} 85% to 90% of women identified an array of prodromal symptoms to their AMI. Some reported ignoring these symptoms, whereas others repeatedly sought medical assistance only to have clinicians minimize, misdiagnose, or ignore their symptoms. Women associated these symptoms with CHD because they either appeared or changed in intensity or frequency before

their AMI and disappeared or returned to previous levels of intensity or frequency afterward.¹³ Women indicated that they needed reflection time after the AMI to accurately identify prodromal symptoms. Because previous studies usually queried women within a week after AMI,^{15,16} they most likely missed important prodromal symptoms.

Accurately describing women's prodromal and acute symptoms of CHD is a vital step in providing a complete picture of women's typical presentation. The current description of "typical" cardiac symptoms is based primarily on the experience of white, middle-aged men, with deviations called "atypical." Researchers^{6,17-19} have speculated that this label contributes to misunderstandings in clinicians and lay individuals, leads to inaccurate diagnosis, and causes women to delay seeking treatment. Accurate information about women's prodromal and acute CHD symptoms would provide a normative description of women's cardiac symptom experience.

Accordingly, the present study determined (1) the most frequent prodromal symptoms of AMI, (2) how prodromal and acute symptoms relate to comorbidities and CHD risk

Received May 16, 2003; revision received August 25, 2003; accepted August 26, 2003.

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Circulation is available at <http://www.circulationaha.org>

DOI: 10.1161/01.CIR.0000097116.29625.7C

factors, and (3) whether prodromal symptoms were predictive of AMI symptomatology.

Methods

Sampling and Setting

We recruited women discharged within the previous 4 to 6 months with a diagnosis of AMI (ICD-9 codes 410.0 to 410.9) from 5 sites in Arkansas, North Carolina, and Ohio. Inclusion criteria were that the respondent be cognitively intact, speak English, and have telephone access.

Measurement

To assess prodromal and acute symptoms of AMI, we used the McSweeney Acute and Prodromal Myocardial Infarction Symptom Survey (MAPMISS).²⁰ The MAPMISS, a telephone-administered instrument, lists 33 prodromal and 37 acute symptoms that women previously identified in our qualitative studies.^{7,13,14} Although the literature substantiates many acute symptoms on the MAPMISS, few studies have reported prodromal symptoms. We incorporated women's actual descriptions into the following definitions of prodromal and acute symptoms. Prodromal symptoms (1) are new or change in intensity or frequency before the AMI, (2) are intermittent before the AMI, and (3) disappear or return to previous levels after the AMI. Acute symptoms appear with the AMI and do not resolve until women receive treatment.

The MAPMISS contains descriptors for each symptom. Women rate prodromal symptoms according to intensity (ie, mild, severe), frequency (ie, daily, weekly), and time frame (ie, week of, more than 1 month). They rate acute symptoms for intensity only. The MAPMISS also contains questions relating to comorbidities, risk factors, medications, and demographics.

We developed the MAPMISS in a series of studies to establish content validity.²¹ Women never added symptoms, indicating that the tool was comprehensive and had content validity. To establish test-retest reliability, we resurveyed 90 women in the present study within 7 to 14 days of the initial interview. We assessed agreement of items across both administrations. The average κ value for prodromal symptoms was 0.49, and for acute symptoms, 0.52. Low κ values were related to the small number of women reporting each symptom. Prodromal scores were constructed from the product of intensity and frequency for each symptom. Then we summed scores for each symptom to create an overall prodromal score. The acute score was constructed from the sum of each acute symptom weighted by its intensity. In our test-retest sample, the average prodromal score was 23.80 ± 24.24 (time 1) and 26.79 ± 30.52 (time 2) with an acceptable Pearson correlation ($r=0.72$; $P \leq 0.01$). The average acute score was 19.4 ± 14.4 (time 1) and 12.4 ± 8.8 (time 2) with Pearson correlation indicating stability ($r=0.84$; $P < 0.01$). The acute and prodromal summary scores remained stable across administrations.

Procedure

After approval by the Institutional Review Board at each site, medical records employees developed a list of potential subjects from hospital discharge ICD-9 codes. They gave the list to site recruiters who telephoned eligible women to obtain permission to release the women's personal information to the team.

From a single location, trained nurse research assistants (RAs) telephoned the women 4 to 6 months after their AMI. This allowed women time to accurately identify their prodromal symptoms and determine which symptoms disappeared or changed after their AMI.¹³ The RAs explained the study, gained verbal consent, verified eligibility, and performed the Blessed cognitive screen²² to ensure that subjects were cognitively intact. Then the RAs conducted the 60-minute telephone survey, first querying women about symptoms that occurred during their AMI. Next, they asked women to identify prodromal symptoms they believed were associated with their heart disease that were new/different, occurred intermittently before their AMI, and changed/disappeared after their AMI. The RAs routinely repeated this definition while asking women to select their symptoms

from a list and to choose appropriate descriptors for their symptoms. They were given the opportunity to add symptoms. Women easily differentiated between acute and prodromal symptoms and added no symptoms.

Data Analysis

Data collection occurred over a period of 3 years. The RAs entered data directly into an ACCESS database that was programmed with checks for data consistency and completeness. We calculated percentages for nominal or ordinal data and medians, means, and SDs for continuously scaled variables; t tests for univariate comparisons between those with and without risk factors; and multiple regression analysis to determine whether acute symptom scores could be predicted from prodromal symptom scores after control for selected risk factors. All probability values were 2-tailed. Using SPSS version 10.0 to analyze data, we defined statistical significance as $\alpha=0.05$.

Results

We received a total of 712 names: 40 declined, 37 could not be located, 10 had died, 4 failed the cognitive screen, and 106 did not meet study criteria. The final sample was 515 women with complete survey data.

Ages ranged from 29 to 97 years (mean, 66.4 ± 12.0 years), and 481 (93%) were white, 32 (6.2%) black, and 2 (0.4%) Native American. Educational levels varied, with 13% ($n=67$) having an eighth grade education or less to 32.3% ($n=166$) with some college. More than 44% of the women reported yearly household incomes \leq \$20 000.

This was the first AMI for 72%, and the remaining 28% reported on their most recent AMI. Most ($n=489$; 95%) reported prodromal symptoms (see Table 1). The average number of prodromal symptoms was 5.71 ± 4.36 (range, 0 to 25). The most frequent prodromal symptoms were unusual fatigue (70.7%), sleep disturbance (47.8%), shortness of breath (42.1%), indigestion (39.4%), and anxiety (35.5%). Of the women reporting these symptoms, 44% and 42%, respectively, rated sleep disturbances and fatigue as severe. Other frequently reported symptoms were rated as equally mild, moderate, and severe. Approximately 78% of women reported experiencing at least one prodromal symptom for more than 1 month either daily or several times a week before their AMI. We combined chest locations (general, high in chest, and left breast) to determine the number with prodromal chest discomfort/pain. Only 29.7% reported chest discomfort, which they described as aching (33%), tightness (33%), pressure (32%), sharpness (23%), burning (21%), fullness (18%), and tingling (18%). Location and sensation descriptors were not mutually exclusive.

The average number of acute symptoms was 7.3 ± 4.8 (range, 0 to 29). The most frequent acute symptoms were shortness of breath (57.9%), weakness (54.8%), unusual fatigue (42.9%), cold sweat (39%), and dizziness (39%). The main locations of discomfort were in the back (37%) and high chest (27.7%). When chest discomfort/pain was experienced, the most common descriptors were pressure (21.9%), ache (15%), and tightness (14.8%); intensity was commonly severe (59.2%). When all chest locations were combined, 43% reported no acute chest discomfort/pain. Again, selections were not mutually exclusive.

The average prodromal score, symptoms weighted by frequency and intensity, was 58.5 ± 52.7 (range, 0 to 289),

TABLE 1. Frequency of Prodromal and Acute Symptoms (n=515)

Symptom	Prodromal Frequency, n (%)	Acute Frequency, n (%)
Discomfort/pain		
General chest	67 (13.0)	102 (19.8)
Centered high in chest	74 (14.4)	157 (30.5)
Left breast	48 (9.3)	76 (14.8)
Neck/throat	38 (7.4)	84 (16.3)
Jaw/teeth	23 (4.5)	49 (9.5)
Back/between or under shoulder blades	67 (13.0)	109 (21.2)
Top of shoulders	26 (5.0)	52 (10.1)
Both arms	28 (5.4)	63 (12.2)
Left arm/shoulder	61 (11.8)	112 (21.7)
Right arm/shoulder	12 (2.3)	24 (4.7)
Leg(s)	18 (3.5)	7 (1.4)
General symptoms		
Cold sweat*	...	201 (39.0)
Hot/flushed*	...	167 (32.4)
Anxious†	183 (35.5)	...
Sleep disturbance†	246 (47.8)	...
Unusual fatigue	364 (70.7)	221 (42.9)
Weakness*	...	282 (54.8)
Cough	95 (18.4)	54 (10.5)
Heart racing	141 (27.4)	118 (22.9)
Shortness of breath	217 (42.1)	298 (57.9)
Difficulty breathing at night†	99 (19.2)	...
Change in taste of cigarettes*	...	15 (2.9)
Choking*	...	49 (9.5)
Loss of appetite	113 (21.9)	100 (19.4)
Indigestion	203 (39.4)	157 (30.5)
Nausea*	...	183 (35.5)
Vomiting*	...	98 (19.0)
Arms weak/heavy	128 (24.9)	179 (34.8)
Arms ache	97 (18.8)	167 (32.4)
Hands/arms tingling	112 (21.7)	108 (21.0)
Arms swollen*	...	21 (4.1)
Numbness/burning in both arms	28 (5.4)	36 (7.0)
Numbness/burning in right arm	7 (1.4)	6 (1.2)
Numbness/burning in left arm	37 (7.2)	45 (8.7)
Numbness in both hands	54 (10.5)	45 (8.7)
Numbness in right hand	10 (1.9)	5 (1.0)
Numbness in left hand	33 (6.4)	44 (8.5)
Dizziness*	...	201 (39.0)
Vision change	119 (23.1)	69 (13.4)
Headache*	...	78 (15.1)
Increased intensity of headaches†	47 (9.1)	...
Increased frequency of headaches†	68 (13.2)	...
Changes in thinking or remembering†	123 (23.9)	...

*Symptoms not asked for prodromal phase.

†Symptoms not asked for acute phase.

TABLE 2. Frequency of Risk Factors and Comorbidities

Risk Factors/Comorbidities	Frequency, n (%)
Personal history of CVD	321 (62.3)
Family history of CVD	496 (96.3)
Age >50 y	457 (88.7)
BMI >29	214 (44.3)
Hyperlipidemia	253 (49.1)
Hypertension	344 (66.8)
Diabetes	172 (33.4)
Hysterectomy	274 (53.2)
Smoker	151 (29.3)
Second-hand smoke	341 (66.2)
Lack of regular exercise	290 (56.3)

CVD indicates cardiovascular disease; BMI, body mass index.

whereas the average acute score, symptoms weighted by intensity, was 16.5 ± 12.1 (range, 0 to 70). These 2 scores were correlated ($r=0.61, P<0.001$).

The women commonly reported risk factors and comorbidities (see Table 2). Most (n=496; 96.3%) reported a positive family history, 321 (62.3%) had a personal history of cardiovascular disease, and 172 (33.4%) had diabetes. The average body mass index was 28.6 ± 6.5 (range, 11.7 to 61.5). Less than half (n=225; 43.7%) reported engaging in regular physical activity before their AMI.

We conducted a series of *t* tests to determine whether the acute or prodromal scores were associated with the risk factors of personal or family history of cardiovascular disease, age >50 years, obesity (body mass index >29), hyperlipidemia, hypertension, diabetes, hysterectomy, smoker, second-hand smoke exposure, and lack of regular exercise before AMI. Prodromal scores were significantly associated with all risk factors except age >50 years, hypertension, and hyperlipidemia. Acute scores were significantly associated with all risk factors except hypertension, hyperlipidemia, and second-hand smoke exposure.

We used multiple regression analysis to determine whether the acute score could be predicted from the prodromal score after controlling for the same risk factors as delineated above. The prodromal score accounted for an additional 33.2% of the variance in acute symptom scores after control for the risk factors, which accounted for only 9.9% of the variance.

Discussion

Failure to recognize prodromal symptoms may be one reason women experience a greater proportion of sudden cardiac deaths than men do²³ and the reason why CHD remains the primary cause of death in women in the United States.²⁴ In the present study, most women (95%) experienced prodromal symptoms, such as unusual fatigue, as our earlier studies reported.^{13,14,25} Women were most likely to rate the 2 most frequent prodromal symptoms, fatigue and sleep disturbances, as severe in intensity. The remaining 3 most frequent symptoms, shortness of breath, indigestion, and anxiety, were just as likely to be rated as severe, medium, or mild.

Most women reported experiencing prodromal symptoms more than 1 month before the AMI. However, it remains unknown how long women experience prodromal symptoms, because the MAPMISS does not include time frames longer than 1 month, because women had difficulty in retrospectively identifying the onset of each symptom. Previous qualitative findings indicate that women experienced prodromal symptoms for an average of 4 to 6 months.¹⁴ Because most women reported experiencing prodromal symptoms for more than 1 month before AMI, theoretically, women could recognize them as prodromal symptoms and immediately seek assistance, and clinicians could implement treatment.

In the present study, most women did not experience prodromal chest discomfort/pain. When they did, they were more likely to describe it as pressure, aching, or tightness, not as pain. Others^{6,12,25} have noted that typical chest pain is not a frequent early CHD symptom in women.^{12,17}

Numerous studies have indicated chest pain as a major acute symptom women experience with AMI.^{8,9,15,26} Others report that women describe chest pain differently^{27,28} or that it is a less significant symptom.^{7,8,14,25} In our study, 43% did not experience any type of chest discomfort with AMI. Canto et al²⁷ reported that of 434 000 patients, 33% had no chest pain but were diagnosed with AMI. Of this number, 49% were women, 38% men. Although Canto et al²⁷ linked lack of chest pain with the presence of diabetes, only 33.4% of our sample had diabetes, with 70% experiencing no prodromal symptoms and 43% no acute chest discomfort. Shlipak et al²⁸ reported that of 11 women who experienced a silent AMI, none had diabetes.

Lack of significant chest pain may be a major reason why women have more unrecognized AMIs^{29–31} than men or are mistakenly diagnosed and discharged from emergency departments¹¹ because clinicians continue to assess for chest pain as the primary symptom of AMI. In a study¹⁸ of 78 emergency and critical care clinicians, 85% of nurses and 66% of physicians stated that they assessed primarily for chest pain in persons with suspected AMI. Importantly, only 35% reported assessing for atypical symptoms, although 92% to 100% had previous experience with persons with atypical presentation. Compounding this problem, Milner et al⁹ and others^{15,27} classified all chest sensations (pressure, heaviness, or tightness) as chest pain and reported that women were more likely to use these descriptors than white men. Failure by clinicians to assess for and differentiate between chest pain and sensations may be a significant contributing factor in the chest pain controversy in women and may lead some clinicians to indicate on medical records the presence of chest pain when women reported no pain or described other sensations.⁹ Because some providers record all chest sensations as pain, retrospective studies auditing medical records may not be able to discern whether pain was present. Thus, our findings may differ, because we did not rely on medical records but had women select their symptoms and descriptors from a list devised from previous interviews with women after AMI. Another reason for our different findings, especially related to absence of chest discomfort in 43% of the subjects, may be that some registries or clinical trials required more classic symptoms for entry into the studies and may

have artificially inflated the number of women with chest pain,³² whereas we entered a more heterogeneous and “typical” community sample.

Although overall prodromal symptoms were not typical of angina, they were significant in predicting the severity of the acute symptoms as indicated by the acute score. Importantly, the prodromal score was a more important predictor than the commonly accepted comorbidities of hypertension, hyperlipidemia, and diabetes. Although it is possible that some women tend to be more descriptive and report more prodromal and acute symptoms, the symptoms reported were different, suggesting that the women were discriminating about the symptoms they reported. This finding supports our assertion that they remembered these symptoms not only because we asked but also because they may be unique female indicators of CHD.

Clinical Implications

Prodromal symptom score was the most important predictor of acute symptoms. It was more important than common CHD risk factors such as diabetes. When women experienced chest discomfort, they used descriptors such as aching, tightness, or pressure, not pain. Clinicians need to include these descriptors when assessing women with suspected CHD or at risk for CHD rather than asking only about chest pain. Unusual fatigue remained the most frequently identified prodromal symptom, as it has been previously. If unexplained fatigue is present, clinicians should assess it in depth and explore the degree of fatigue, because some women previously described it as so severe that they could not make a bed without resting. Because such prodromal symptoms as fatigue are nonspecific and may be associated with noncardiac diseases, they should be assessed thoroughly, in conjunction with known CHD risk factors, to guide the clinician in determining which women may be at greatest risk for CHD and need further diagnostic evaluation.

Although 95% of the women in this study retrospectively reported experiencing prodromal symptoms, it is unknown whether prodromal symptoms themselves predict future CHD events or whether the location, frequency, and intensity of the symptoms are more important than the number of symptoms. In addition, we do not know whether or what level of prodromal scores may be predictive of abnormal cardiovascular diagnostic tests. Because this sample was primarily white, it is unknown whether women's prodromal and acute symptoms or scores differ by race. Prospective longitudinal research is essential to address these issues to clarify the clinical significance of prodromal symptoms.

Because no women in this study added acute symptoms or descriptors to our list, we believe that this list of acute symptoms and descriptors may be useful in educating women and clinicians about women's typical AMI symptoms. However, before undertaking mass educational efforts, we must explore possible racial differences to develop a normative description of women's AMI symptoms. This description should facilitate earlier recognition of AMI symptoms by the public and clinicians.

Limitations

Our convenience sample of primarily white women from limited sections of the country may have limited generalizability. This was a retrospective study of women's self-reported acute and prodromal symptoms. It is plausible that women may describe symptoms differently during the AMI or that certain symptoms stand out afterward, but life-altering events such as AMI are often recalled in vivid detail.^{33,34} We do not know whether prodromal symptoms are predictive of a CHD event. Because we enrolled only women with AMI, it is unknown how many women without diagnosed CHD experience similar prodromal symptoms. However, in a pilot study²¹ of a convenience sample of 100 self-identified healthy women, 83% white and 17% black, the women reported a mean of 2.74 (SD, 4.0) prodromal symptoms, compared with 5.77 (SD, 4.8) for women with CHD, a significant difference ($t=7.32$, $P<0.000$). Healthy women had a mean prodromal score of 14.2 ± 22 , compared with 58.5 ± 52.7 for women with CHD ($t=20.12$, $P<0.000$). These findings suggest that healthy women experience fewer symptoms than women with CHD.

Acknowledgment

This study was funded by the National Institute of Nursing Research (R01-NR04908).

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