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Gender differences in first medical contact and delay in ST-elevation myocardial infarction - a prospective multicentre survey study

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Abstract

Introduction

Timely reperfusion therapy is critical in ST-elevation myocardial infarction [STEMI]. Disconcertingly, pre-hospital delay times [PHDT] have hardly changed over the decades and especially women seem to delay. Prospective studies are needed to better understand the relation between gender and care-seeking in STEMI.

Objective

We aimed to compare the genders in STEMI regarding 1) first medical contact [FMC] 2) PHDT 3) factors associated with PHDT

Method

SymTime was a cross-sectional survey study based on self-reported data using a validated questionnaire. Patients were enrolled from five Swedish hospitals with catheterisation facilities 24/7 Nov 2012 to Jan 2014. Eligible patients were included within 24 hours after admittance.

Results

Among 449 patients, women more often called an advisement nurse as FMC (28 vs 18%, p=0.02). They had longer PHDT until FMC, 90 (interquartile range [IQR] 39-221) vs. 66 min (28-161), p=0.04, and until ECG, 146 (68-316) vs. 103 (61-221) min, p=0.03. Men went to hospital because of believing they were stricken by MI to a higher extent than women (25 vs 15%, p=0.04), and were more often recommended to call Emergency Medical Services [EMS] by bystanders (38 vs 22%, p<0.01). Women more often did not tell about their symptoms (7 vs 2%, p=0.02). Hesitating going to hospital and experiencing pain in the stomach/back/shoulders were factors associated with long PHDT in women. Believing the symptoms should disappear or interpreting them as nothing serious were corresponding factors in men. In both genders bystanders acting to contact EMS was explaining short delay.

Conclusion

In STEMI women differed from men in FMC and they had longer PHDT. This was partly due to atypical symptoms and a longer decision time. Bystanders acted more promptly when men than when women fell ill. The public knowledge of MI symptoms, and how to properly act when diseased, seems still not sufficient.

Article summary

Strength and limitations of this study

- The specific aim with the SymTime project was to prospectively evaluate thoughts, actions, symptoms and pre-hospital delays in ST elevation myocardial infarction [STEMI] from a gender perspective. The focus on the pre-hospital setting, together with the prospective design using self-reported data with a validated questionnaire is unique, using wide inclusion criteria but selecting the inclusion to STEMI where delay is most devastating.
- Approximately 1/10 of the hospitalised Swedish STEMI patients during the inclusion period filled in the questionnaire within 24 hours of admittance making the results generalizable and with limited risk of recall bias.
- Female gender has been found associated with increased delay to reperfusion therapy in STEMI but reasons why are still obscure. Whereas systems delay times have been successively shortened, pre-hospital delay times [PHDT] are still long and hard to influence. The current study compared PHTD between men and women in the modern primary percutaneous coronary intervention [PPCI] era but also explored gender specific predictors of delay.
- Using other forms of first medical contact [FMC] than the Emergency Medical Services [EMS] are known to increase delays. The current study is to the best of our knowledge the first ever study of investigating gender differences in FMC in STEMI.
- With the observational design of this study, we can only report associations rather than causation. In addition, there may be factors associated with delay not covered by the questionnaire, such as deeper knowledge about MI and about risk factors. Patients having difficulties in reading and speaking Swedish were excluded from the study and thus we cannot draw firm conclusion about refugees and immigrants stricken by STEMI.

INTRODUCTION

In ST-elevation myocardial infarction [STEMI], timely administration of reperfusion therapy is critical for improving survival.[1, 2] Short term outcomes in STEMI differ between the genders, with approximately twice as high in-hospital mortality in women.[3] In addition,

women receive appropriate reperfusion therapy less often than men, and have higher rates of adverse events.[3] During the last decades focus has mainly been on shortening system delay times where a clear association between longer delay and worse prognosis has been found.[1] Less focus has been on the pre-hospital phase where the actions of the patients play a major part, and is proven difficult to influence.[4, 5] Disconcertingly, pre-hospital delay times [PHDT] have hardly changed over the past decades.[6, 7] Female gender has been found associated with PHDT according to several studies,[7, 8, 9, 10] but measurements of PHDT have been inconsistent[11] and data on gender differences on first medical contact [FMC] are very sparse. PHDT consist of, (1) symptom onset to the decision to seek care, (2) decision to FMC, and (3) FMC to hospital arrival.[12] Mostly all these phases has been studied together,[6, 7, 13, 14] and further studies are needed to better understand the relation between gender and care-seeking behaviour in STEMI, restricting the PHDT to the pre-hospital phase and using prospective designs.

Aim of the study

In STEMI patients compare the genders as to,

1. FMC
2. PHDT defined as from symptom onset to a) FMC and b) diagnostic ECG
3. Factors associated with PHDT (symptom onset to FMC)

METHOD

This Swedish multicentre study (SymTime) has been previously described.[15] Shortly, it has a descriptive and comparative cross-sectional design of self-reported data. A previously validated self-administered questionnaire developed and tested in a Swedish chest pain population was used,[9] with small changes and clarifications. The questionnaire covers 35 items; including (1) baseline characteristics, (2) symptoms, (3) course of events including multiple time point measurements and (4) description of transport mode. We enrolled participants from five Swedish hospitals with a diverged geographic locations, all with catheterisation facilities and primary percutaneous coronary intervention [PCI] enabled 24/7. Data were collected in the cardiac care unit [CCU] in each participating hospital from November 2012 to January 2014. Eligible patients were planned to be consecutively included within 24 h after admittance. Inclusion criteria were: (1) STEMI, defined as ST-elevation on

admission ECG and a diagnosis of acute MI at discharge according to ESC's guidelines,[16] (2) ability to fill in the questionnaire and (3) willing to participate. Patients were pain free and hemodynamically stable when they were asked to participate. The staff nurse obtained clinical data such as information on diagnosis, FMC, important time point measurements (e.g., ECG and FMC) and comorbidities from the patients as well as from the medical records.

Ethical aspects

Permission for the study was obtained from the regional Ethical Review Board, Linköping, Sweden (D-nr 2012/201–31), and complied with the Declaration of Helsinki.[17] Informed consent was obtained from all included patients.

Statistical analysis

Patient delay time was defined as the interval between time-of-onset-of-symptoms until first FMC. FMC was defined as the time point when contacting the Primary Healthcare Centre [PHC], the national service telephone number; Swedish Healthcare Direct [SHD], Emergency Medical Service [EMS]) or Emergency Room [ER]. We used frequencies and proportions to describe the history of patients' characteristics, the sociodemographic, clinical and contextual variables, and their FMC. Continuous variables were reported as mean ± SD or median (interquartile range [IQR]), and gender comparisons done with Student T-test or Mann Whitney U-test depending on if the variable was normally distributed or not. Multiple linear regression analyses were performed in men and women separately in order to sort out relevant predictors of patient delay. The time variable had to be log-transformed in order to be normally distributed. Background characteristics, clinical presentation, context when falling ill, thoughts and actions as well as reactions from bystanders were included in five blocks in order to analyse the relevance of each block in terms of R^2 change. Included variables were chosen through literature research and/or deemed to be important by the research group. There were few missing values in the data collection - regarding the most important outcome measurements there were no (symptoms) or minor (FMC, 0.9% and delay from symptom onset until FMC, 3.8%) missing values. All statistical analyses were performed using IBM SPSS Statistics 23.0.

RESULTS

Background characteristic and clinical presentation

In total 449 STEMI patients were included. Women were five years older than men, with lower educational status and more often living on their own. Women had higher prevalence of hypertension as well as diabetes mellitus. (Table I)

Among chief complaints, chest pain /discomfort was prevalent in 92% of men compared to 73% of women p<0.001. Pain in the throat/neck, back and/or shoulder as twice as common in women as in men, as well as a feeling of fear. Nausea was prevalent in half of the women compared to one third of the men. There was no gender difference in pain intensity. (Table II)

Thoughts, actions and context when falling ill

When falling ill in STEMI women were more often together with their children, relatives or friends, whereas men were more often together with colleagues. There was no gender difference in being alone or being at home at the time. Self-medication with aspirin was as common in both gender as well as nitro-glycerine, whereas women took pain-killers almost twice as often as men (27 vs 15%, p<0.01). The first person to talk to about the symptoms was the partner, which was the case in more than half of both men and women. Women more often than men informed their children first of all about their symptoms, whereas men more often than women first talked to friends or relatives. More than one third of the women compared to one fourth of the men spoke to the SHD before they went to the hospital (28 vs 18%, p=0.02) and less than 1/5 of both men and women talked to their PHC without any gender difference. Both genders had heard of angioplasty or clot-dissolving as treatment of MI to a great extent.

The most common reason why STEMI patients went to the hospital was severe symptoms, with no difference between the genders. Men went to hospital because of believing they were struck by MI to a higher extent compared to women (25 vs 15%, p=0.04). There was neither any gender difference in hesitating going to the hospital, nor in reasons why hesitating. The most common reason why hesitating in both genders was believing the symptoms should disappear. (Table III)

Reactions from bystanders

Men were more often recommended to call 112 (38 vs 22%, p<0.01) by the bystanders. Women more often had bystanders calling SHD (36 vs 25%, p=0.03), but also more often did not tell anyone about their symptoms (7 vs 2%, p=0.02). (Table IV)

Delay times and first medical contact

In the total study population the median PHDT from symptom onset to FMC was 70 min (IQR 30-178) and to diagnostic ECG 110 min (IQR 64-238). The system delay from FMC to diagnostic ECG was 27 min (IQR 15-50).

Women waited in median 90 min (IQR 39-221) before taking their FMC compared to 66 min (IQR 28-161) in men, p=0.04. Moreover women more often contacted SHD as FMC compared to men. (Figure 1)

System delay time in form of FMC to diagnostic ECG did not differ between the genders, (25 [15-49] min in men vs. 33 [15-61] min in women, p=0.09). Altogether, women had longer delay from symptom onset until diagnostic ECG (146 [68-316] min in women, vs. 103 [61-221] min in men p=0.03). Divided in subgroups on short, medium and long delay, women more often had a long delay compared to men, both from symptom onset to FMC, and from symptom onset to diagnostic ECG. (Figure 2-4)

Factors associated with delay in men and women

In women, sociodemographic, contextual, cognitive, behavioural and clinical factors included in the survey explained 53% of the variance of PHDT compared to 26% in men. In both genders the clinical presentation explained most of the delay, followed by thoughts and actions when falling ill. In women hesitating going to the hospital, stomach pain and pain in the back/shoulders were the variables strongest associated with increased delay, while cold sweat and bystanders calling - or recommending calling - EMS were the variables strongest associated with short delay. In men, believing the symptoms should disappear or interpreting the symptoms as nothing serious had the strongest association with increased delay, whereas bystanders calling EMS was the variable strongest associated with reduced delay. (Table V)

DISCUSSION

The main findings of the present study are the far longer delay times in women vs. men among Swedish STEMI patients - from symptom onset until 1) FMC of 26 min and 2)

diagnostic ECG of 43 min. This was due to primarily three things; more atypical symptoms and a longer decision time in women and a gender difference in choice of FMC, were women more often than men called for advice to the national SHD service number.

A short system delay has been found associated with prognosis in STEMI patients undergoing primary percutaneous coronary intervention [PPCI], and timely reperfusion is recommended in current guidelines.[16] Anyhow, total ischemic time may be a better metric to study the effect of time on clinical outcomes. De Luca et al. examined the total ischemic time in a large cohort of STEMI patients treated with PPCI. After multivariable adjustment every additional 30 min of reperfusion delay increased 1-year mortality by 8%.[2] In another analysis of two large STEMI trials Brodie et al. found that only patients with a short PHDT (<90 min) had long term benefit of shorter system delay to reperfusion.[18] PHDT accounts for the largest proportion of total ischemic time[4] but has remained virtually unchanged over the last decades in the western world.[7] Although interventions aimed at shortening PHDT has been discouraging,[4, 5] a more recent report from Denmark on STEMI patients calling EMS service have found a temporal trend of decrease in PHDT (symptom onset until calling EMS) from 101 to 85 min between year 2003 to 2009. This was after introduction of PPCI to all STEMI patients, which the authors claim could have had potential positive effects on public awareness.[19]

Few STEMI studies have focused on patient-related delays based on self-reported data, and studies focusing on symptom onset to FMC are even sparser. In the meta-analysis from Nguyen et al., in terms of the measurement of PHDT, the majority of investigations defined pre-hospital delay as the time interval from the onset of symptoms to arrival at the hospital, such as studies from the MONICA, NRMI and GRACE registries.[6, 7, 13, 14, 20] Thus there is no possibility to differ patient delay from system delay, i.e., from FMC to ECG and from ECG to arrival. In addition previous studies exploring gender differences in PHDT in MI have shown inconsistent results and have several limitations such as using restricted patient samples,[20] that may have resulted in limited generalisability, or relying primarily on information from medical records, which may be associated with information bias.[20] Finally, many studies have included mixed acute coronary syndrome [ACS] populations not restricting the inclusion to STEMI.[9, 13] In the current study focusing on the patient delay in STEMI, women delayed 1.5 h before their FMC compared to approximately 1 h in men. In the total study population, the median PHDT from symptom onset to FMC of 70 min, and to

diagnostic ECG of 110 min, is substantially better than reported in studies from other American and European countries.[21, 22] but much longer than the goal time of 5 minutes advised by guidelines.[23] More than 40% of the women compared to 30% of the men waited over 2 hours before seeking medical attention in our study. Reducing the delay in this time interval has a great potential to improve the outcomes of STEMI patients, given that many deaths occur early.[24] It is important to analyse care-seeking behaviour in different regions of the world as differences in medical insurance and health care systems do certainly play a part as well as cultural factors reflecting differences in awareness and interpretation of and actions upon MI symptoms. In a study by Alshahrani et al. women in Saudi Arabia were found to have a tremendously long PHDT of 12.9 h, and female gender was the strongest predictor of PHDT. Several possible explanations were identified, such as women requiring a male relative's permission to seek medical care and to be accompanied to the hospital, and women prioritising family responsibilities as well as a lack of knowledge of MI symptoms and treatments.[25] In our Swedish STEMI cohort only small gender differences were found in context, thoughts and actions when falling ill. Men more often first talked about their symptoms with a spouse, relative or friend whereas women more often talked with their child/children. This probably reflects the fact that women are older than men when falling ill into STEMI, and thus more often living on their own because of being widowed. Older studies from other geographic regions have found that "not wanting to trouble anyone" is a factor associated with prolonged delay in women, but not in men.[26] In the present study no difference was found as regards worries of disturbing or waking attention.

One important difference in action was found in the present study; women and men differed in FMC. In Sweden SHD, a joint service number, was launched in 2003 and is staffed by advisement nurses 24/7 in order to answer questions, determine the need for further care, and provide advice and/or contact with other healthcare providers. Media campaigns have informed the general public about the possibility to contact an advisement nurse by telephone instead of seeking immediate care at the ER or general practitioner [GP] for non-life-threatening symptoms. SHD has become a very important way of contacting the health care system and gets around 500 000 calls every month. In our study, as many as 1/3 of the women compared to 1/5 of the men, called SHD as the FMC. This is worrying as we have shown in a previous study that patients turning to SHD as FMC had 38 min longer delay from symptom onset until first ECG compared to patients calling EMS.[15] The reluctance to call EMS – and the prolonged delay before FMC - may be explained by several factors such as

misinterpretation of symptoms, as well as women's lack of perceived potential risk for ACS.[27] Consistent with other studies,[14] women were less educated than men and in the multivariable analysis this variable was associated with longer PHDT in women, although with borderline significance (p=0.06). This could be attributed to low socioeconomic status and lack of ACS knowledge.

A large difference in chest pain prevalence - the most well recognized symptom of MI presentation in the society - was found between the genders. In the same time less well known MI symptoms such as pain in the neck, throat, back or shoulders or nausea were more than twice as common in women as in men. Previous studies have found that MI symptoms looked upon as typical such as chest pain or pain in the left arm are most important for a correct attribution to the heart.[28] In accordance, men more often than women responded that believing that they had an MI was the reason going to the hospital in the current study. The importance of the clinical presentation for the PHDT was shown in the multivariable regression with an R^2 change of 23% in women compared to 10% in men, and the presence of symptoms such pain in the back, shoulders or stomach was associated with longer delay in women. Symptoms that are perceived as threatening have been described associated with shorter PHDT.[29] Accordingly, in the present study, cold sweat was associated with shorter delay in women and anguish/fear was associated with shorter delay in men.

Finally, bystanders can be crucial in obtaining appropriate care. In the present study bystanders calling EMS was one of the strongest factors associated with short delay although a gender difference in bystanders' responses on described symptoms depending on the patient's gender was found - whereas men more often had bystanders recommending contact with the EMS, women more often had bystanders calling SHD for advice. A previous study has found that relatives are more dissatisfied with the information given by the hospital staff compared to the patient. This illustrates the need to involve the next of kin in secondary prevention education and care seeking behaviour,[30] as a well-informed bystander can help diminish the patients' decision time.[30]

CONCLUSION

In conclusion, this study showed that women differ from men on several self-reported symptoms, thoughts, actions and PHDT – and partly also in reasons why delaying. Based on

our findings, women may have different educational needs compared to men which has to be taken into account when educating the public about how to recognize and act when an evolving MI emerge.

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Contributorship statement

SSL and IT contributed to the study planning, design, preparation, validation of the slightly modified questionnaire and data analysis. KHÄ, ME and SSL contributed to the data collection. KHÄ, ME, RMI, SSL and IT contributed to the manuscript preparation and approved the final version of the manuscript.

Data sharing statement

No additional data available.

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Competing interests

None declared.

Ethics approval

The Regional Ethical Review Board, Linköping, Sweden (D-nr 2012/201-31, 2012/338-32).

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Table I. Baseline and clinical characteristics

	Men n=340	Women n=109	p-values
Socio-demographic variables			
Age, mean (SD)	64.5 (11.0)	69.8 (10.7)	*<0.001*
Education level, compulsory school	120 (35.3)	53 (48.6)	*0.02*
Marital status, single	68 (20.0)	34 (31.2)	*0.02*
Clinical variables			
Current Smoker	87 (25.6)	34 (31.2)	0.25
Hypertension	162 (47.6)	68 (62.4)	*0.007*
Diabetes	46 (13.5)	24 (22.0)	*0.03*
Previous Myocardial Infarction	44 (12.9)	16 (14.7)	0.64
LAD as culprit artery	144 (42.4)	42 (38.5)	0.48

SD, Standard Deviation; LAD, Left Artery Descending. Missing values, none.

Table II. Clinical presentation

	Men n=340	Women n=109	p-values
Pain/pressure/discomfort in			
Chest/thorax	313 (92.1)	80 (73.4)	*<0.001*
Throat/neck	57 (16.8)	40 (36.7)	*<0.001*
Back	42 (12.4)	32 (29.4)	*<0.001*
Stomach	30 (8.8)	6 (5.5)	0.27
Shoulders	53 (15.6)	36 (33.0)	*<0.001*
Arms/hands	183 (53.8)	71 (65.1)	*0.04*
Associated symptoms			
Tiredness/fatigue	102 (30.0)	45 (41.3)	*0.03*
Nausea/vomiting	94 (27.6)	53 (48.6)	*<0.001*
Cold sweat	197 (57.9)	70 (64.2)	0.25
Fear	57 (16.8)	34 (31.2)	*0.001*
Symptom intensity			
Pain intensity, NRS, median (IQR)	7 (6,8)	7 (6,8)	0.65

NRS, Numeric Rating Scale; IQR, Interquartile range. Missing values; 3 (<1%) patients did not grade any pain/discomfort on the NRS scale. No missing values regarding other variables.

Table III. Thoughts, actions and context when falling ill into STEMI

	Men n=340	Women n=109	p-values
With whom did your first talk about your symptoms?			
My wife/husband/partner	202 (60.3)	60 (55.6)	0.38
A relative or friend	31 (9.3)	3 (2.8)	*0.03*
My children	23 (6.9)	18 (16.7)	*0.002*
The Swedish Healthcare Direct	11 (3.3)	7 (6.5)	0.14
The Emergency Medical Service	20 (6.0)	4 (3.7)	0.36
The Primary Healthcare Centre	15 (4.5)	5 (4.6)	0.95
Someone else	30 (9.0)	11 (10.2)	0.70
Did you call any of the following before you went to the hospital?			
The Primary Healthcare Centre	66 (19.8)	17 (15.6)	0.33
The Swedish Healthcare Direct	81 (24.3)	33.9 (37)	*0.05*
Did you take any medication un order to relieve the symptoms?			
Painkillers	50 (14.7)	29 (26.6)	*0.005*
Nitro-glycerine	44 (12.9)	20 (18.3)	0.16
Have you heard of angioplasty or clot-dissolving treatment in case of myocardial infarction?			
Yes, I have	319 (94.1)	99 (93.4)	0.79
Why did you decide to go to the hospital			
The symptoms were severe	108 (33.9)	36 (34.3)	0.94
I thought I had a myocardial infarction	79 (24.8)	16 (15.2)	*0.04*
I was told to seek care by my wife/husband/partner	38 (11.9)	14 (13.3)	0.70
Another reason for going to the hospital	22 (6.9)	12 (11.4)	0.14
Did you hesitate to go to the hospital? If yes, why?			
I did not hesitate	249 (73.5)	74 (67.9)	0.26
I though the symptoms would disappear	85 (25.1)	31 (28.4)	0.49
I did not thought it was anything serious	27 (8.9)	8 (7.3)	0.83
I did not want to make my family worried	17 (5.0)	5 (4.6)	0.86
I did want to wake attention	4 (1.2)	2 (1.8)	0.61
I did not want to disturb	10 (2.9)	3 (2.8)	0.92
I felt a discomfort in the face of being hospitalised	11 (3.2)	5 (4.6)	0.51
Context when falling ill			
At home	253 (74.4)	90 (82.6)	0.08
I was alone	91 (26.8)	29 (26.6)	0.97
Weekend	95 (29.3)	34 (31.8)	0.49
Weekdays, out of office time	118 (35.4)	38 (35.8)	0.94
Transport mode			
I went by ambulance to the hospital	280 (82.4)	91 (83.5)	0.79
Missing values; 25 (5.6%) patients did not answer the question about why hesitating going to the hospital. No or minor missing regarding all other variables.			

Table IV. Reactions from bystanders when falling ill.

	Men n=340	Women n=109	p-values
He/she/they suggested that I should rest	47 (14.0)	13 (12.0)	0.61
He/she/they suggested medication	11 (3.3)	7 (6.5)	0.14
He/she/they suggested that I should call EMS	126 (37.5)	24 (22.2)	*0.003*
He/she/they suggested that I should call SHD	85 (25.3)	85 (78.7)	0.40
He/she/they called EMS	175 (52.1)	55 (51.4)	0.90
He/she/they called SHD	85 (25.3)	39 (36.1)	*0.03*
He/she/they brought me to the hospital	63 (18.8)	23 (21.3)	0.56
I did not tell anyone	8 (2.4)	8 (7.4)	*0.02*

EMS, Emergency Medical Services; SHD, Swedish Health Care Direct. Missing values; 5 (1.1%) patients did not answer question about reaction from bystanders.

Table V. Predictions of patient delay times in men and women separately

	Men n=340			**Women n=109**		
	Standardized Beta	**p-value**	**R^2 change**	**Standardized Beta**	**p-value**	**R^2 change**
Block 1. Background characteristics			**0.04**			**0.13**
Age	0.12	*0.05*		0.07	0.54	
Current smoker	0.14	*0.01*		0.19	*0.05*	
Block 2. Symptoms			**0.10**			**0.23**
Chest pain	0.15	*0.01*		0.05	0.55	
Pain in back/shoulders	-0.03	0.60		0.25	*0.01*	
Stomach pain	0.09	0.07		0.30	*0.00*	
Cold sweat	-0.07	0.19		-0.18	*0.04*	
Anguish/fear	-0.13	*0.01*		-0.08	0.38	
Block 3. Context when falling ill			**0.02**			**0.08**
At home	-0.11	*0.03*		-0.04	0.62	
Out of office time	0.06	0.27		0.18	*0.03*	
Block 4. Reactions from bystanders			**0.08**			**0.12**
They suggested rest	-0.13	*0.02*		0.10	0.28	
They suggested calling EMS	-0.04	0.41		-0.22	*0.02*	
They called EMS	-0.28	*0.00*		-0.23	*0.01*	
They drove me to the hospital	0.02	0.75		-0.14	0.12	
Block 5. Thoughts and actions			**0.09**			**0.13**
I took some medication to relieve the symptoms	0.12	*0.03*		0.06	0.47	
I hesitated going to the hospital	-0.11	0.26		0.62	*0.00*	
I thought the symptoms should go away/it was not anything serious	0.25	*0.01*		-0.31	0.06	
I did not want to make my relatives worried	0.09	0.11		-0.17	*0.05*	
I was afraid of the reaction from the hospital staff	0.05	0.34		0.20	*0.04*	

Multiple linear regression with log-transformed pre-hospital delay time in minutes as the dependent variable. Independent variables entered in five blocks, significant predictors in the multivariable analyses shown in table. R^2 for the complete model 0.53 in women, 0.26 in men. EMS, emergency medical service.

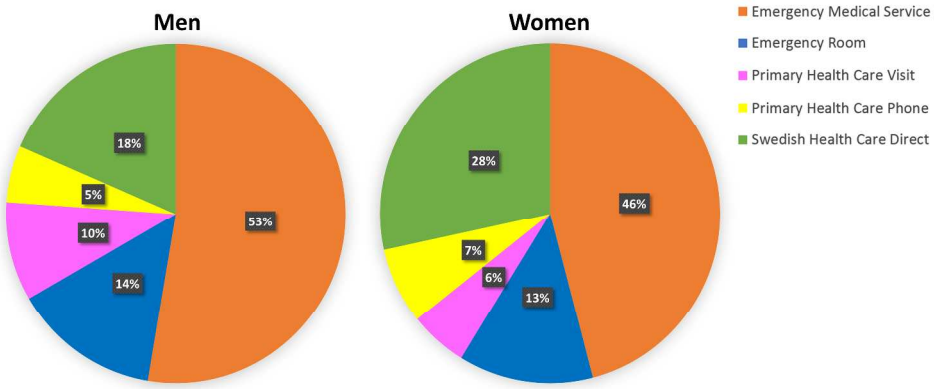

Figure 1. First medical contact in men and women with STEMI

338x190mm (300 x 300 DPI)

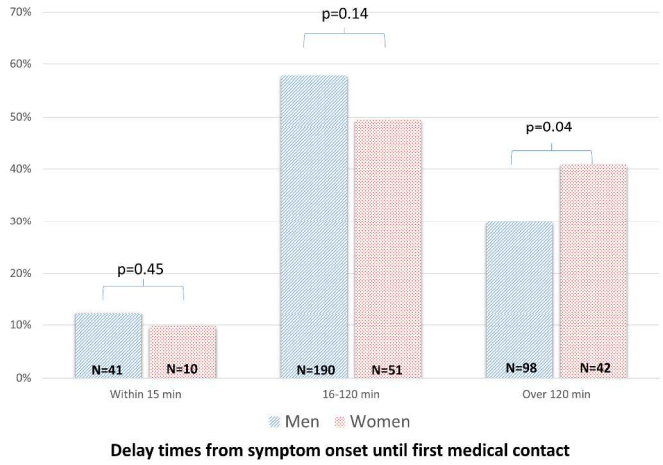

Figure 2. Delay times from symptom onset until first medical contact

338x190mm (300 x 300 DPI)

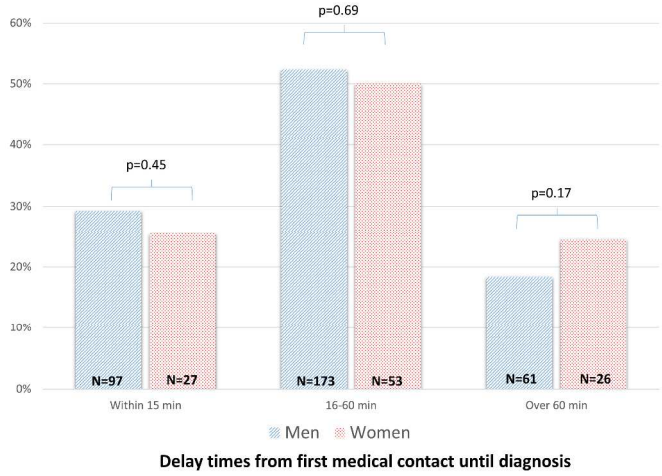

Figure 3. Delay times from first medical contact until diagnosis

338x190mm (300 x 300 DPI)

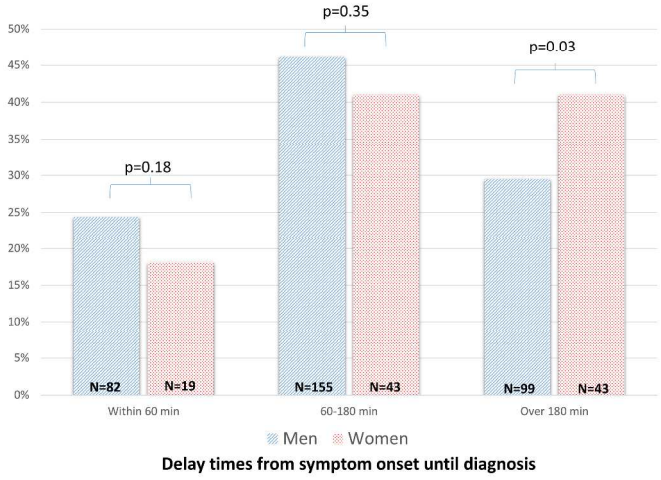

Figure 4. Delay times from symptom onset until diagnosis

338x190mm (300 x 300 DPI)

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract **Indicated in the title (page 1), in the abstract (page 2) and in the method section (page 4-5)**
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found **Done (page 2)**
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported **Done (page 3-4)**
Objectives	3	State specific objectives, including any prespecified hypotheses **Objectives specified in the introduction section (aim of the study, page 4)**
Methods		
Study design	4	Present key elements of study design early in the paper **Presented in title (page 1), abstract (page 2) and method section (page 4-5)**
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection **Summarised in the method section (page 4-5) as all details are given in a previous publication that we refer to**
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants **Done, in the method section (page 4-5)**
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable **Done, in the method and statistical sections (page 4-5)**
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group **Done, in the method section (page 4-5). Details of the questionnaire given in a previous publication that we refer to**
Bias	9	Describe any efforts to address potential sources of bias **Done, in the method section (page 4-5). We have made an effort to include eligible STEMI patients on a consecutive basis within 24 hours after admittance, reducing the risk of selection and recall bias**
Study size	10	Explain how the study size was arrived at **No power calculation was done as this is a descriptive observational study (page 4-5). We planned for one year inclusion and that we then should include approximately 500 STEMI patients which would be enough to do the gender (and other) comparisons we planned for**
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why **Explained in the statistical section (page 5)**
Statistical methods	12	Describe all statistical methods, including those used to control for confounding **Multivariable linear regression analyses performed – not to control for confounding, but to find variables associated to delay in women and in men, separately. Explained in the statistical section (page 5)**
		(*b*) Describe any methods used to examine subgroups and interactions **NA**
		(*c*) Explain how missing data were addressed **We had very little missing data, specified in the statistical section (page 5)**

		(*d*) If applicable, describe analytical methods taking account of sampling strategy **NA**
		(*e*) Describe any sensitivity analyses **NA**
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed **SymTime was supposed to consecutively include eligible STEMI-patients at five hospitals with cath lab facilities (page 4-5). The patients could not be included the first hours because of the acute nature of this disease. Thus they had to stay a while at the participating hospital in order to be able to be included. Patients were then included within 24 h, most often at day 2. The total study population consisted of 532 STEMI patients comprising 36% of all STEMI patients that ever touched down (including those only coming to cath lab and then leaving the including hospital very fast) at the five hospitals during the study period (n=1473) according to the Swedish quality register SWEDEHEART. The first couple of months FMC was not registered. Thus the present study consists of the 449 STEMI patients included after the start of FMC registering.**
		(b) Give reasons for non-participation at each stage **Inclusion and exclusion criteria presented in the method section (page 4-5).**
		(c) Consider use of a flow diagram **Considered, but not deemed necessary. Data given in text.**
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders **Presented in Table 1 and in the result section (page 6)**
		(b) Indicate number of participants with missing data for each variable of interest **There was very little missing data in the current study, specified in the statistical section (page 5)**
Outcome data	15*	Report numbers of outcome events or summary measures **No outcome events were measured**
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included **Absolut numbers, percentages, multivariable adjusted linear regression analyses for the main measurements are presented in the result section. Selection of variables in the multivariable analyses and how these were chosen is described in the statistics section.**
		(*b*) Report category boundaries when continuous variables were categorized **NA**
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period **NA**
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses **NA**
Discussion		
Key results	18	Summarise key results with reference to study objectives **Summarised in the discussion section (page 7-8)**
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision.

		Discuss both direction and magnitude of any potential bias **Summarised in the strength and limitation section (page 3)**
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence **Done in the discussion (page 8-10) and in the conclusion (page 10-11)**
Generalisability	21	Discuss the generalisability (external validity) of the study results **Done in the strength and limitation section (page 3)**
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based **Done in the funding section (page 11)**

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Gender disparities in first medical contact and delay in ST-elevation myocardial infarction - a prospective multicentre survey study

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Gender disparities in first medical contact and delay in ST-elevation myocardial infarction - a prospective multicentre survey study

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Abstract

Introduction

Timely reperfusion therapy is critical in ST-elevation myocardial infarction [STEMI]. Disconcertingly, pre-hospital delay times [PHDT] have hardly changed over the decades and especially women seem to delay. Prospective studies are needed to better understand the relation between gender and care-seeking in STEMI.

Objective

We aimed to compare gender disparities in STEMI regarding 1) choice of first medical contact [FMC], 2) delay from symptom onset-to-FMC and to-diagnostic ECG, and 3) factors associated with symptom onset-to-FMC in men and women.

Method

SymTime was a cross-sectional survey study based on self-reported data using a validated questionnaire. Patients were enrolled from five Swedish hospitals with catheterisation facilities 24/7 Nov 2012 to Jan 2014. Eligible patients were included within 24 hours after admittance.

Results

Among 449 patients, women more often called an advisement nurse as FMC (28 vs 18%, p=0.02). They had longer delay until FMC, 90 (interquartile range [IQR] 39-221) vs. 66 (28-161) min, p=0.04, and until ECG, 146 (68-316) vs. 103 (61-221) min, p=0.03. Men went to hospital because of believing they were stricken by MI to a higher extent than did women (25 vs 15%, p=0.04), and were more often recommended to call Emergency Medical Services [EMS] by bystanders (38 vs 22%, p<0.01). Hesitating going to hospital and experiencing pain in the stomach/back/shoulders were factors associated with long delay in women. Believing the symptoms should disappear or interpreting them as nothing serious were corresponding factors in men. In both genders bystanders acting to contact EMS was explaining shorter delay.

Conclusion

In STEMI women differed from men in FMC and they had longer delays. This was partly due to atypical symptoms and a longer decision time. Bystanders acted more promptly when men

than when women fell ill. The public knowledge of MI symptoms, and how to properly act, seems still not sufficient.

Article summary

Strength and limitations of this study

- The current study is to the best of our knowledge the first ever study of gender disparities in choice of - and time to - first medical contact [FMC] in STEMI, using self-reported data.
- With the use of wide inclusion criteria approximately 1/10 of the hospitalised Swedish STEMI patients during the inclusion period filled in the questionnaire within 24 hours of admittance making the results generalizable and with limited risk of recall bias.
- The study compared pre-hospital delay times [PHDT] between the genders in the primary percutaneous coronary intervention [PPCI] era and thoroughly explored gender specific predictors of delay in order to facilitate a possible future intervention aiming at shortening delays in both men and women with STEMI.
- With the observational study design, we can only report associations rather than causations, and there may be factors associated with PHDT not covered by the questionnaire, such as health literacy and deeper knowledge about MI.
- Patients having difficulties in reading and speaking Swedish were excluded from the study and thus we cannot draw firm conclusion about refugees and immigrants stricken by STEMI.

INTRODUCTION

Myocardial infarction [MI] mortality has decreased substantially the last decades in the western world, because of more active prevention and better treatment.[1] Still, outcomes in ST-elevation MI [STEMI] differ between the genders, with approximately twice as high in-hospital mortality in women,[2, 3] who receive reperfusion therapy less often than men.[2, 4] In STEMI timely administration of reperfusion therapy is critical for improving survival.[5, 6] During the last decades focus has mainly been on shortening system delay times where a clear association between longer delay and worse prognosis has been found.[5] Consequently, STEMI guidelines strongly recommend that the diagnosis is made already in

the pre-hospital setting.[7] In Sweden, ECG is taken in by the Emergency Medical Services [EMS] paramedics in patients with symptoms indicating an evolving MI. The ECG is then transferred to the nearest hospital where the cardiologist/internist on call judge if the patient has a probable STEMI or not. Thus, in patients calling EMS, the diagnosis of STEMI can be done well in advance before admission to hospital and the patient can be directed straightforward to the cath lab or could be given pre-hospital fibrinolytics.[8] Less focus has been on the patient delay in the pre-hospital phase, which has been proven difficult to influence.[9, 10] Disconcertingly, pre-hospital delay times [PHDT] have hardly changed over the past decades.[11, 12, 13] In order to diverse patient from system delay it has been suggested to include also the time point of first medical contact [FMC] in the analysis of PHDT.[14] Still, previous studies have mostly focused on total PHDT.[11, 12, 15] Since STEMI patients do not always call EMS as their FMC, studying the different phases of PHDT as well as choice of FMC is imperative. Female gender has been found associated with PHDT according to several studies,[12, 16, 17, 18, 19] but measurements have been inconsistent[20] and data on gender disparities on FMC are very sparse. Consequently, further studies are needed to better understand the relation between gender and care-seeking behaviour in STEMI .

Aim of the study

We aimed to compare gender disparities in STEMI regarding 1) choice of FMC, 2) PHDT from symptom onset-to-FMC as well as from symptom onset-to-diagnostic ECG and, 3) factors associated with symptom onset-to-FMC in men and women separately.

METHOD

This Swedish multicentre study (SymTime) has been previously described.[21] Shortly, it has a descriptive and comparative cross-sectional design of self-reported data. A previously validated self-administered questionnaire developed and tested in a Swedish chest pain population was used,[17] with some minor changes and clarifications. The questionnaire covers 35 items; including (1) baseline characteristics, (2) symptoms, (3) course of events including multiple time point measurements and (4) description of transport mode. We enrolled participants from five Swedish hospitals with a diverged geographic locations, all with catheterisation facilities and primary percutaneous coronary intervention [PCI] enabled 24/7. Data were collected in the cardiac care unit [CCU] in each participating hospital from

November 2012 to January 2014. Eligible patients were planned to be consecutively included within 24 h after admittance. Inclusion criteria were: (1) STEMI, defined as ST-elevation on admission ECG and a diagnosis of acute MI at discharge according to ESC's guidelines,[7] (2) ability to fill in the questionnaire and (3) willing to participate. Patients were pain free and hemodynamically stable when they were asked to participate and when filling in the questionnaire. The staff nurse simultaneously obtained clinical data such as information on diagnosis, FMC, important time point measurements (e.g., ECG and FMC) and comorbidities from the patients as well as from the medical records.

In this study, two parts of PHDT were studied, 1) the interval between time of symptom onset-to-FMC and 2) the interval from symptom onset-to-diagnostic ECG. FMC was defined as the time point when contacting any health care personnel either by phone or in person and was divided into five categories; 1) the Primary Healthcare Centre [PHC] by phone, 2) the PHC directly, 3) the Swedish Healthcare Direct [SHD] by phone, 4) the EMS by phone or 5) the Emergency Room [ER] directly. All patients chose any of these five ways of contacting the Swedish health care system.

Ethical aspects

Permission for the study was obtained from the regional Ethical Review Board, Linköping, Sweden (D-nr 2012/201–31), and complied with the Declaration of Helsinki.[22] Informed consent was obtained from all included patients.

Statistical analysis

We used frequencies and proportions to describe the history of patients' characteristics, the sociodemographic, clinical and contextual variables, and their FMC. Categorical variables were reported by numbers and percentages and groups were compared with the use of the Chi-Square test. Continuous variables were reported as means ± standard deviations [SD] or as medians with interquartile ranges [IQR], and gender comparisons were done with the two-tailed Student T-test or the Mann Whitney U-test depending on if the variable was normally distributed or not. Multiple linear regression analyses were performed in men and women separately in order to sort out relevant predictors of patient delay. The time variable had to be log-transformed in order to be normally distributed. Background characteristics, clinical presentation, context when falling ill, thoughts and actions as well as reactions from

bystanders were included in five blocks in order to analyse the relevance of each block in terms of R^2 change. Included variables were chosen through literature research and/or deemed to be important by the research group. There were few missing values in the data collection - regarding the most important outcome measurements there were no (symptoms) or minor (FMC, 0.9% and delay from symptom onset until FMC, 3.8%) missing values. All tests were two-tailed and a p-value of less than 0.05 was deemed indicating a statistically significant difference between compared groups. All statistical analyses were performed using IBM SPSS Statistics V23.0 (SPSS Inc, Chicago, Illinois, USA) for Windows.

RESULTS

Background characteristic and clinical presentation

In total 449 STEMI patients were included. Women were five years older than men, with lower educational status and more often living on their own. Women had higher prevalence of hypertension as well as diabetes mellitus. (Table I)

Among chief complaints, chest pain /discomfort was prevalent in 92% of men compared to 73% of women p<0.001. Pain in the throat/neck, back and/or shoulder as twice as common in women as in men, as well as a feeling of fear. Nausea was prevalent in half of the women compared to one third of the men. There was no gender difference in pain intensity. (Table II)

Thoughts, actions and context when falling ill

When falling ill in STEMI women were more often together with their children, relatives or friends, whereas men were more often together with colleagues. There was no gender difference in being alone or being at home at the time. Self-medication with aspirin was as common in both gender as well as nitro-glycerine, whereas women took pain-killers almost twice as often as men (27 vs 15%, p<0.01). The first person to talk to about the symptoms was the partner, which was the case in more than half of both men and women. Women more often than men informed their children first of all about their symptoms, whereas men more often than women first talked to friends or relatives. More than one third of the women compared to one fourth of the men spoke to the SHD before they went to the hospital (28 vs 18%, p=0.02) and less than 1/5 of both men and women talked to their PHC, with no difference between the gender. Both genders had heard of angioplasty or clot-dissolving as treatment of MI to a great extent.

The most common reason why STEMI patients went to the hospital was severe symptoms, with no difference between the genders. Men went to hospital because of believing they were struck by MI to a higher extent compared to women (25 vs 15%, p=0.04). There was neither any gender difference in hesitating going to the hospital, nor in reasons why hesitating. The most common reason why hesitating in both genders was a belief the symptoms should disappear. (Table III)

Reactions from bystanders

Men were more often recommended to call 112 by bystanders (38 vs 22%, p<0.01). Women more often had bystanders calling SHD (36 vs 25%, p=0.03), but also more often did not tell anyone about their symptoms (7 vs 2%, p=0.02). (Table IV)

Delay times and first medical contact

In the total study population the median patient delay from symptom onset to FMC was 70 min (IQR 30-178) and to diagnostic ECG 110 min (IQR 64-238). The system delay from FMC to diagnostic ECG was 27 min (IQR 15-50).

Women waited in median 90 min (IQR 39-221) before taking their FMC compared to 66 min (IQR 28-161) in men, p=0.04. EMS was the most common FMC used by approximately half of the patient regardless of sex, but women more often contacted SHD as FMC compared to men, 28 vs 18% (p=0.02). (Figure 1) In total, 83% of patients were finally arriving to the hospital by ambulance (data not shown).

System delay time in form of FMC to diagnostic ECG did not differ between the genders, (25 [15-49] min in men vs. 33 [15-61] min in women, p=0.09). Altogether, women had longer delay from symptom onset until diagnostic ECG (146 [68-316] min in women, vs. 103 [61-221] min in men p=0.03). Divided in subgroups on short, medium and long delay, women more often had a long delay compared to men, both from symptom onset to FMC, and from symptom onset to diagnostic ECG. (Figure 2-4)

Factors associated with delay in men and women

In women, sociodemographic, contextual, cognitive, behavioural and clinical factors included in the survey explained 53% of the variance of PHDT compared to 26% in men (i.e., the R^2 for the complete model, men and women studied separately). In both genders the clinical

presentation explained most of the delay from symptom onset-to-FMC, followed by thoughts and actions when falling ill. In women hesitating going to the hospital, stomach pain and pain in the back/shoulders were the variables strongest associated with increased delay, while cold sweat and bystanders calling - or recommending calling - EMS were the variables strongest associated with short delay. In men, believing the symptoms should disappear or interpreting the symptoms as nothing serious had the strongest association with increased delay, whereas bystanders calling EMS was the variable strongest associated with reduced delay. (Table V)

DISCUSSION

The main findings of the present study are the far longer delay times in women vs. men among Swedish STEMI patients; from symptom onset-to-FMC of 26 min and from symptom onset-to-diagnostic ECG of 43 min. This was due to primarily three things; more atypical symptoms and a longer decision time in women and a gender difference in choice of FMC, where women more often than men called for advice to the national SHD service number.

A short system delay has been found associated with prognosis in STEMI patients undergoing primary percutaneous coronary intervention [PPCI], and timely reperfusion is recommended in current guidelines.[7] Anyhow, total ischemic time may be a better metric to study the effect of time on clinical outcomes, i.e. measuring the time from symptom onset-to-reperfusion therapy. De Luca et al. examined the total ischemic time in a large cohort of STEMI patients treated with PPCI. After multivariable adjustment every additional 30 min of reperfusion delay increased 1-year mortality by 8%.[6] In another analysis of two large STEMI trials Brodie et al. found that only patients with a short PHDT (<90 min) had a long term benefit of shorter system delay to reperfusion.[23] PHDT accounts for the largest proportion of the total ischemic time[9] but has remained virtually unchanged over the last decades.[12] Although interventions aimed at shortening PHDT has been discouraging,[9, 10] a more recent report from Denmark on STEMI patients calling EMS service have found a temporal trend of decrease in PHDT (symptom onset until calling EMS) from 101 to 85 min between year 2003 to 2009. This was after introduction of PPCI to all STEMI patients, which the authors claim could have had potential positive effects on public awareness.[24]

Few studies have focused on delays to FMC in STEMI. The majority of previous studies have defined PHDT as the time interval from symptom onset-to-hospital arrival, without

separating the patient from the system delay, i.e. before and after FMC.[11, 12, 15, 25, 26] Studies on gender disparities in PHDT have shown inconsistent results and have limitations such as using restricted patient samples,[25] or relying primarily on information from medical records [25] or registries not specifically formed to study delay.[11, 25, 26] Finally, many studies have included mixed MI patients not restricting the inclusion to STEMI.[11, 17, 25] In the current study focusing on patient delay from symptom onset-to-FMC and from symptom onset-to-diagnosis of STEMI, women delayed 1.5 h until FMC compared to approximately 1 h in men. In the total study population, the median delay from symptom onset to FMC of 70 min, and to diagnostic ECG of 110 min, is substantially better than reported in studies from other American and European countries.[19, 27] but much longer than the goal time of 5 minutes advised by guidelines.[28] A study based on the French eMUST registry including STEMI patients that have been taken care of by special mobile intensive care units found in accordance to our data that women waited longer before calling to the EMS. They also found very similar delay until calling as we did until any FMC (78 min in women vs 54 min in men, $p<0.0001$).[19] In the current study, more than 40% of the women compared to 30% of the men waited over 2 hours before seeking medical attention. Reducing patient caused delay has a great potential to improve the outcomes of STEMI patients, given that many deaths occur early.

It is important to analyse care-seeking behaviour in different regions of the world as differences in medical insurance and health care systems do play a part as well as cultural factors and gender equality reflecting differences in awareness, interpretation and actions upon MI symptoms. In Sweden, counted as one of the most gender equal countries in the world, with a complete health care coverage for all citizens, only small gender disparities were found in context, thoughts and actions when falling ill. Men more often first talked about their symptoms with a spouse, relative or friend whereas women more often talked with their child/children. This probably reflects the fact that women are older than men when falling ill into STEMI, and thus more often living on their own because of being widowed. Older studies from other geographic regions have found that “not wanting to trouble anyone” is a factor associated with prolonged delay in women, but not in men.[29] In the present study no difference was found as regards worries of disturbing or waking attention.

Women and men differed in FMC in the current study. EMS was the FMC in only half of the patients (53% of men and 46% of women) and instead as many as 1/3 of the women and 1/5 of the men called SHD as the FMC in spite of suffering from a very urgent disease. In

Sweden SHD, a joint service number, was launched in 2003 and is staffed by advisement nurses 24/7 in order to answer questions, determine the need for further care, and provide advice and/or contact with other healthcare providers. SHD has become a very important way of contacting the health care system and gets around 500 000 calls every month. The use of SHD in STEMI is worrying as we have shown in a previous study that patients turning to SHD as FMC had 38 min longer delay from symptom onset until first ECG compared to patients calling EMS.[21] The reluctance to call EMS may be explained by several factors such as misinterpretation of symptoms, as well as women's lack of perceived potential risk for ACS.[30] Consistent with other studies,[15] women were less educated than men and in the multivariable analysis this variable tended to be associated with longer PHDT in women (p=0.06). This could be attributed to low socioeconomic status and lack of ACS knowledge. Anyhow, it is reassuring is that although far too few patients, both men and women, chose EMS as FMC, 83% of patients were finally arriving to the hospital by ambulance (data not shown).We have previously shown that this was the case regardless if the patient chose calling/visiting PHC, calling EMS or calling SHD as their FMC.[21]

A large gender disparity in chest pain prevalence - the most well recognized symptom of MI presentation in the society - was found, which is in accordance with previous studies.[31] In the same time less well known MI symptoms such as pain in the neck, throat, back or shoulders or nausea were more than twice as common in women as in men. Previous studies have found that MI symptoms looked upon as typical such as chest pain or pain in the left arm are most important for a correct attribution to the heart,[32] and that the prognosis is worse in MI patients with atypical symptoms.[31] In accordance, men more often than women responded that believing that they had an MI was the reason going to the hospital in the current study. The importance of the clinical presentation for the patient delay was shown in the multivariable regression with an R^2 change of 23% in women compared to 10% in men, and the presence of symptoms such as pain in the back, shoulders or stomach was associated with longer delay in women. Symptoms that are perceived as threatening have been described associated with shorter PHDT.[33] Accordingly, in the present study, cold sweat was associated with shorter delay in women and anguish/fear was associated with shorter delay in men.

Finally, bystanders can be crucial in obtaining appropriate care. In the present study bystanders calling EMS was one of the strongest factors associated with short delay although

a gender difference in bystanders' responses on described symptoms depending on the patient's gender was found - whereas men more often had bystanders recommending contact with the EMS, women more often had bystanders calling SHD for advice. A previous study has found that relatives are more dissatisfied with the information given by the hospital staff compared to the patient. This illustrates the need to involve the next of kin in secondary prevention education and care seeking behaviour,[34] as a well-informed bystander can help diminish the patients' decision time.[34]

CONCLUSION

In conclusion, this study showed that women differ from men on several self-reported symptoms, thoughts, actions and PHDT – and partly also in reasons why delaying. Based on our findings, women may have different educational needs compared to men which has to be taken into account when educating the public about how to recognize and act when an evolving MI emerge.

Acknowledgements

The authors hereby acknowledge all participating hospitals and their staff who included patients on a daily bases, making this project possible. We especially acknowledge Elisabeth Logander, a highly skilled research nurse at Linköping University Hospital, who supported the study group throughout the project.

Contributorship statement

SSL and IT contributed to the study planning, design, preparation, validation of the slightly modified questionnaire and data analysis. KHÄ, ME and SSL contributed to the data collection. KHÄ, ME, RMI, SSL and IT contributed to the manuscript preparation and approved the final version of the manuscript.

Data sharing statement

No additional data available.

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Competing interests

None declared.

Ethics approval

The Regional Ethical Review Board, Linköping, Sweden (D-nr 2012/201-31, 2012/338-32).

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Table I. Baseline and clinical characteristics

	Men n=340	Women n=109	p-values
Socio-demographic variables			
Age, mean (SD)	64.5 (11.0)	69.8 (10.7)	*<0.001*
Education level, compulsory school	120 (35.3)	53 (48.6)	*0.02*
Marital status, single	68 (20.0)	34 (31.2)	*0.02*
Clinical variables			
Current Smoker	87 (25.6)	34 (31.2)	0.25
Hypertension	162 (47.6)	68 (62.4)	*0.007*
Diabetes	46 (13.5)	24 (22.0)	*0.03*
Previous Myocardial Infarction	44 (12.9)	16 (14.7)	0.64
LAD as culprit artery	144 (42.4)	42 (38.5)	0.48

SD, Standard Deviation; LAD, Left Artery Descending. Missing values, none.

Table II. Clinical presentation

	Men n=340	Women n=109	p-values
Pain/pressure/discomfort in			
Chest/thorax	313 (92.1)	80 (73.4)	*<0.001*
Throat/neck	57 (16.8)	40 (36.7)	*<0.001*
Back	42 (12.4)	32 (29.4)	*<0.001*
Stomach	30 (8.8)	6 (5.5)	0.27
Shoulders	53 (15.6)	36 (33.0)	*<0.001*
Arms/hands	183 (53.8)	71 (65.1)	*0.04*
Associated symptoms			
Tiredness/fatigue	102 (30.0)	45 (41.3)	*0.03*
Nausea/vomiting	94 (27.6)	53 (48.6)	*<0.001*
Cold sweat	197 (57.9)	70 (64.2)	0.25
Fear	57 (16.8)	34 (31.2)	*0.001*
Symptom intensity			
Pain intensity, NRS, median (IQR)	7 (6,8)	7 (6,8)	0.65

NRS, Numeric Rating Scale; IQR, Interquartile range. Missing values; 3 (<1%) patients did not grade any pain/discomfort on the NRS scale. No missing values regarding other variables.

Table III. Thoughts, actions and context when falling ill into STEMI

	Men n=340	Women n=109	p-values
With whom did your first talk about your symptoms?			
My wife/husband/partner	202 (60.3)	60 (55.6)	0.38
A relative or friend	31 (9.3)	3 (2.8)	*0.03*
My children	23 (6.9)	18 (16.7)	*0.002*
The Swedish Healthcare Direct	11 (3.3)	7 (6.5)	0.14
The Emergency Medical Service	20 (6.0)	4 (3.7)	0.36
The Primary Healthcare Centre	15 (4.5)	5 (4.6)	0.95
Someone else	30 (9.0)	11 (10.2)	0.70
Did you call any of the following before you went to the hospital?			
The Primary Healthcare Centre	66 (19.8)	17 (15.6)	0.33
The Swedish Healthcare Direct	81 (24.3)	33.9 (37)	*0.05*
Did you take any medication un order to relieve the symptoms?			
Painkillers	50 (14.7)	29 (26.6)	*0.005*
Nitro-glycerine	44 (12.9)	20 (18.3)	0.16
Have you heard of angioplasty or clot-dissolving treatment in case of myocardial infarction?			
Yes, I have	319 (94.1)	99 (93.4)	0.79
Why did you decide to go to the hospital			
The symptoms were severe	108 (33.9)	36 (34.3)	0.94
I thought I had a myocardial infarction	79 (24.8)	16 (15.2)	*0.04*
I was told to seek care by my wife/husband/partner	38 (11.9)	14 (13.3)	0.70
Another reason for going to the hospital	22 (6.9)	12 (11.4)	0.14
Did you hesitate to go to the hospital? If yes, why?			
I did not hesitate	249 (73.5)	74 (67.9)	0.26
I though the symptoms would disappear	85 (25.1)	31 (28.4)	0.49
I did not thought it was anything serious	27 (8.9)	8 (7.3)	0.83
I did not want to make my family worried	17 (5.0)	5 (4.6)	0.86
I did want to wake attention	4 (1.2)	2 (1.8)	0.61
I did not want to disturb	10 (2.9)	3 (2.8)	0.92
I felt a discomfort in the face of being hospitalised	11 (3.2)	5 (4.6)	0.51
Context when falling ill			
At home	253 (74.4)	90 (82.6)	0.08
I was alone	91 (26.8)	29 (26.6)	0.97
Weekend	95 (29.3)	34 (31.8)	0.49
Weekdays, out of office time	118 (35.4)	38 (35.8)	0.94
Transport mode			

I went by ambulance to the hospital	280 (82.4)	91 (83.5)	0.79
Missing values; 25 (5.6%) patients did not answer the question about why hesitating going to the hospital. *No or minor missing regarding all other variables.*			

Table IV. Reactions from bystanders when falling ill.

	Men n=340	Women n=109	p-values
He/she/they suggested that I should rest	47 (14.0)	13 (12.0)	0.61
He/she/they suggested medication	11 (3.3)	7 (6.5)	0.14
He/she/they suggested that I should call EMS	126 (37.5)	24 (22.2)	*0.003*
He/she/they suggested that I should call SHD	85 (25.3)	85 (78.7)	0.40
He/she/they called EMS	175 (52.1)	55 (51.4)	0.90
He/she/they called SHD	85 (25.3)	39 (36.1)	*0.03*
He/she/they brought me to the hospital	63 (18.8)	23 (21.3)	0.56
I did not tell anyone	8 (2.4)	8 (7.4)	*0.02*

EMS, Emergency Medical Services; SHD, Swedish Health Care Direct. Missing values; 5 (1.1%) patients did not answer question about reaction from bystanders.

Table V. Predictions of patient delay times in men and women separately

	Men n=340			**Women n=109**		
	Standardized Beta	**p-value**	**R^2 change**	**Standardized Beta**	**p-value**	**R^2 change**
Block 1. Background characteristics			**0.04**			**0.13**
Age	0.12	*0.05*		0.07	0.54	
Current smoker	0.14	*0.01*		0.19	*0.05*	
Block 2. Symptoms			**0.10**			**0.23**
Chest pain	0.15	*0.01*		0.05	0.55	
Pain in back/shoulders	-0.03	0.60		0.25	*0.01*	
Stomach pain	0.09	0.07		0.30	*0.00*	
Cold sweat	-0.07	0.19		-0.18	*0.04*	
Anguish/fear	-0.13	*0.01*		-0.08	0.38	
Block 3. Context when falling ill			**0.02**			**0.08**
At home	-0.11	*0.03*		-0.04	0.62	
Out of office time	0.06	0.27		0.18	*0.03*	
Block 4. Reactions from bystanders			**0.08**			**0.12**
They suggested rest	-0.13	*0.02*		0.10	0.28	
They suggested calling EMS	-0.04	0.41		-0.22	*0.02*	
They called EMS	-0.28	*0.00*		-0.23	*0.01*	
They drove me to the hospital	0.02	0.75		-0.14	0.12	
Block 5. Thoughts and actions			**0.09**			**0.13**
I took some medication to relieve the symptoms	0.12	*0.03*		0.06	0.47	
I hesitated going to the hospital	-0.11	0.26		0.62	*0.00*	
I thought the symptoms should go away/it was not anything serious	0.25	*0.01*		-0.31	0.06	
I did not want to make my relatives worried	0.09	0.11		-0.17	*0.05*	
I was afraid of the reaction from the hospital staff	0.05	0.34		0.20	*0.04*	

Multiple linear regression with log-transformed pre-hospital delay time in minutes as the dependent variable. Independent variables entered in five blocks, significant predictors in the multivariable analyses shown in table. R^2 for the complete model 0.53 in women, 0.26 in men. EMS, emergency medical service.

Figure legends

Figure 1. First medical contact in men and women with STEMI

Figure 2. Delay times from symptom onset until first medical contact

Figure 3. Delay times from first medical contact until diagnosis

Figure 4. Delay times from symptom onset until diagnosis

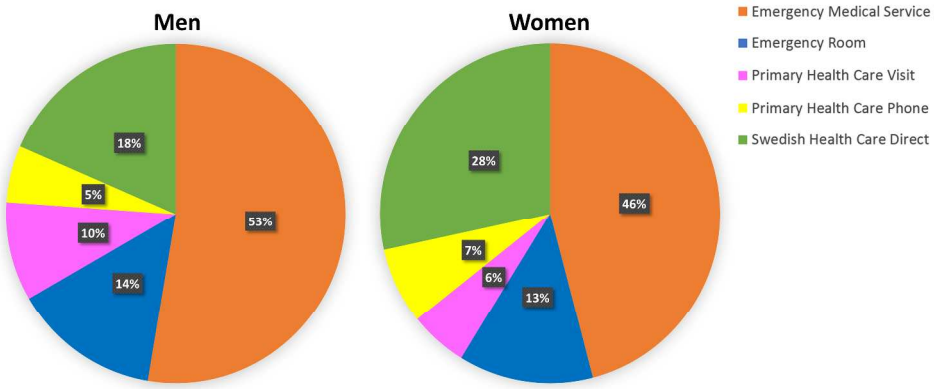

Figure 1. First medical contact in men and women with STEMI

338x190mm (300 x 300 DPI)

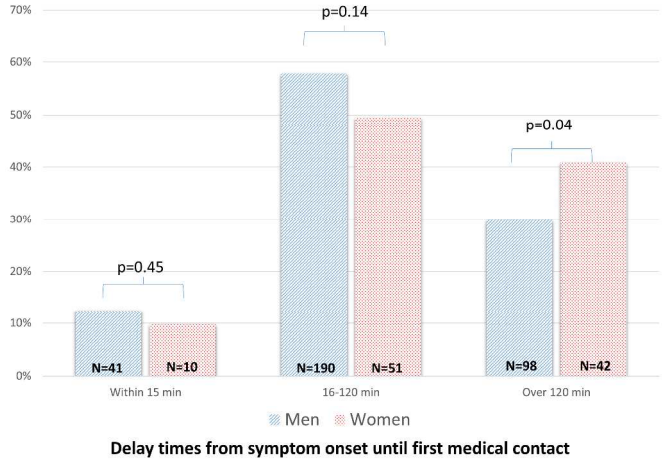

Figure 2. Delay times from symptom onset until first medical contact

338x190mm (300 x 300 DPI)

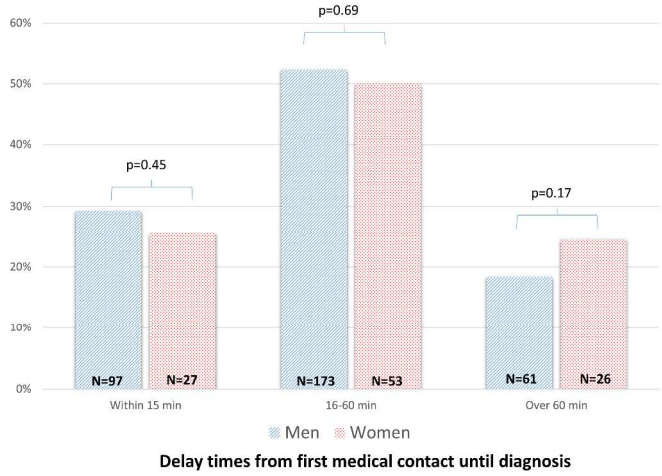

Figure 3. Delay times from first medical contact until diagnosis

338x190mm (300 x 300 DPI)

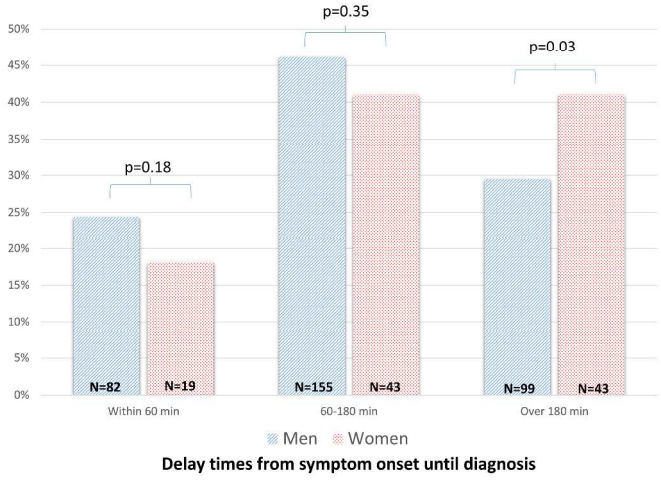

Figure 4. Delay times from symptom onset until diagnosis

338x190mm (300 x 300 DPI)

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract **Indicated in the title (page 1), in the abstract (page 2) and in the method section (page 4-5)**
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found **Done (page 2)**
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported **Done (page 3-4)**
Objectives	3	State specific objectives, including any prespecified hypotheses **Objectives specified in the introduction section (aim of the study, page 4)**
Methods		
Study design	4	Present key elements of study design early in the paper **Presented in title (page 1), abstract (page 2) and method section (page 4-5)**
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection **Summarised in the method section (page 4-5) as all details are given in a previous publication that we refer to (ref 21, page 14)**
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants **Done, in the method section (page 4-5)**
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable **Done, in the method and statistical sections (page 4-6)**
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group **Done, in the method section (page 4-5). Details of the questionnaire given in a previous publication that we refer to (ref 21, page 14)**
Bias	9	Describe any efforts to address potential sources of bias **Done, in the method section (page 4-5). We have made an effort to include eligible STEMI patients on a consecutive basis within 24 hours after admittance, reducing the risk of selection and recall bias**
Study size	10	Explain how the study size was arrived at **No power calculation was done as this is a descriptive observational study (page 4-5). We planned for one year inclusion and that we then should include approximately 500 STEMI patients which would be enough to do the gender (and other) comparisons we planned for**
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why **Explained in the statistical section (page 5-6)**
Statistical methods	12	Describe all statistical methods, including those used to control for confounding **Multivariable linear regression analyses performed – not to control for confounding, but to find variables associated to delay in women and in men, separately. Explained in the statistical section (page 5-6)**
		(*b*) Describe any methods used to examine subgroups and interactions **NA**
		(*c*) Explain how missing data were addressed **We had very little missing data, specified in the statistical section (page 5-6)**

		(*d*) If applicable, describe analytical methods taking account of sampling strategy **NA**
		(*e*) Describe any sensitivity analyses **NA**
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed **SymTime was supposed to consecutively include eligible STEMI-patients at five hospitals with cath lab facilities (method section, page 4-5). The patients could not be included the first hours because of the acute nature of this disease. Thus they had to stay a while at the participating hospital in order to be able to be included. Patients were then included within 24 h, most often at day 2. The total study population consisted of 532 STEMI patients comprising 36% of all STEMI patients that ever touched down (including those only coming to cath lab and then leaving the including hospital very fast) at the five hospitals during the study period (n=1473) according to the Swedish quality register SWEDEHEART. The first couple of months FMC was not registered. Thus the present study consists of the 449 STEMI patients included after the start of FMC registering.**
		(b) Give reasons for non-participation at each stage **Inclusion and exclusion criteria presented in the method section (page 4-5).**
		(c) Consider use of a flow diagram **Considered, but not deemed necessary. Data given in text.**
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders **Presented in Table 1 and in the result section (page 6)**
		(b) Indicate number of participants with missing data for each variable of interest **There was very little missing data in the current study, specified in the statistical section (page 5-6)**
Outcome data	15*	Report numbers of outcome events or summary measures **No outcome events were measured**
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included **Absolut numbers, percentages, multivariable adjusted linear regression analyses for the main measurements are presented in the result section (page 6-8). Selection of variables in the multivariable analyses and how these were chosen is described in the statistics section (page 5-6).**
		(*b*) Report category boundaries when continuous variables were categorized **NA**
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period **NA**
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses **NA**
Discussion		
Key results	18	Summarise key results with reference to study objectives **Summarised in the discussion section (page 7-8)**

Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias **Summarised in the strength and limitation section (page 3)**
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence **Done in the discussion (page 8-10) and in the conclusion (page 11)**
Generalisability	21	Discuss the generalisability (external validity) of the study results **Done in the strength and limitation section (page 3)**
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based **Done in the funding section (page 11)**

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Gender disparities in first medical contact and delay in ST-elevation myocardial infarction - a prospective multicentre survey study

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Date Submitted by the Author:	30-Jan-2018
Complete List of Authors:	Sederholm Lawesson, Sofia; Department of Cardiology and Department of Medical and Health Sciences, Linköping University; Isaksson, Rose-Marie; Department of Research, Norrbotten County Council, Luleå, Sweden, and Department of Medical and Health Sciences, Linköping University, Eriksson, Maria; Department of Cardiology and Department of Medical and Health Sciences, Linköping University Hellström Ängerud, Karin; Cardiology, Heart Centre and Department of Nursing, Umeå University, Umeå, Sweden, Thylén, Ingela; Department of Cardiology and Department of Medical and Health Sciences, Linköping University
Primary Subject Heading:	Cardiovascular medicine
Secondary Subject Heading:	Cardiovascular medicine, Epidemiology
Keywords:	Adult cardiology < CARDIOLOGY, Coronary heart disease < CARDIOLOGY, Myocardial infarction < CARDIOLOGY, Ischaemic heart disease < CARDIOLOGY

Gender disparities in first medical contact and delay in ST-elevation myocardial infarction - a prospective multicentre survey study

Sofia Sederholm Lawesson[1], Rose-Marie Isaksson[2], Maria Ericsson[3], Karin Hellström Ängerud[3], and Ingela Thylén[1] on behalf of the SymTime study group

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Keywords: ST-elevation myocardial infarction, gender, first medical contact, pre-hospital delay time

Abstract

Introduction

Timely reperfusion therapy is critical in ST-elevation myocardial infarction [STEMI]. Disconcertingly, pre-hospital delay times have hardly changed over the decades and especially women seem to delay. Prospective studies are needed to better understand the relation between gender and care-seeking in STEMI.

Objective

We aimed to compare gender disparities in STEMI regarding 1) choice of first medical contact [FMC], 2) delay from symptom-onset-to-FMC and to-diagnostic ECG, and 3) factors associated with symptom-onset-to-FMC in men and women.

Method

SymTime was a cross-sectional survey study based on self-reported data using a validated questionnaire. Patients were enrolled from five Swedish hospitals with catheterisation facilities 24/7 Nov 2012 to Jan 2014. Eligible patients were included within 24 hours after admittance.

Results

Among 449 patients, women more often called an advisement nurse as FMC (28 vs 18%, p=0.02). They had longer delay until FMC, 90 (interquartile range [IQR] 39-221) vs. 66 (28-161) min, p=0.04, and until ECG, 146 (68-316) vs. 103 (61-221) min, p=0.03. Men went to hospital because of believing they were stricken by MI to a higher extent than did women (25 vs 15%, p=0.04), and were more often recommended to call Emergency Medical Services [EMS] by bystanders (38 vs 22%, p<0.01). Hesitating going to hospital and experiencing pain in the stomach/back/shoulders were factors associated with long delay in women. Believing the symptoms should disappear or interpreting them as nothing serious were corresponding factors in men. In both genders bystanders acting to contact EMS was explaining shorter pre-hospital delay.

Conclusion

In STEMI women differed from men in FMC and they had longer delays. This was partly due to atypical symptoms and a longer decision time. Bystanders acted more promptly when men

than when women fell ill. The public knowledge of MI symptoms, and how to properly act, seems still not sufficient.

Article summary

Strength and limitations of this study

- The present study is to the best of our knowledge the first published study of gender disparities and first medical contact [FMC] in STEMI, using self-reported data covering not only symptoms, multiple time point measurements and actions, but also self-reported reasons for delay and interpretation of symptoms as explaining factors for pre-hospital delay.
- With the use of wide inclusion criteria approximately 1/10 of the hospitalised Swedish STEMI patients during the inclusion period filled in the questionnaire within 24 hours of admittance making the results generalizable and with limited risk of recall bias.
- With the observational study design, we can only report associations rather than causations, and there may be factors associated with pre-hospital delay times not covered by the questionnaire, such as health literacy and deeper knowledge about MI.
- Patients not being pain free and hemodynamically stable were excluded from participation, but we do not have any demographic data on this cohort making it impossible to compare those participating in the study with those being excluded.
- We have not collected data on all traditional risk factor variables history of hypercholesterolemia and heredity), which can be seen as a limitation.

INTRODUCTION

Myocardial infarction [MI] mortality has decreased substantially the last decades in the western world, because of more active prevention and better treatment.(1) Still, outcomes in ST-elevation MI [STEMI] differ between the genders, with approximately twice as high in-hospital mortality in women,(2, 3) who receive reperfusion therapy less often than men.(2, 4) In STEMI timely administration of reperfusion therapy is critical for improving survival.(5, 6) During the last decades focus has mainly been on shortening system delay times where a clear association between longer delay and worse prognosis has been found.(5)

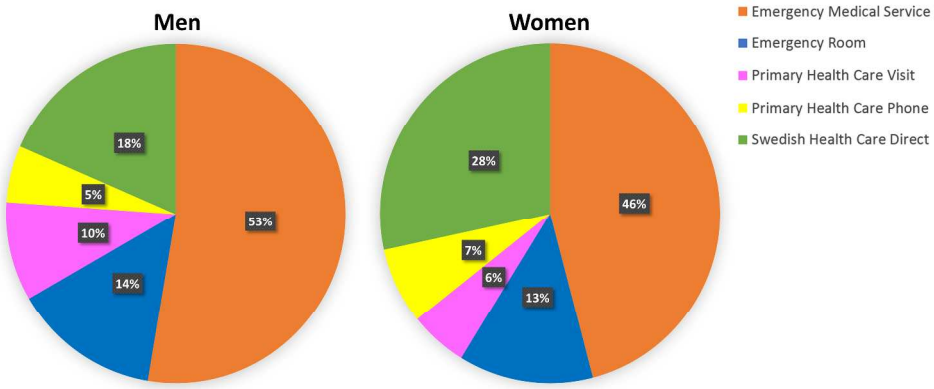

Figure 1. First medical contact in men and women with STEMI

338x190mm (300 x 300 DPI)

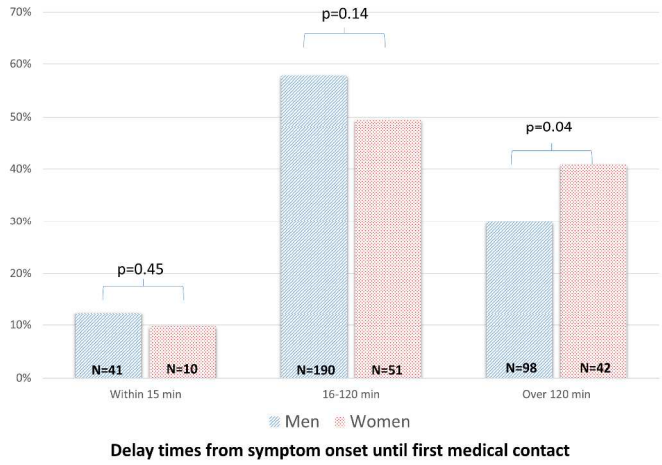

Figure 2. Delay times from symptom onset until first medical contact

338x190mm (300 x 300 DPI)

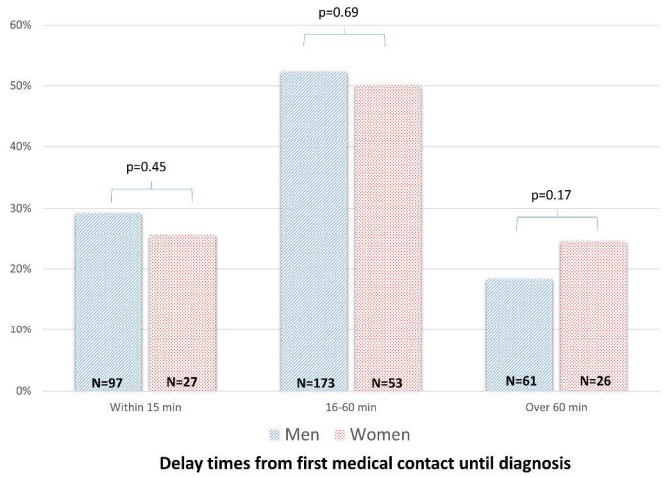

Figure 3. Delay times from first medical contact until diagnosis

338x190mm (300 x 300 DPI)

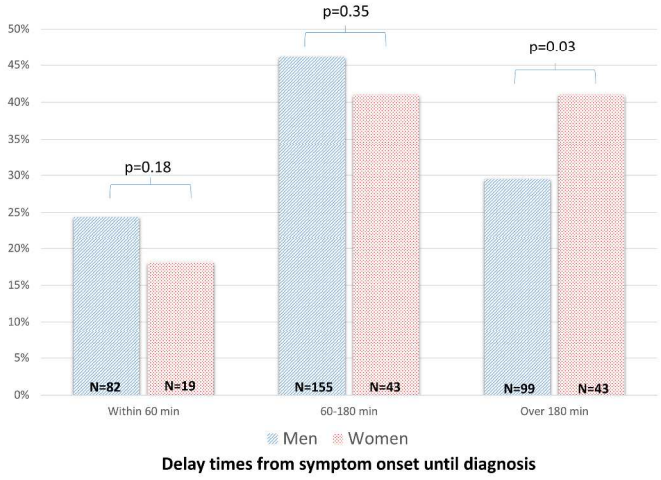

Figure 4. Delay times from symptom onset until diagnosis

338x190mm (300 x 300 DPI)

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract **Indicated in the title (page 1), in the abstract (page 2) and in the method section (page 4-5)**
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found **Done (page 2)**
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported **Done (page 3-4)**
Objectives	3	State specific objectives, including any prespecified hypotheses **Objectives specified in the introduction section (aim of the study, page 4)**
Methods		
Study design	4	Present key elements of study design early in the paper **Presented in title (page 1), abstract (page 2) and method section (page 4-5)**
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection **Summarised in the method section (page 4-5) as all details are given in a previous publication that we refer to (ref 21, page 14)**
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants **Done, in the method section (page 4-5)**
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable **Done, in the method and statistical sections (page 4-6)**
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group **Done, in the method section (page 4-5). Details of the questionnaire given in a previous publication that we refer to (ref 21, page 14)**
Bias	9	Describe any efforts to address potential sources of bias **Done, in the method section (page 4-5). We have made an effort to include eligible STEMI patients on a consecutive basis within 24 hours after admittance, reducing the risk of selection and recall bias**
Study size	10	Explain how the study size was arrived at **No power calculation was done as this is a descriptive observational study (page 4-5). We planned for one year inclusion and that we then should include approximately 500 STEMI patients which would be enough to do the gender (and other) comparisons we planned for**
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why **Explained in the statistical section (page 5-6)**
Statistical methods	12	Describe all statistical methods, including those used to control for confounding **Multivariable linear regression analyses performed – not to control for confounding, but to find variables associated to delay in women and in men, separately. Explained in the statistical section (page 5-6)**
		(*b*) Describe any methods used to examine subgroups and interactions **NA**
		(*c*) Explain how missing data were addressed **We had very little missing data, specified in the statistical section (page 5-6)**

		(*d*) If applicable, describe analytical methods taking account of sampling strategy **NA**
		(*e*) Describe any sensitivity analyses **NA**
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed **SymTime was supposed to consecutively include eligible STEMI-patients at five hospitals with cath lab facilities (method section, page 4-5). The patients could not be included the first hours because of the acute nature of this disease. Thus they had to stay a while at the participating hospital in order to be able to be included. Patients were then included within 24 h, most often at day 2. The total study population consisted of 532 STEMI patients comprising 36% of all STEMI patients that ever touched down (including those only coming to cath lab and then leaving the including hospital very fast) at the five hospitals during the study period (n=1473) according to the Swedish quality register SWEDEHEART. The first couple of months FMC was not registered. Thus the present study consists of the 449 STEMI patients included after the start of FMC registering.**
		(b) Give reasons for non-participation at each stage **Inclusion and exclusion criteria presented in the method section (page 4-5).**
		(c) Consider use of a flow diagram **Considered, but not deemed necessary. Data given in text.**
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders **Presented in Table 1 and in the result section (page 6)**
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Outcome data	15*	Report numbers of outcome events or summary measures **No outcome events were measured**
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included **Absolut numbers, percentages, multivariable adjusted linear regression analyses for the main measurements are presented in the result section (page 6-8). Selection of variables in the multivariable analyses and how these were chosen is described in the statistics section (page 5-6).**
		(*b*) Report category boundaries when continuous variables were categorized **NA**
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Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses **NA**
Discussion		
Key results	18	Summarise key results with reference to study objectives **Summarised in the discussion section (page 7-8)**

Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias **Summarised in the strength and limitation section (page 3)**
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence **Done in the discussion (page 8-10) and in the conclusion (page 11)**
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Gender disparities in first medical contact and delay in ST-elevation myocardial infarction - a prospective multicentre Swedish survey study

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Primary Subject Heading:	Cardiovascular medicine
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Keywords:	Adult cardiology < CARDIOLOGY, Coronary heart disease < CARDIOLOGY, Myocardial infarction < CARDIOLOGY, Ischaemic heart disease < CARDIOLOGY

Gender disparities in first medical contact and delay in ST-elevation myocardial infarction - a prospective multicentre Swedish survey study

Sofia Sederholm Lawesson[1], Rose-Marie Isaksson[2], Maria Ericsson[3], Karin Hellström Ängerud[3], and Ingela Thylén[1] on behalf of the SymTime study group

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Word count: (excluding title page, abstract, references, figures and tables) 3615

Keywords: ST-elevation myocardial infarction, gender, first medical contact, pre-hospital delay times

Abstract

Objectives: Compare gender disparities in ST-elevation myocardial infarction [STEMI] regarding first medical contact [FMC] and pre-hospital delay times and explore factors associated with pre-hospital delay in men and women separately.

Design: Cross-sectional study based on medical records and a validated questionnaire. Eligible patients were enrolled within 24 hours after admittance to hospital.

Setting: Patients were included Nov 2012-Jan 2014 from five Swedish hospitals with catheterisation facilities 24/7.

Participants: 340 males and 109 females aged between 31-95 years completed the survey.

Main outcome measures: FMC were divided into five possible contacts: Primary Healthcare Centre [PHC] by phone or directly, national advisory nurse by phone, Emergency Medical Services [EMS] and Emergency Room directly. Two parts of pre-hospital delay times were studied: time-from-symptom-onset-to-FMC and time-from-symptom-onset-to-diagnostic ECG.

Results: Women more often called an advisory nurse as FMC (28 vs 18%, p=0.02). They had a longer delay until FMC, 90 (interquartile range [IQR] 39-221) vs. 66 (28-161) min, p=0.04, and until ECG, 146 (68-316) vs. 103 (61-221) min, p=0.03. Men went to hospital because of believing they were stricken by an MI to a higher extent than women did (25 vs. 15%, p=0.04) and were more often recommended to call EMS by bystanders (38 vs. 22%, p<0.01). Hesitating about going to hospital and experiencing pain in the stomach/back/shoulders were factors associated with longer delays in women. Believing the symptoms would disappear or interpreting them as nothing serious were corresponding factors in men. In both genders bystanders acting by contacting EMS explained shorter pre-hospital delays.

Conclusions: In STEMI, women differed from men in FMC and they had longer delays. This was partly due to atypical symptoms and a longer decision time. Bystanders acted more promptly when men than when women fell ill. Public knowledge of MI symptoms, and how to-act properly, still seems insufficient.

Article summary

Strength and limitations of this study

- The present study is to the best of our knowledge the first published study of gender disparities and first medical contact [FMC] in ST-elevation myocardial infarction [STEMI], using self-reported data covering not only symptoms, multiple time point measurements and actions, but also self-reported reasons for delay and interpretation of symptoms as explanatory factors for pre-hospital delay.
- With the use of wide inclusion criteria approximately 1/10 of the hospitalised Swedish STEMI patients during the inclusion period filled in the questionnaire within 24 hours of admittance, making the results generalizable and with limited risk of recall bias.
- Regarding the observational study design, we can only report associations rather than causations and there may be factors associated with pre-hospital delay times not covered by the questionnaire, such as health literacy and deeper knowledge about MI.
- Patients not being pain free and hemodynamically stable were excluded from participation, but we do not have any demographic data on this cohort making it impossible to compare those participating in the study with those excluded.
- We have not collected data on all traditional risk factor variables (such as history of hypercholesterolemia), which can be seen as a limitation.

INTRODUCTION

Myocardial infarction [MI] mortality has decreased substantially during the last decades in the western world, because of more active prevention and better treatment.(1) Still, outcomes in ST-elevation MI [STEMI] differ between the genders, with approximately twice as high in-hospital mortality in women,(2, 3) who receive reperfusion therapy less often than men.(2, 4) In STEMI timely administration of reperfusion therapy is critical for improving survival.(5, 6) During the last decades focus has mainly been on shortening system delay times where a clear association between longer delay and worse prognosis has been found.(5) Consequently, STEMI guidelines strongly recommend that the diagnosis is made already in the pre-hospital setting.(7) In Sweden, an ECG is taken by the Emergency Medical Services

[EMS] paramedics in patients with symptoms indicating an evolving MI. The ECG is then transferred to the nearest hospital where the cardiologist/internist on call judges if the patient has a probable STEMI or not. Thus, in patients calling EMS, the diagnosis of STEMI can be made well in advance before admission to hospital and the patient can be directed straight to the cath lab or could be given pre-hospital fibrinolytics.(8)

Less focus has been on the patient delay in the pre-hospital phase, which has been proven difficult to influence.(9, 10) The pre-hospital delay times have been unchanged over the past decades (11-13) but it is unknown whether the delay is due to difficulty with symptom recognition, symptom interpretation, or decisions related to care seeking (including the mode of transportation to the hospital). In order to distinguish patient delay from system delay times it has been suggested to also include the time point of first medical contact [FMC] in the analysis of pre-hospital delay times.(14) However, previous studies have mostly focused on *total* pre-hospital delay times.(11, 12, 15) Since STEMI patients do not always call EMS as their FMC, studying the different phases of pre-hospital delay times as well as choice of FMC is imperative. Female gender has been found to be associated with pre-hospital delay times according to several studies,(12, 16-19) but measurements have been inconsistent(20) and data on gender disparities on FMC in STEMI are very sparse. Consequently, further studies are needed to better understand the relation between gender and care-seeking behaviour in a STEMI population.

Aim of the study

We aimed to compare gender disparities in STEMI regarding: 1) first FMC, 2) pre-hospital delay times from symptom-onset-to-FMC as well as from symptom-onset-to-diagnostic ECG and 3) factors associated with symptom-onset-to-FMC in men and women separately.

METHOD

This Swedish multicentre study (SymTime) has been previously described.(21) In short, it has a descriptive and comparative cross-sectional design of self-reported data. A previously validated self-administered questionnaire developed and tested in a Swedish chest pain population was used,(22) with some minor changes and clarifications. The questionnaire covers 35 items including: (1) baseline characteristics, (2) symptoms, (3) course of events including multiple time point measurements and (4) description of transport mode. We

enrolled participants from five Swedish hospitals with diverged geographic locations, all with catheterisation facilities and primary percutaneous coronary intervention [PCI] enabled 24/7. Data were collected in the cardiac care unit [CCU] in each participating hospital from November 2012 to January 2014. Eligible patients were planned to be consecutively included within 24 hours after admittance and were invited to answer the questionnaire after the primary PCI/reperfusion therapy had been given. Inclusion criteria were: (1) a confirmed STEMI diagnosis, (2) ability to fill in the questionnaire and, (3) willingness to participate. Patients were pain free and hemodynamically stable when they were asked to participate and fill in the questionnaire. The staff nurse simultaneously obtained clinical data such as information on diagnosis, FMC, important time point measurements (e.g., ECG and FMC) and comorbidities from the patients as well as from the medical records.

In this study, two parts of pre-hospital delay times were studied: 1) the interval between time of symptom-onset-to-FMC and 2) the interval from symptom-onset-to-diagnostic ECG. FMC was defined as the time point when contacting any healthcare personnel either by phone or in person and was divided into five possible contacts: 1) the Primary Healthcare Centre [PHC] by phone, 2) the PHC directly, 3) the Swedish Healthcare Direct [SHD] by phone (i.e., advisory nurses), 4) the EMS by phone or 5) the Emergency Room [ER] directly. All patients chose any of these five ways of contacting the Swedish healthcare system.

Ethical aspects

Permission for the study was obtained from the regional Ethical Review Board, Linköping, Sweden (D-nr 2012/201–31) and complied with the Declaration of Helsinki.(23) Informed consent was obtained from all included patients.

Patient and Public Involvement

We originally involved patients in the development and the revision of the questionnaire used in this study when testing the user-friendliness and content in the modified questionnaire. We also collaborated with a patient representative from the national Heart & Lung foundation when planning the design of SymTime. The knowledge gain from this project will be disseminated to the public at different meeting and seminars at local patient organisations in Sweden. Participants interesting in the results have been advised to contact the study coordinator for information.

Statistical analysis

We used frequencies and proportions to describe the history of patients' characteristics, the sociodemographic, clinical and contextual variables and their FMC. Categorical variables were reported by numbers and percentages and groups were compared with the use of the Chi-Square test. Continuous variables were reported as means ± standard deviations [SD] or as medians with interquartile ranges [IQR], and gender comparisons were made with the two-tailed Student T-test or the Mann Whitney U-test depending on if the variable was normally distributed or not. Multiple linear regression analyses were performed in men and women separately in order to sort out relevant predictors of patient delay. The time variable had to be log-transformed in order to be normally distributed. Background characteristics, clinical presentation, context when falling ill, thoughts and actions as well as reactions from bystanders were included in five blocks in order to analyse the relevance of each block in terms of R^2 change. Residual plots were run, and no violations of assumptions were noted. Included variables were chosen through literature research and/or deemed to be important by the research group. There were few missing values in the data collection - regarding the most important outcome measurements there were no (symptoms) or minor (FMC, 0.9% and delay from symptom onset until FMC, 3.8%) missing values. All tests were two-tailed and a p-value of less than 0.05 was deemed as indicating a statistically significant difference between compared groups. All statistical analyses were performed using IBM SPSS Statistics V23.0 (SPSS Inc, Chicago, Illinois, USA) for Windows.

RESULTS

Background characteristics and clinical presentation

In total, 449 STEMI patients were included. Women were five years older than men, with lower educational status and more often living on their own. Women had a higher prevalence of hypertension as well as diabetes mellitus. (Table I) Among chief complaints, chest pain/discomfort was prevalent in 92% of men compared to 73% of women p<0.001. Pain in the throat/neck, back and/or shoulder was twice as common in women as in men, as well as a feeling of fear. Nausea was prevalent in half of the women compared to one third of the men. There was no gender difference in pain intensity. (Table II)

Thoughts, actions and context when falling ill

When falling ill in STEMI women were more often together with their children, relatives or friends, whereas men were more often together with colleagues. There was no gender difference in being alone or being at home at the time. Self-medication with aspirin was as common in both genders as well as nitro-glycerine, whereas women took pain-killers almost twice as often as men (27 vs 15%, p<0.01). The first person to talk to about the symptoms was the partner, which was the case in more than half of both men and women. Women more often than men informed their children first of all about their symptoms, whereas men more often than women first talked to friends or relatives. More than one third of the women compared to one fourth of the men spoke to the SHD before they went to the hospital (28 vs. 18%, p=0.02) and less than 1/5 of both men and women talked to their PHC, with no difference between the genders. To a great extent both genders had heard of angioplasty or clot-dissolving as treatment for MI.

The most common reason why STEMI patients went to the hospital was severe symptoms, with no difference between the genders. Men went to hospital because of believing they were struck by an MI to a higher extent compared to women (25 vs 15%, p=0.04). There was neither any gender difference in hesitating going to the hospital, nor in reasons why hesitating. The most common reason for why hesitating was a belief the symptoms would disappear, with no difference between the genders. (Table III)

Reactions from bystanders

Men were more often recommended to call 112 by bystanders (38 vs. 22%, p<0.01). Women more often had bystanders calling SHD (36 vs 25%, p=0.03), but also more often did not tell anyone about their symptoms (7 vs 2%, p=0.02). (Table IV)

Delay times and first medical contact

In the total study population, the median patient delay from symptom-onset-to-FMC was 70 min (IQR 30-178) and to diagnostic ECG 110 min (IQR 64-238). The system delay from FMC to diagnostic ECG was 27 min (IQR 15-50). Women waited in median 90 min (IQR 39-221) before taking their FMC compared to 66 min (IQR 28-161) in men, p=0.04. EMS was the most common FMC used by approximately half of the patients regardless of sex, but

women more often contacted SHD as FMC compared to men, 28 vs 18% (p=0.02). (Figure 1) After being urged to contact the EMS by the general practitioner [GP] or the advisory nurse at the SHD, 83% of patients finally arrived at the hospital by ambulance while the remainder transported themselves directly to the ER. System delay time in form of FMC to diagnostic ECG did not differ between the genders, (25 [15-49] min in men vs. 33 [15-61] min in women, p=0.09). Altogether, women had a longer delay from symptom-onset-to-diagnostic ECG (146 [68-316] min in women, vs. 103 [61-221] min in men p=0.03). Divided in subgroups on short, medium and long delay, women more often had a long delay compared to men, both from symptom-onset-to-FMC, and from symptom-onset-to-diagnostic ECG. (Figure 2-4)

Factors associated with delay in men and women

In women, sociodemographic, contextual, cognitive, behavioural and clinical factors included in the survey explained 53% of the variance of pre-hospital delay times from symptom-onset-to-FMC compared to 26% in men (i.e., the R^2 for the complete model, men and women studied separately). In both genders the clinical presentation explained most of the delay from symptom-onset-to-FMC, followed by thoughts and actions when falling ill. In women hesitating to go to the hospital, stomach pain and pain in the back/shoulders were the variables most strongly associated with increased delay, while cold sweat and bystanders calling - or recommending calling - EMS were the variables most strongly associated with short delay. In men, believing the symptoms would disappear or interpreting the symptoms as nothing serious had the strongest association with increased delay, whereas bystanders calling EMS was the variable most strongly associated with reduced delay. (Table V)

DISCUSSION

The main findings of the present study are the far longer delay times in women vs. men among Swedish STEMI patients, from symptom-onset-to-FMC of 26 min and from symptom-onset-to-diagnostic ECG of 43 min. This was due to primarily three factors: 1) more atypical symptoms in women and 2) a longer decision time in women and 3) a gender difference in choice of FMC, where women more often than men called the national SHD service number for advice.

Pre-hospital delay times account for the largest proportion of the total ischemic time(9) but have remained virtually unchanged over the last decades.(12) This is important since only STEMI patients with a short pre-hospital delay (< 90 min) have a long term benefit of shorter system delay to reperfusion.(24) Although interventions aimed at shortening pre-hospital delay times have been discouraging,(9, 10) a more recent report from Denmark on STEMI patients calling EMS services have found a temporal trend of decrease in pre-hospital delay times (symptom-onset-to-calling EMS) from 101 to 85 min between year 2003 to 2009. This was after introduction of primary PCI to all STEMI patients, which the authors claim could have had potentially positive effects on public awareness.(25) Still, further efforts are needed in order to increase public awareness and in the recent scientific statements from the American Heart Association, the authors emphasise improved methods to disseminate information about women's risks, symptoms, and behaviours and necessary responses to symptoms of acute MI.(19)

Few studies have focused on delays to FMC in STEMI. The majority of previous studies have defined pre-hospital delay time as the time interval from symptom-onset-to-hospital arrival, without separating the patient from the system delay, i.e., before and after FMC.(11, 12, 15, 26, 27) However, in a recent registry based study, Bugiardini et al.(28) report time lapses from symptom-onset-to-calls-to-EMS or a GP's office and found no significant time differences among men and women (50 min vs. 60 min) while we did find a significant delay between genders (66 min delay in men vs. 90 min in women). Still, the time lapses are not completely comparable since our FMC, beyond calls to the EMS and the GP's office, also included in-office visits to the GP, a phone contact with an advisory nurse or a direct contact with the ER. Studies on gender disparities in pre-hospital delay times have shown inconsistent results and have limitations such as using restricted patient samples,(26) or relying primarily on information from medical records (26) or registries not specifically designed to study delay.(11, 26, 27) Finally, many studies have included mixed MI patients not restricting the inclusion to STEMI.(11, 22, 26) In the current study focusing on patient delay from symptom-onset-to-FMC and from symptom-onset-to-diagnosis of STEMI, women delayed 1.5 h until FMC compared to approximately 1 h in men. In the total study population, the median delay from symptom-onset-to-FMC of 70 min, and to diagnostic ECG of 110 min, is substantially better than reported in studies from other American and European countries (18, 28, 29) but still exceeding the recommendations advised by guidelines by several minutes.(30) A study based on the French eMUST registry, including STEMI patients

that have been taken care of by special mobile intensive care units, found in accordance with our data that women waited longer before calling the EMS. They also found a very similar delay until calling as we did to any FMC (78 min in women vs. 54 min in men, p<0.0001).(18) In the present study, more than 40% of the women compared to 30% of the men waited over 2 hours before seeking medical attention. Reducing patient-caused delay has a great potential to improve the outcomes of STEMI patients, given that many deaths occur early after symptom onset.

It is important to analyse care-seeking behaviour in different regions of the world, as differences in medical insurance and healthcare systems do play a part as well as cultural factors and gender equality reflecting differences in awareness, interpretation and actions upon MI symptoms. In Sweden, counted as one of the most gender equal countries in the world, with complete healthcare coverage for all citizens, only small gender disparities were found in context, thoughts and actions when falling ill. Men more often first talked about their symptoms with a spouse, relative or friend whereas women more often talked with their child/children. This probably reflects the fact that women are older than men when falling ill with STEMI, and thus more often living on their own because of being widowed.(31) Older studies from other geographic regions have found that "not wanting to trouble anyone" is a factor associated with prolonged delay in women, but not in men.(32) In the present study no difference was found as regards worries of disturbing or drawing attention.

Women and men differed in FMC in the current study. EMS was the FMC in only half of the patients (53% of men and 46% of women) and instead as many as 1/3 of the women and 1/5 of the men called SHD as the FMC despite suffering from a very serious disease. In Sweden, SHD - a joint service number - was launched in 2003 and is staffed by advisory nurses 24/7 in order to answer questions, determine the need for further care and provide advice and/or contact with other healthcare providers. SHD has become a very important way of contacting the healthcare system and gets around 500 000 calls every month. The use of SHD in STEMI is worrying as we have shown in a previous study that patients turning to SHD as FMC had a 38 min longer delay from symptom onset until first ECG compared to patients calling EMS.(21) The reluctance to call EMS may be explained by several factors such as misinterpretation of symptoms, as well as women's lack of perceived potential risk for acute coronary syndrome [ACS].(33) The women in our study were less educated than the men and in the multivariable analysis this variable tended to be associated with longer pre-hospital

delay times in women (p=0.06). This could be attributed to low socioeconomic status and lack of ACS knowledge in women.(19) Anyhow, it is reassuring that although far too few patients, both men and women chose EMS as FMC, with 83% of patients finally arrived at the hospital by ambulance while the remainder transported themselves directly to the ER. We have previously shown that this was the case regardless of if the patient chose calling/visiting PHC, calling EMS or calling SHD as their FMC.(21)

A large gender disparity in chest pain prevalence - the most well recognized symptom of MI presentation in society - was found. The fact that women are less likely to experience chest pain has also been noted in two recent scientific statements from the American Heart Association (19, 31) and is in accordance with a previous large registry study in a mixed MI population.(34) At the same time less well known MI symptoms such as pain in the neck, throat, back or shoulders or nausea were more than twice as common in women as in men. Previous studies have found that MI symptoms looked upon as typical such as chest pain or pain in the left arm are most important for a correct attribution to the heart (35) and that the prognosis is worse in MI patients with atypical symptoms.(34) In accordance, men more often than women responded that believing that they had an MI was the reason for going to the hospital in the current study. The importance of the clinical presentation for patient delay was shown in the multivariable regression with the presence of symptoms such as pain in the back, shoulders or stomach being associated with longer delay in women but not in men. Symptoms that are perceived as threatening have been described associated with shorter pre-hospital delay times.(36) Accordingly, in the present study, cold sweat was associated with shorter delay in women and anguish/fear was associated with shorter delay in men.

Finally, bystanders can be crucial in obtaining appropriate care. In the present study bystanders calling EMS was one of the strongest factors associated with short delay although a gender difference in bystanders' responses to described symptoms depending on the patient's gender was found - whereas men more often had bystanders recommending contact with the EMS, women more often had bystanders calling SHD for advice. A previous study has found that relatives are more dissatisfied with the information given by the hospital staff compared to the patient.(37) This illustrates the need to involve the next of kin in secondary prevention education and care-seeking behaviour, as a well-informed bystander can help diminish the patients' decision time.

CONCLUSION

In conclusion, this study showed that women differ from men regarding several self-reported symptoms, thoughts, actions and pre-hospital delay times – and partly also in reasons as to why delaying. Based on our findings, women may have different educational needs compared to men, which has to be considered when educating the public about how to recognize and act when an evolving MI emerges.

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Contributorship statement

SSL and IT contributed to the study planning, design, preparation, validation of the slightly modified questionnaire and data analysis. KHÄ, ME and SSL contributed to the data collection. KHÄ, ME, RMI, SSL and IT contributed to the manuscript preparation and approved the final version of the manuscript.

Data sharing statement

No additional data available.

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Competing interests

None declared.

Ethics approval

The Regional Ethical Review Board, Linköping, Sweden (D-nr 2012/201-31, 2012/338-32).

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Table I. Baseline and clinical characteristics

	Men n=340	Women n=109	p-values
Socio-demographic variables			
Age, mean (SD)	64.5 (11.0)	69.8 (10.7)	*<0.001*
Education level, compulsory school	120 (35.3)	53 (48.6)	*0.02*
Marital status, single	68 (20.0)	34 (31.2)	*0.02*
Clinical variables			
Current Smoker	87 (25.6)	34 (31.2)	0.25
Hypertension	162 (47.6)	68 (62.4)	*0.007*
Diabetes	46 (13.5)	24 (22.0)	*0.03*
Previous Myocardial Infarction	44 (12.9)	16 (14.7)	0.64
LAD as culprit artery	144 (42.4)	42 (38.5)	0.48

SD, Standard Deviation; LAD, Left Artery Descending. Missing values, none.

Table II. Clinical presentation

	Men n=340	Women n=109	p-values
Pain/pressure/discomfort in			
Chest/thorax	313 (92.1)	80 (73.4)	*<0.001*
Throat/neck	57 (16.8)	40 (36.7)	*<0.001*
Back	42 (12.4)	32 (29.4)	*<0.001*
Stomach	30 (8.8)	6 (5.5)	0.27
Shoulders	53 (15.6)	36 (33.0)	*<0.001*
Arms/hands	183 (53.8)	71 (65.1)	*0.04*
Associated symptoms			
Tiredness/fatigue	102 (30.0)	45 (41.3)	*0.03*
Nausea/vomiting	94 (27.6)	53 (48.6)	*<0.001*
Cold sweat	197 (57.9)	70 (64.2)	0.25
Fear	57 (16.8)	34 (31.2)	*0.001*
Symptom intensity			
Pain intensity, NRS, median (IQR)	7 (6,8)	7 (6,8)	0.65

NRS, Numeric Rating Scale; IQR, Interquartile range. Missing values; 3 (<1%) patients did not grade any pain/discomfort on the NRS scale. No missing values regarding other variables.

Table III. Thoughts, actions and context when falling ill with STEMI

	Men n=340	Women n=109	p-values
With whom did you first talk about your symptoms?			
My wife/husband/partner	202 (60.3)	60 (55.6)	0.38
A relative or friend	31 (9.3)	3 (2.8)	*0.03*
My children	23 (6.9)	18 (16.7)	*0.002*
The Swedish Healthcare Direct	11 (3.3)	7 (6.5)	0.14
The Emergency Medical Service	20 (6.0)	4 (3.7)	0.36
The Primary Healthcare Centre	15 (4.5)	5 (4.6)	0.95
Someone else	30 (9.0)	11 (10.2)	0.70
Did you call any of the following before you went to the hospital?			
The Primary Healthcare Centre	66 (19.8)	17 (15.6)	0.33
The Swedish Healthcare Direct	81 (24.3)	33.9 (37)	*0.05*
Did you take any medication in order to relieve the symptoms?			
Painkillers	50 (14.7)	29 (26.6)	*0.005*
Nitro-glycerine	44 (12.9)	20 (18.3)	0.16
Have you heard of angioplasty or clot-dissolving treatment in case of myocardial infarction?			
Yes, I have	319 (94.1)	99 (93.4)	0.79
Why did you decide to go to the hospital?			
The symptoms were severe	108 (33.9)	36 (34.3)	0.94
I thought I had a myocardial infarction	79 (24.8)	16 (15.2)	*0.04*
I was told to seek care by my wife/husband/partner	38 (11.9)	14 (13.3)	0.70
Another reason for going to the hospital	22 (6.9)	12 (11.4)	0.14
Did you hesitate to go to the hospital? If yes, why?			
I did not hesitate	249 (73.5)	74 (67.9)	0.26
I thought the symptoms would disappear	85 (25.1)	31 (28.4)	0.49
I did not think it was anything serious	27 (8.9)	8 (7.3)	0.83
I did not want to worry my family	17 (5.0)	5 (4.6)	0.86
I did want to draw attention	4 (1.2)	2 (1.8)	0.61
I did not want to disturb anyone	10 (2.9)	3 (2.8)	0.92
I felt discomfort in facing being hospitalised	11 (3.2)	5 (4.6)	0.51
Context when falling ill			
At home	253 (74.4)	90 (82.6)	0.08
I was alone	91 (26.8)	29 (26.6)	0.97
Weekend	95 (29.3)	34 (31.8)	0.49
Weekdays, out of office time	118 (35.4)	38 (35.8)	0.94
Transport mode			

I went by ambulance to the hospital	280 (82.4)	91 (83.5)	0.79
Missing values; 25 (5.6%) patients did not answer the question about why hesitating before going to the hospital. No, or minor, details missing regarding all other variables.			

Table IV. Reactions from bystanders when a person fell ill

	Men n=340	Women n=109	p-values
He/she/they suggested that I should rest	47 (14.0)	13 (12.0)	0.61
He/she/they suggested medication	11 (3.3)	7 (6.5)	0.14
He/she/they suggested that I should call EMS	126 (37.5)	24 (22.2)	*0.003*
He/she/they suggested that I should call SHD	85 (25.3)	85 (78.7)	0.40
He/she/they called EMS	175 (52.1)	55 (51.4)	0.90
He/she/they called SHD	85 (25.3)	39 (36.1)	*0.03*
He/she/they brought me to the hospital	63 (18.8)	23 (21.3)	0.56
I did not tell anyone	8 (2.4)	8 (7.4)	*0.02*

EMS, Emergency Medical Services; SHD, Swedish Health Care Direct. Missing values; 5 (1.1%) patients did not answer question about reactions from bystanders.

Table V. Predictions of patient delay times in men and women separately

	Men n=340			**Women n=109**		
	Standardized Beta	**p-value**	**R^2 change**	**Standardized Beta**	**p-value**	**R^2 change**
Block 1. Background characteristics			**0.04**			**0.13**
Age	0.12	*0.05*		0.07	0.54	
Current smoker	0.14	*0.01*		0.19	*0.05*	
Block 2. Symptoms			**0.10**			**0.23**
Chest pain	0.15	*0.01*		0.05	0.55	
Pain in back/shoulders	-0.03	0.60		0.25	*0.01*	
Stomach pain	0.09	0.07		0.30	*0.00*	
Cold sweat	-0.07	0.19		-0.18	*0.04*	
Anguish/fear	-0.13	*0.01*		-0.08	0.38	
Block 3. Context when falling ill			**0.02**			**0.08**
At home	-0.11	*0.03*		-0.04	0.62	
Out of office time	0.06	0.27		0.18	*0.03*	
Block 4. Reactions from bystanders			**0.08**			**0.12**
They suggested rest	-0.13	*0.02*		0.10	0.28	
They suggested calling EMS	-0.04	0.41		-0.22	*0.02*	
They called EMS	-0.28	*0.00*		-0.23	*0.01*	
They drove me to the hospital	0.02	0.75		-0.14	0.12	
Block 5. Thoughts and actions			**0.09**			**0.13**
I took some medication to relieve the symptoms	0.12	*0.03*		0.06	0.47	
I hesitated about going to the hospital	-0.11	0.26		0.62	*0.00*	
I thought the symptoms would go away/it was not anything serious	0.25	*0.01*		-0.31	0.06	
I did not want to worry my relatives	0.09	0.11		-0.17	*0.05*	
I was afraid of the reaction from the hospital staff	0.05	0.34		0.20	*0.04*	

Multiple linear regression with log-transformed pre-hospital delay time from symptom-onset-to-first-medical contact in minutes as the dependent variable. Independent variables entered in five blocks, significant predictors in the multivariable analyses shown in table. R^2 for the complete model 0.53 in women, 0.26 in men. EMS, emergency medical service.

Figure legends

Figure 1. First medical contact in men and women with STEMI

Figure 2. Delay times from symptom onset until first medical contact

Figure 3. Delay times from first medical contact until diagnosis

Figure 4. Delay times from symptom onset until diagnosis

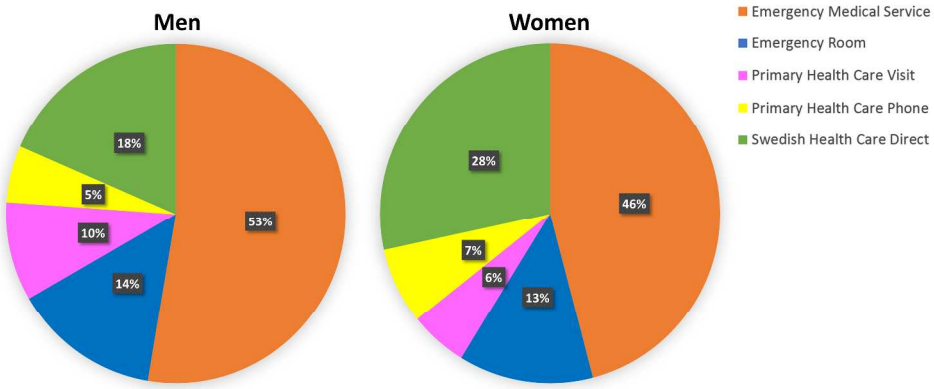

Figure 1. First medical contact in men and women with STEMI

338x190mm (300 x 300 DPI)

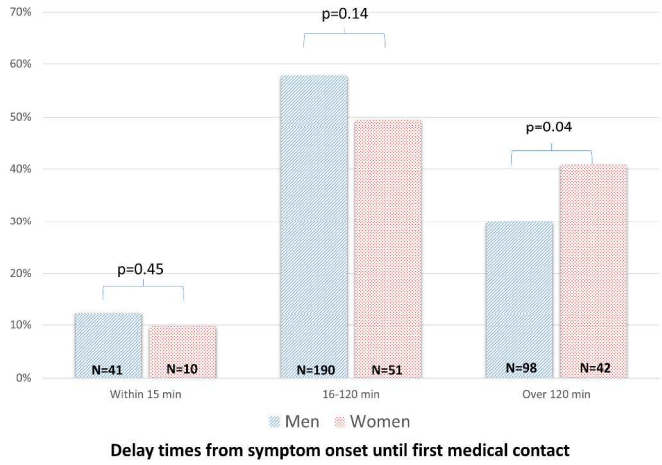

Figure 2. Delay times from symptom onset until first medical contact

338x190mm (300 x 300 DPI)

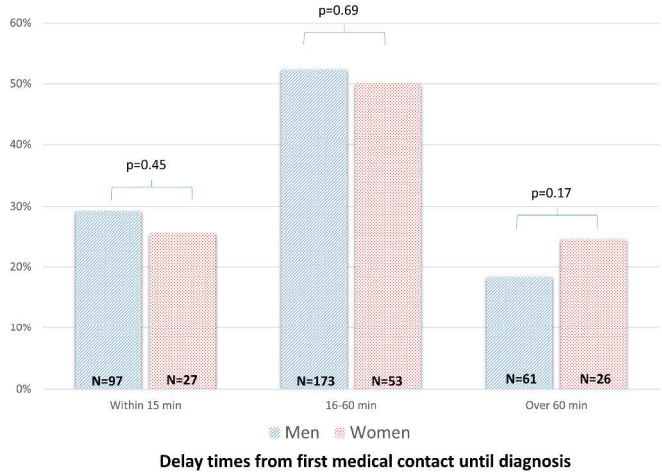

Figure 3. Delay times from first medical contact until diagnosis

338x190mm (300 x 300 DPI)

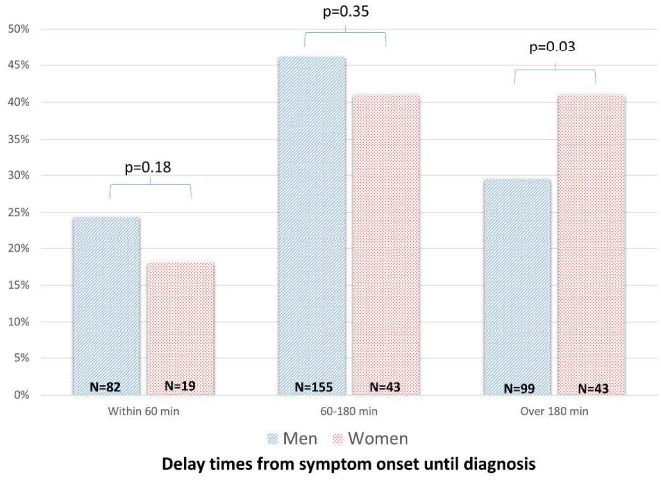

Figure 4. Delay times from symptom onset until diagnosis

338x190mm (300 x 300 DPI)

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract **Indicated in the title (page 1), in the abstract (page 2) and in the method section (page 4-5)**
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found **Done (page 2)**
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported **Done (page 3-4)**
Objectives	3	State specific objectives, including any prespecified hypotheses **Objectives specified in the introduction section (aim of the study, page 4)**
Methods		
Study design	4	Present key elements of study design early in the paper **Presented in title (page 1), abstract (page 2) and method section (page 4-5)**
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection **Summarised in the method section (page 4-5) as all details are given in a previous publication that we refer to (ref 21, page 14)**
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants **Done, in the method section (page 4-5)**
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable **Done, in the method and statistical sections (page 4-6)**
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group **Done, in the method section (page 4-5). Details of the questionnaire given in a previous publication that we refer to (ref 21, page 14)**
Bias	9	Describe any efforts to address potential sources of bias **Done, in the method section (page 4-5). We have made an effort to include eligible STEMI patients on a consecutive basis within 24 hours after admittance, reducing the risk of selection and recall bias**
Study size	10	Explain how the study size was arrived at **No power calculation was done as this is a descriptive observational study (page 4-5). We planned for one year inclusion and that we then should include approximately 500 STEMI patients which would be enough to do the gender (and other) comparisons we planned for**
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why **Explained in the statistical section (page 5-6)**
Statistical methods	12	Describe all statistical methods, including those used to control for confounding **Multivariable linear regression analyses performed – not to control for confounding, but to find variables associated to delay in women and in men, separately. Explained in the statistical section (page 5-6)**
		(*b*) Describe any methods used to examine subgroups and interactions **NA**
		(*c*) Explain how missing data were addressed **We had very little missing data, specified in the statistical section (page 5-6)**

		(*d*) If applicable, describe analytical methods taking account of sampling strategy **NA**
		(*e*) Describe any sensitivity analyses **NA**
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed **SymTime was supposed to consecutively include eligible STEMI-patients at five hospitals with cath lab facilities (method section, page 4-5). The patients could not be included the first hours because of the acute nature of this disease. Thus they had to stay a while at the participating hospital in order to be able to be included. Patients were then included within 24 h, most often at day 2. The total study population consisted of 532 STEMI patients comprising 36% of all STEMI patients that ever touched down (including those only coming to cath lab and then leaving the including hospital very fast) at the five hospitals during the study period (n=1473) according to the Swedish quality register SWEDEHEART. The first couple of months FMC was not registered. Thus the present study consists of the 449 STEMI patients included after the start of FMC registering.**
		(b) Give reasons for non-participation at each stage **Inclusion and exclusion criteria presented in the method section (page 4-5).**
		(c) Consider use of a flow diagram **Considered, but not deemed necessary. Data given in text.**
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders **Presented in Table 1 and in the result section (page 6)**
		(b) Indicate number of participants with missing data for each variable of interest **There was very little missing data in the current study, specified in the statistical section (page 5-6)**
Outcome data	15*	Report numbers of outcome events or summary measures **No outcome events were measured**
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included **Absolut numbers, percentages, multivariable adjusted linear regression analyses for the main measurements are presented in the result section (page 6-8). Selection of variables in the multivariable analyses and how these were chosen is described in the statistics section (page 5-6).**
		(*b*) Report category boundaries when continuous variables were categorized **NA**
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period **NA**
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses **NA**
Discussion		
Key results	18	Summarise key results with reference to study objectives **Summarised in the discussion section (page 7-8)**

Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias **Summarised in the strength and limitation section (page 3)**
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence **Done in the discussion (page 8-10) and in the conclusion (page 11)**
Generalisability	21	Discuss the generalisability (external validity) of the study results **Done in the strength and limitation section (page 3)**
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based **Done in the funding section (page 11)**

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.