Maturitas 115 (2018) 45–50

Contents lists available at ScienceDirect

Maturitas

journal homepage: www.elsevier.com/locate/maturitas

Women's Health in the Lund Area (WHILA) study. Health problems and acute myocardial infarction in women – A 17-year follow-up study

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ARTICLE INFO

Keywords:
Myocardial infarction
Women
Risk factors
Signs and symptoms

ABSTRACT

Objectives: The literature has highlighted the importance of identifying symptoms predictive of acute myocardial infarction (AMI) in women, in addition to traditional cardiovascular risk factors. The objective was to study subjective health problems, in relation to later AMI, in a large sample of women, adjusted for age, educational status, smoking, waist/hip ratio, blood pressure, total cholesterol/HDL ratio, diabetes and neighbourhood socioeconomic status.

Study design: From December 1995 to February 2000 a cohort of 6711 women aged 50–59 years in southern Sweden underwent a physical examination and answered a questionnaire that had 18 items on health problems such as stress symptoms, tiredness and pain.

Main outcome measures: Incidence of AMI during a mean follow-up of 17 years, drawn from national registers.

Results: The number of health problems showed a J-shaped relationship with AMI, with the lowest hazard ratio (HR) in women with a median of 4 health problems. The HR for AMI in women with 0 health problems was 1.58 (95% CI: 0.95–2.63) and in those with 13 problems HR 1.65 (95% CI 1.16–2.36), after adjusting for potential confounding factors.

Conclusions: The presence of several health problems, including pain and stress symptoms, is associated with an increased risk of later AMI in middle-aged women. Awareness among clinicians of predictive risk factors for AMI is important for the early identification of individuals at higher risk.

1. Introduction

Although ischemic heart disease including acute myocardial infarction (AMI) has declined during the last decades, it still remains the number one cause of death in most Western countries [1]. Among women, a recent increase of coronary events has been reported in the United States, [2,3]. Most knowledge on the prevention, diagnosis and treatment of AMI is based on studies conducted predominantly on men [4]. It is well known that the symptomatology of AMI in women differs from that in men, and under-recognition of women's symptoms is a clinical problem [5,6]. The predictive risk pattern in women also differs, but this area is not fully studied [7]. The literature highlights the importance of identifying symptoms predictive of AMI in women [4,7].

The development of AMI is multifactorial and complex. In addition to traditional cardiac risk factors adverse pregnancy outcomes, systemic autoimmune disorders and osteoporosis are associated with AMI in women [7]. Previous research studying the predictive cardiac symptomatology in women found that discomfort in jaws/teeth, unusual fatigue, discomfort in arms, general chest discomfort, and shortness of breath were symptoms strongly associated with an increased risk of a cardiac event during 2 years of follow up [5]. In addition to somatic complaints, psychosocial factors have gained an increasing interest as cardiac risk factors in women [8]. Depression and anxiety have been related to AMI [7,9,10]. In addition, a previous study from our research group showed that depression was a predictor of developing coronary heart disease strongest for those aged < 40; the risk was 2.17 [11]. Also mild mental problems like sleep disturbances, fatigue and self-perceived stress have been related to AMI [12].

Whether common somatic and mental health problems, such as tiredness, stress symptoms and pain are early predictors of AMI in women is not studied thoroughly, and previous studies had only short follow-ups. Another novelty with the present study was that it includes middle aged women with multiple common somatic and mild mental problems, unlike previous studies which include major mental disorders

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https://doi.org/10.1016/j.maturitas.2018.06.003
Received 16 January 2018; Received in revised form 26 April 2018; Accepted 3 June 2018

and focus on men.

Accordingly, the aim was to study 18 different subjective health problems, and their association with AMI during a 17 year long follow-up, adjusted for age and traditional cardiac risk factors such as educational status, smoking, waist-hip ratio, blood pressure, total cholesterol/HDL-ratio, diabetes and neighbourhood socioeconomic status measured by Care Need Index (CNI). The hypothesis was that these health problems are associated with an increased risk of AMI.

2. Methods

Data was retrieved from the Women's Health in the Lund Area (WHILA) study [13], in which women 50–59 years (born between 1935 and 1945) in southern Sweden were invited to take part in a health survey. Between Dec 1995 and Feb 2000, 6916 women underwent a physical and laboratory examination and completed a self-administered questionnaire. The physical examination included measurement of body weight, height, minimal waist and maximal hip circumference. Blood pressure (mmHg) was measured twice in the right arm, after 15 min and 20 min rest in sitting position, and the average of the recordings was used. Non-fasting serum levels of total cholesterol, HDL-cholesterol and LDL cholesterol were measured on capillary whole blood. In the present study, 6711 women were included, after exclusion of individuals with missing values on education, smoking and diabetes.

The questionnaire has been described previously [13]. In short, after written consent the participants answered a questionnaire including 104 questions about medical history, lifestyle, sociodemographic data and health problems. If any uncertainties, they could ask a nurse. There was no financial reimbursement for participation.

2.1. Follow up and outcome variable

The data was linked to the Hospital Discharge Register, and the women were followed from the day of screening until first hospitalization of AMI, or until the end of the study May 31st 2015. The mean follow-up time was 17 years.

Acute myocardial infarction (AMI) was based on the International Classification of Diseases, i.e. code I21 (ICD-10) or code 410 (ICD-8). Those who had an AMI before screening were excluded.

2.2. Explanatory variables

The explanatory variables were based on the examinations and questionnaires at baseline.

Agec, age at screening, continuous, centered around its mean (56 years).

Education; Educational level was categorized into low/middle ($\leq$12 years) and high (university).

Waist hip ratio (WHR) was calculated as waist circumference (cm) divided by hip circumference (cm), and categorized into $\leq$0.78/ $>$ 0.78. WHR is a significant predictor of AMI in both men and women [14,15]. The cut-off point recommended by WHO (0.85) could not be used because of the small sample size and that the women lived in more affluent areas (Care Need Index, CNI = -6.7) than the Swedish population in general (CNI = 0). Therefore, we chose the cutoff 0.78 as the optimal limit for this sample.

Ratio between total-cholesterol to HDL (Tch/HDL) was treated as a continuous variable, linearly related to risk of AMI. Tch/HDL ratio has been shown to be the best single predictor of ischemic heart disease risk in the Quebec Cardiovascular Study [16].

Blood pressure was categorized into three levels, based on the distribution: 1) systolic blood pressure $<$ 140 mmHg and diastolic blood pressure $<$ 90 mmHg, 2) systolic blood pressure 140–149 mmHg or diastolic blood pressure 90–99 mmHg, and 3) systolic blood pressure $\geq$150 mmHg or diastolic blood pressure $\geq$100 mmHg. Due to the small sample size, we could not use the grades of hypertension according to international guidelines [17].

Self-reported diabetes: Yes/ No

Smoking was categorized into 1) non-smoker 2) former smoker and 3) daily smoker.

Health problems were based on the questions as follow," Have you been bothered by any of the following conditions during the last three months? (yes/no): dizziness, headache, tiredness, sleeping problems, nervousness, sweating problems, shortness of breath, chest pain, felt irritable, overworked, concentration difficulties, restlessness, down and gloomy, easy to cry, hard to relax, stomach ache, nausea and back pain". For those who didn't answer any of the items, a zero (0) was imputed. A factor analysis (iterated principal factors of 18 health problems (Yes = 1/No = 0)) based on tetrachoric correlations, resulted in a one-factor solution (Eigenvalue = 6.53). All factor loadings, after varimax rotation, were positive and $>$ 0.4, supporting that all of the symptoms are indicators of health problems. The factor scores were linearly related to the risk of AMI.

Based on the factor scores health problems were categorized into four levels: (1) -0.53 to -0.48; (2) -0.48 to 0.058; (3) 0.058 to 0.39; (4) 0.39 to 0.93. The mean of the factor scores for the four levels were -0.52, -0.21, 0.22, and 0.57, the higher factor score the more health problems. The median numbers of Health problems in the four categories were 0, 4, 8 and 13, respectively.

Care Need Index (CNI) was used as a proxy for socioeconomic status of the neighborhood area, and has previously been described in detail [18]. Information on CNI was obtained from Swedish public registers on 31 December 1995, with individual information on the entire adult population. The CNI included proportions of seven material, sociodemographic, and cultural variables for each neighborhood: elderly people living alone, children under age 5, unemployed people, people with low educational status, single parents, residents who have moved house during the past year, and foreign born people from Southern and Eastern Europe, Asia, Africa, and South America. The higher the CNI score, the more deprived the neighbourhood. In the present study, CNI was dichotomized into affluent (0) and deprived (1) areas. As there was a relatively high number of missing values for CNI (e.g. individuals who were registered in other areas than they lived in), this variable was analysed in a reduced sample of 6234 women. In the sample, 71% of the women lived in more affluent areas (CNI $<$ 0). In the statistical analyses, the variable was treated at the same level as the other individual variables in the statistical analyses, as the small sample size was not suited for multi-level analysis.

The following variables were analysed as potential confounders: postmenopausal therapy use, age at menopause, alcohol use and family history of cardiovascular disease. None of them was associated with acute myocardial infarction. When added to the multivariate full model, the result were almost identical. They were therefore not included as covariates in the models.

2.3. Statistical method

In order to compensate for missing we weighted data by age and county: N_i/nresponders per one-year age-group (50–59) and municipality. The response rate varied in the different age-groups between 58.9 (youngest) and 66.7% (oldest), in average 64.2%. The weights sum up to population size 1995.

We estimated incidence rates of AMI (formed from the number of failures divided by the person-time, per 10,000 person years at risk) with 95% confidence intervals (STPTIME in STATA) per variable.

In order to analyse the association between health problems and AMI, we applied a Cox regression model, adjusted for potential confounders. All included variables satisfied the proportional hazard assumption. There were no interactions between number of health problems and any of the other included covariates. In a reduced sample the same analyses were conducted including education and CNI.

STATA version 13 was used for the statistical analyses.