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Age and Sex Differences in Duration of Pre-hospital Delay in Patients with Acute Myocardial Infarction: A Systematic Review

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Abstract

Background—Coronary heart disease is the leading cause of morbidity and mortality in American men and women. While there have been dramatic changes in the management of patients hospitalized with acute myocardial infarction (AMI) over the past several decades, a considerable proportion of patients with AMI continue to delay seeking medical care in a timely manner. This review provides an overview of the published literature that has examined age and sex differences in extent of pre-hospital delay in patients hospitalized with AMI.

Methods and Results—A systematic review of the literature from 1960 to 2008, including publications that provided data on duration of pre-hospital delay in patients hospitalized with AMI, was conducted. A total of 44 articles (42 studies) were included in the present analysis. The majority of studies showed that, in patients hospitalized with AMI, women and older persons were more likely to arrive at the hospital later than men and younger persons. Several factors associated with duration of pre-hospital delay, including sociodemographic, medical history, clinical, and contextual characteristics differed according to sex.

Conclusions—The elderly and women were more likely to exhibit longer delays in seeking medical care after the development of symptoms suggestive of acute coronary disease compared to other groups. Further research remains needed to more fully understand the reasons for delay in these vulnerable groups.

Keywords

Acute myocardial infarction; pre-hospital delay; age and sex differences; systematic review

Background

Coronary heart disease (CHD) is the leading cause of mortality in American men and women; in 2009, it is estimated that more than one million Americans will experience an acute myocardial infarction (AMI).[1] Older individuals and women have been shown to be at greater risk for dying after AMI than respective comparison groups. Persons with an AMI have a sudden death rate four to six times that of the general population and upwards of one half of patients with AMI will die before reaching the hospital with men more likely to die out-of-hospital than women. [1]

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Coronary reperfusion therapies and thrombolytic medications have been consistently shown to be more effective at reducing mortality and the development of important clinical complications if patients are treated with these interventions as promptly as possible.[2–4] However, more than one-half of patients with AMI delay seeking medical care by more than 2 hours, and more than one-quarter of patients with AMI delay seeking care by more than 6 hours.[5–8] Although considerable efforts have been made to educate the general public about the symptoms of AMI, and the importance of seeking medical care immediately in the setting of possible acute coronary disease, little change in medical care seeking behavior has occurred over the past several decades.[8–10]

A number of studies have examined possible age and sex differences in the extent of pre-hospital delay in patients with AMI.[7–9,11–22] Several studies have found that women are more likely to experience longer delays compared with men,[9,10,12,23–25] while other studies have suggested that there are no sex differences in duration of pre-hospital delay.[6,8] In terms of age, most prior studies have found that older individuals are more likely to experience prolonged delay in seeking medical care in the setting of AMI than younger persons.[8–10,24] However, several studies have found that there were no age differences in medical care seeking behavior in patients hospitalized with AMI.[11,12,25,26]

Some studies have suggested that socio-demographic factors, acute symptom profile, associated co-morbidities, psychological, and acute contextual factors are associated with patient's care seeking behavior;[7,8,22] little is known, however, about whether these associations differ according to age or according to sex.

The primary objectives of this review are to summarize the published literature that has examined age and sex differences in duration of pre-hospital delay in patients hospitalized with AMI. This review will also examine whether factors associated with pre-hospital delay differ according to patient's age and sex and provide recommendations for future research in this important area.

Methods

Data sources

A formal search of the electronic literature through Ovid including Medline, PsycINFO, the CINAHL database, as well as a manual search of relevant journals from 1960 to September, 2008, was performed using the following search terms as key words (chest pain OR myocardial infarction OR heart attack OR unstable angina OR angina pectoris OR acute coronary syndromes OR heart disease) AND (delay OR pre-hospital delay OR treatment seeking OR care seeking OR help seeking OR timely treatment OR treatment delay OR hospital arrival OR emergency medical care OR decisions OR decision making) AND (age differences OR sex differences OR women).

Review papers, expert opinions or discussions, case reports, studies that did not clearly define pre-hospital delay, had sample sizes less than 50 subjects, and those that did not report delay times according to sex or age were excluded. In addition, since we were unable to review non-English publications, they were excluded from the present review.

Definition of pre-hospital delay

Duration of pre-hospital delay was defined as the time interval between the onset of signs and symptoms suggestive of AMI and arrival in the hospital emergency department. Pre-hospital delay was normally reported in minutes, hours, or days.

Data extraction

A data abstraction form was used to extract the following information from published studies: (1) study description: author, study year, study design, study population, study setting/location, definition of AMI, inclusion/exclusion criteria, sample size (by age and sex if available), mean age, sex distribution, and definition of pre-hospital delay, (2) information on distribution of pre-hospital delay by age and/or by sex, (3) possible factors associated with pre-hospital delay including socio-demographic (e.g., race, education, insurance), clinical (e.g., medical history, clinical presentation), and psychosocial (e.g., knowledge, anxiety, coping mechanisms) factors by age and/or by sex and (4) information on whether the study findings were adjusted for possible confounding factors.

Quality assessment and grading

The quality of each study reviewed was assessed using Downs and Black criteria.[27] The checklist includes 27 items in 5 categories (reporting, external validity, internal validity-bias, internal validity-confounding, and power). The quality score was the number of items from the checklist addressed in the article under review as a percentage of the total number of items applicable (minimum of 23 and maximum of 27). Studies with a quality score of <50% were excluded from further consideration.

Data analysis

We characterized duration of pre-hospital delay by mean, median, and distribution, with further stratification according to patient's age and sex. Given the heterogeneity of studies included, no formal meta-analytic techniques were performed.

The authors had full access to the data and take responsibility for its integrity. All authors have read and agreed to the manuscript as written.

Results

Search

The initial search identified 729 articles/abstracts from Medline, PsyINFO, and the CINHL databases (Figure 1). We initially excluded 180 duplicate articles, 47 non-English studies, and 11 non-human subject studies. Abstracts from 491 studies were reviewed; 421 abstracts determined not to be relevant were excluded. An additional 17 potential studies were identified from the review of bibliographies of published studies. A total of 87 full articles were reviewed and 43 of these were excluded based on previously described criteria, resulting in full abstraction of 44 articles representing 42 independent studies (Figure 1).

Characteristics of Included Studies

The characteristics of studies included[5,7–26,28–50] in this review are shown in Table 1. All studies were conducted after 1985. There was significant heterogeneity between these investigations in terms of study design, population demographic and clinical characteristics, inclusion criteria, and sample sizes. A majority of the studies (54%) were prospective cohort investigations, 29% were cross-sectional in nature, 12% were retrospective cohort studies, and a limited number (5%) were randomized clinical trials.

In terms of the patient populations, most of the studies (90%) included all cases of AMI, regardless of a history of MI (the prevalence of prior MI ranged from 7% to 33%), whereas the remaining investigations focused on patients with a first AMI only. A majority (88%) of the studies were conducted in the U.S., Canada or Europe, with one multi-national registry of patients with acute coronary syndromes. The sample sizes of the published studies ranged widely from 51 to upwards of 480,000 participants. The average age of the patient populations ranged from 52 to 76 years and women accounted for between 20% and 50% of study participants. Women were considerably older than men in the majority of the studies reviewed.

In terms of the measurement of pre-hospital delay, the majority of investigations defined pre-hospital delay as the time interval from the onset of symptoms suggestive of AMI to arrival at the hospital or emergency department (ED). While some studies specifically examined patient associated delay (time from onset of acute symptoms to seeking medical help, such as calling 911), some also included physician related delay (time between the call for assistance and call for an ambulance by the doctor) or transportation delay (period between initiation of travel to the emergency room and ED arrival). Information about duration of pre-hospital delay was abstracted from hospital medical records in 27 studies and was obtained from in-person interviews or self reported questionnaires in 15 studies. Most interviews were conducted between 3–5 days after hospitalization for AMI. Duration of pre-hospital delay was slightly longer in studies in which patients were interviewed[11,12,40] than in studies using data from hospital medical records.[36,38]

Sex Differences in Pre-hospital Delay

In general, the median duration of pre-hospital delay in women ranged from 1.8 hours to 7.2 hours while the range in men was from 1.4 to 3.5 hours (Table 2). A total of 24 studies (median sample size=3,700 patients) found that women were more likely to experience longer delays than men (Tables 2, 3 and 4).[9,14,23,28–30,32,33,36–41,43] In these studies, the median differences in duration of pre-hospital delay between women and men ranged from 0.3 to 3.7 hours. Fourteen studies, with a median sample size of 280 patients, found no differences between men and women in terms of pre-hospital delay (Tables 2, 3 and 4).[11,17,20–22,35,49] In these studies, the median differences between women and men ranged from 0.02 to 0.9 hours.

In summarizing differences in the distributions of men and women according to cutoffs at 2 hours and 6 hours after the onset of AMI[5,7,8,16,18,33], patients arriving at the hospital within 2 hours of symptom onset were more likely to be male (range: 64%–76%) compared to those arriving after 2 hours (range: 59%–69%); similar findings were observed when we used a cutpoint at 6 hours to separate early from late care seekers (range: 55%–73% vs. range 51%–67%).

A limited number of studies have examined changes over time in duration of pre-hospital delay in patients hospitalized with AMI according to sex[8–10,19,39]. The majority of these studies[8,9,19] reported that there were either inconsistent or no changes in delay patterns in general, as well as between women and men. On the other hand, the multi-site ARIC study of nearly 19,000 patients hospitalized with AMI over a 14 year period (1987–2000) reported that, although there were no significant changes in the proportion of patients delaying 4 or more hours after acute symptom onset, there was a narrowing of differences between men and women in duration of pre-hospital delay during the period under study.[10] Similar findings of narrowing gaps between men and women were observed in NRMI 2.[39]

Age Specific Differences in Pre-hospital Delay

In general, the median duration of pre-hospital delay in older patients hospitalized with AMI (≥ 65 years) ranged from 1.4 hours to 2.5 hours while the range in younger patients was between 1.1 hours to 2.0 hours (Table 2). In examining the relation between age and duration of pre-hospital delay, the findings from 24 studies (median sample size: 3,700 patients) suggested that older individuals were more likely to exhibit prolonged delay than younger patients (Tables 2, 3, and 4).[5,7–10,15,16,18,26,30–33,38,39,43] On the other hand, nine studies with a median sample size of approximately 280 patients found no age-related differences in extent of pre-hospital delay (Tables 2, 3 and 4).[11,12,14,20,26,49] Only one small study (n=79) in Jordan found younger age to be associated with prolonged delay in seeking acute medical care.[44]

In summarizing differences in the distribution of age according to care seeking cutpoints at 2 hours and 6 hours after the onset of AMI[7,8,18,33], patients arriving at the hospital within 2 hours of symptom onset were more likely to be younger than 65 years of age (range: 44%–57%) compared to those arriving after 2 hours (range: 36%–46%); similar findings were observed when we used a cutpoint at 6 hours to separate early from late care seekers (range: 41%–52% vs. range 35%–45%).

Studies examining potentially changing trends in pre-hospital delay in patients with AMI according to age have shown that the previously observed gaps between patients of different age groups have not narrowed over time.[8,9,39] Two publications from the Worcester Heart Attack Study, which included nearly 4,000 patients hospitalized with AMI in central New England medical centers between 1986 and 2005, found that patients ≥75 years were more likely to delay seeking medical care than patients <55 years and these differences were relatively unchanged over the 20 year period under study.[8,51] On the other hand, data from the NRMI 2 suggest that these gaps have slightly narrowed over time (patients 70 years and older delayed longer than younger patients by an average of 39 minutes in 1995 and by 25 minutes in 2004).[39]

Interaction Between Age and Sex and Extent of Pre-hospital Delay

The interaction between age and sex is important when examining the impact of these demographic characteristics on patient's care seeking behavior since sex differences in pre-hospital delay may be modified by age and vice versa. A limited number of studies have suggested that differences in duration of pre-hospital delay were greater between older men and women compared to those who were younger.[19,25,34]

Factors associated with pre-hospital delay according to sex and age

A variety of socio-demographic (in addition to age and sex), clinical, situational, and psychological factors have been associated with prolonged care seeking behavior. These factors included non-White race,[5,9,10,21,22,39] low socioeconomic status,[15,26] history of angina,[5,8,29,33,39] diabetes,[5,8,9,11,12,15,16,23,26,29,33,38,39] and hypertension,[8,10,18,26,45] consulting a spouse or other relative,[20] consulting a physician,[21,22,43,50] self treatment,[21,22,50] waiting for symptoms to go away, stuttering symptom pattern,[12,25] not viewing symptoms as serious or experiencing anxiety about them,[25,40] and lack of knowledge about the symptoms of AMI.[12,25] On the other hand, having Medicare or private health insurance,[16,23,43] history of MI,[5,7,9,23,29,33,39] sudden onset of severe chest pain,[10,18,23,26,39] onset of symptoms in the evening,[39] calling EMS,[10,21,22] presenting with shock,[30,39] sweating,[23] recognition by patient that symptoms were heart related[26,46], and concordance between expected and experienced symptoms[21,22,49,50] were associated with shortened delay times. Socio-demographic and clinical factors were typically investigated in large cohort studies in which data were collected through the review of hospital medical records, whereas psychological factors were primarily examined in small studies, where data were gathered through self-reported questionnaires or direct patient interviews.

Among men, low education,[22] having a partner with low education,[22] having symptom onset at home,[12] not asking for help or calling 911,[12] not taking the ambulance,[12] experiencing early musculoskeletal pain,[21] developing a non-Q wave AMI,[25] lack of consistency between

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expected and experienced symptoms[50], and not knowing about thrombolytic therapy when having symptoms of AMI[25] placed men at greater risk for prolonged pre-hospital delay; a history of a previous MI[25] and symptom appraisal[21] were associated with reduced pre-hospital delay in men.

Factors associated with delays in seeking medical care in women slightly differed from those noted in men. Women who were older,[25] single,[12] had a history of a previous MI,[25] were alone during symptom onset,[12] and did not want to trouble anyone[12,25] were more likely to seek medical care at a later time than women who did not have these characteristics; women who were transported to the hospital by ambulance were more likely to arrive at the hospital earlier than those who were transported by other methods.[36]

Among studies included in the present review, we could not identify any study that examined whether factors associated with pre-hospital delay differed in persons of different age groups.

Discussion

Overall, the findings of the studies reviewed were somewhat mixed with regards to possible age and sex differences in duration of pre-hospital delay in patients hospitalized with AMI. A significant number of studies found that women were more likely to present at the hospital later than men, and older persons were more likely to experience longer delays than younger persons; these associations were particularly noted in studies that were broader in scale and that adjusted for the role of other potentially confounding variables. There were some suggestions for an interaction between age and sex with regards to extent of pre-hospital delay, in which differences in pre-hospital delay between men and women were less pronounced in younger as compared to older individuals. Several factors were differentially associated with care seeking behavior between men and women.

Sex Differences in Duration of Pre-hospital Delay

The majority of studies reviewed found that women were more likely to delay seeking medical care than men, even after adjustment for the important potentially confounding influence of age and other comorbidities. There are several possible explanations for this finding. First, women were considerably older than men when experiencing their first AMI[12,13,17,21,25,35,36,41,43,49,50] and many studies have found that advancing age is associated with prolonged delay in seeking medical care in patients hospitalized with AMI.[8,9,15,30,38,39,43] Second, women were more likely to report atypical symptoms of AMI than men.[52] Women may lack knowledge about the symptoms of AMI or consider heart attack as a “male disease”; therefore, they may not recognize the importance of their symptoms in seeking medical care in a timely fashion. Women were more likely to contact their physician initially than men which likely contributed to the more prolonged delay patterns observed.[50] Women were also more likely to be widowed and living alone at the time of symptom onset[21] and living alone has been previously shown to be an independent predictor of prolonged delay.[12,18] Women were more likely to have additional comorbidities present than men, including diabetes, hypertension, and heart failure,[21,35] and these conditions have been associated with prolonged delay times.[5,7,8,18,39] Women also tended to cope with their illness by themselves and these coping mechanisms have been previously associated with longer delay times.[12,25] Interventional strategies specifically targeting women may be needed to improve their understanding about the nature of this disease, differences in symptom patterns between women and men, and the need for seeking medical care promptly after developing symptoms suggestive of AMI.

Age Differences in Duration of Pre-hospital Delay

Older individuals were more likely to experience greater delays in seeking acute medical care than younger individuals in the setting of AMI. Several factors may have contributed to this observation. Older patients are more likely to have atypical symptoms of AMI,[31,53] and have additional comorbidities present compared to younger patients,[6–8,19,43,31] that may lead to delays in seeking medical care in a timely manner. Other factors such as limited health care access, denial and embarrassment, living alone, or failure to recognize the symptoms associated with AMI in older patients may also have contributed to the longer delays noted in older persons.

Given the markedly increased risk for initial coronary events in older as compared to younger individuals, as well as in the risk of recurrent coronary events in patients with an initial AMI, older persons need to be educated about the symptoms of AMI they may experience and appropriate care seeking steps they should take when experiencing these symptoms. Family members as well as care providers should be encouraged to become involved in these educational programs since they play important roles in the decision making process of older persons.

Interaction between Age and Sex and Duration of Pre-hospital Delay

A limited number of studies have examined the interaction between age and sex with regards to extent of pre-hospital delay showing that sex differences in pre-hospital delay were greater in older compared to younger persons with older women more likely to exhibit greater delay, highlighting the need for targeted interventions in older women.[19,25,34]

Limitations of Published Studies

The studies we included in this summary overview have several limitations. First, some studies used either convenience[11,12,20,40,44,47,49] or restricted patient samples[16,20–22,32,39,47] that may have resulted in selection biases or findings with limited generalizability. Several studies had small sample sizes,[11,12,20,40,44,47,49] with a consequent lack of statistical power. Many studies relied primarily on information from medical records which may be associated with information bias[5,7–9,16–18,30,37,39] and may not have precisely characterized extent of delay in comparison to data collected through in person interviews. Indeed, differences were noted in average delay times based on information collected from medical records as compared to data collected by direct standardized patient interviews. Similarly, studies that relied exclusively on patient interviews[15,44,46,49] may have been subject to recall bias, depending on the patient's cognitive status and time when the interviews were performed. None of the studies reviewed adjusted for cognitive impairment status. Lastly, a number of studies did not report on, or perform, multivariate analyses which may have led to concerns in the interpretation of the study findings.[11,12,15,17,28,34,36,38,41]

Future Research

Women and older persons, particularly older women, have been shown to delay seeking medical care for AMI to a greater extent compared to respective comparison groups. In addition, factors associated with delay are likely to differ by age and according to sex which needs to be confirmed in well designed future studies. Further qualitative studies (e.g., in-depth interviews or focus groups) are needed to better understand the relation between age and sex with care seeking behavior in patients developing an AMI. Greater understanding of differences in, and reactions to, premonitory, as well as acute, symptoms of coronary disease is needed and of the steps that individuals take in seeking acute medical care. Future studies should report means, medians, and distributions of pre-hospital delay by age and by sex for more meaningful comparisons. Multivariate as well as stratified analyses should also be performed to minimize the effects of other potentially confounding variables.

Interventions to Reduce Extent of Pre-hospital Delay

Several community intervention trials have been undertaken with the goal of reducing extent of pre-hospital delay in patients with signs and symptoms of AMI, with inconsistent results. Some trials, using interventions ranging from mass to specialized media campaigns, have shown significant reductions in either median delay times or increases in the proportion of patients presenting for medical care relatively soon after the onset of acute coronary symptoms.[54–57] On the other hand, several studies have failed to observe reductions in delay times in patients experiencing symptoms of AMI.[58–65] The results of these trials, especially 2 recent trials which employed both broad population approaches and more personalized interventions,[64,65] suggest that our understanding of the reasons for delay in seeking care in patients with symptoms suggestive of AMI may be inadequate as may be our educational approaches and intervention efforts.

Conclusions and Implications for Clinical Practice

Women and older individuals are more likely to delay seeking medical care after the onset of AMI. Factors associated with duration of pre-hospital delay including socio-demographic, medical history, clinical presentation, and psychological variables have been shown to affect medical care seeking behavior; the role of these and additional factors that may affect acute care seeking behavior need to be more systematically examined in future studies. Research remains needed to particularly address delays in seeking medical care after the onset of acute coronary symptoms in vulnerable groups.

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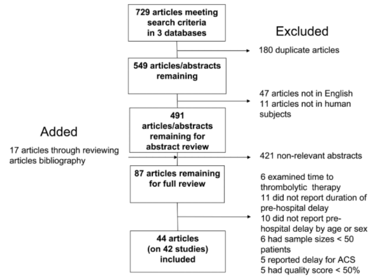

Figure 1.
Flow Chart of Review Process

Table 1

Characteristics of Included Studies

First Author	Study period	Study Design	Study location/Setting	Sample Size	Male (%)	Age (mean, yrs)	Sources of pre- hospital delay
Karlson et al[28]	1986–1987	Prospective	Goteborg, Sweden, 1 local hospital	912	76	NA	Medical record
Meischke et al[29]	1988–1991	Prospective	Washington State, 19 hospitals	2,947	66	66	Medical record
Goldberg et al[8]	1986–1997	Prospective	Worcester, MA, 16 area hospitals	3,837	61	NA	Medical record
Leizorovicz et al[30]	1988–1992	RCT	15 European countries and Canada	5,469	77	61	Medical record
McGinn et al[10]	1987–2000	Retrospective	ARIC, U.S., 31 hospitals	18,928	67	NA	Medical record
Barakat et al[31]	1988–1994	Prospective	England, 1 district hospital	1,225	76	NA	Medical record
Magid et al[32]	1989–1994	Retrospective	MITI, Washington, 19 hospitals,	1,331	66	NA	Medical record
Isaksson et al[19]	1989–2003	Prospective	MONICA, Sweden, 2 counties	6,542	78	NA	Medical record
Ottesen et al[33]	1990–1992	Prospective	TRACE, Denmark, 27 hospitals	5978	68	NA	Medical record
Gibler et al*[16]	1990–1993	RCT	GUSTO I - U.S., Multiple sites	23,105	73	61	Medical record
Maynard et al[34]	1990–1994	Prospective	NRMI- U.S., 904 hospitals	212,990	65	65	Medical record
Meischke et al[23]	1991–1993	Prospective	Washington State, 19 hospitals	4,497	66	67	Medical record
Behar et al[13]	1992	Cross sectional	Israel, 25 CCUs	1,014	76	NA	Medical record
Gurwitz et al[18]	1992–1993	Retrospective	Minnesota, 37 hospitals	2,409	62	NA	Medical record
Kaplan et al[35]	1993–1994	Retrospective	Rochester, NY, 4 hospitals	573	67	NA	Medical record
Lambrew et al[36]	1993–1994	Prospective	NRMI-1- San Francisco, CA, 42 hospitals	1,755	72	NA	Medical record
Bouma et al[14]	1993–1995	Prospective	Netherlands, 3 hospitals	400	78	NA	Interview
Sheifer et al[5]	1994–1996	Prospective	U.S. Medicare	102,339	54	76	Medical record
Goldberg et al[9]	1994–1997	Prospective	NRMI 2-1624 hospitals	364,131	67	66	Medical record
Heer et al[37]	1994–1997	Prospective	Southwest Germany, 54 hospitals	6,066	66	NA	Medical record
Brophy et al[38]	1995–1996	Prospective	Quebec, Canada, 40 hospitals	1,357	74	60	Questionnaire
Gibler et al*[16]	1995–1997	RCT	GUSTO III U.S., Multiples sites	4,744	70	62	Medical record
Ting et al[39]	1995–2004	Prospective	NRMI 2 U.S.	482,327	67	NA	Medical record
Sawaya et al[24]	1996	Prospective	Lebanon,18 medical centers	432	77	NA	Medical record

First Author	Study period	Study Design	Study location/Setting	Sample Size	Male (%)	Age (mean, yrs)	Sources of pre- hospital delay
Lovlien et al[20]	1999	Cross sectional	Norway,13 hospitals	82	54	NA	Questionnaire
Goldberg et al ||[7]	1999–2001	Prospective	GRACE,14 countries, 94 hospitals	3,693	72	NA	Medical record
Walsh et al[40]	2000	Cross sectional	Galway, Ireland, 1 university hospital	61	72	62	Interview
Carrabba et al[41]	2000–2001	Prospective	Florence, Italy, 6 hospitals	920	68	NA	Medical record
Morgan et al[42]	2001–2002	Cross sectional	Northeast U.S., 2 rural hospitals	98	63	NA	Interview
O'Donnell et al[43]	2001–2002	Prospective	Dublin, Ireland, 6 hospitals	890	69	NA	Medical record
Al-Hassan et al[44]	2002	Cross sectional	Northern Jordan, 3 district hospitals	83	69	52	Interview
Pitsovos et al †[45]	2003–2004	Prospective	Athens, Lamia, Kardista, Halkida, Kalamata, Zakynthos, Greece, 6 hospitals	2,172	76	NA	Medical record
Lovlien et al[21,22]	2003–2004	Prospective	Norway, 5 hospitals	533	72	NA	Questionnaire
Bleeker et al[46]	NA	Retrospective	Rotterdam, Netherlands, 3 hospitals	300	79	NA	Interview
Dracup et al[15]	NA	Cross sectional	North America, 43 hospitals	277	72	58	Questionnaire
McKinley et al*[26]	NA	Prospective	GUSTO, Australia, 2 hospitals	145	66	62	Interview
McKinley et al*[26]	NA	Prospective	GUSTO, U.S., Canada, 41 hospitals	277	71	58	Interview
Grace et al[17]	NA	Cross sectional	Ontario, Canada, 12 CCUs	482	72	62	Questionnaire, Medical record
Rosenfeld et al[47]	NA	Cross sectional	Pacific Northwest, 3 tertiary hospitals	52	0	NA	Interview
Moser et al[25]	NA	Cross sectional	Midwest, 2 hospitals/medical centers	194	51	NA	Interview
Quinn et al[48]	NA	Cross sectional	Rochester, NY, 1 hospital	100	59	63	Medical record
King et al[49]	NA	Cross sectional	Rochester, NY, 1 medical center	60	50	NA	Interview
Zerwic et al[50]	NA	Cross sectional	Midwestern state, 3 hospitals	212	53	NA	Interview

RCT: Randomized Clinical Trial; NA: Not available

||GRACE study included AMI and Unstable Angina (UA). Data presented in Table 1 were for ST-segment elevation myocardial infarction only, data for ST-segment elevation myocardial infarction were not presented since they could not be separated from unstable angina

†The GREESC study included AMI and UA. Data presented in Table 1 were for all patients since no information about sample size, sex distribution, and mean age specific for AMI and UA was available. However, information about pre-hospital delay was available for each group presented in Table 2.

*These studies included two populations, data were extracted separately.

Table 2

Summary of Selected Studies Reporting Duration of Pre-hospital Delay According to Age and Sex

	Mean Delay (hours)			Median Delay (hours)				
First Author	Men (M)	Women (W)	Age groups	Men (M)	Women (W)	Age groups	Adjusted confounders	Conclusions
Ting et al[39]	1.9	2.4	<60y: 1.8 60–69y: 2.0 70–79y: 2.3 ≥80y: 2.6	NA	NA	NA	Yes	Women increased delay (↑) Older patients >60 y ↑ Age and sex differences slightly narrowed over time
Maynard et al[34]	NA	NA	NA	NA	NA	<60y: 1.8 >75y: 2.5	No	Women ↑ least apparent in patients <60y Older patients >75y↑
Heer et al[37]	NA	NA	NA	2.5	3.3	NA	Yes	Women↑
Ottesen et al[33]	NA	NA	NA	3	3.8	NA	No	Women↑
Leizorovicz et al[30]	NA	NA	NA	1.2*	1.5*	<65y: 1.1 >65y: 1.4	Yes	Women↑ Older patients >65y↑
Lambrew et al[36]	2.5±0.1	3.1±0.2	NA	1.4	1.9	NA	No	Women ↑
Brophy et al[38]	NA	NA	NA	1.5	2.0	≤65y: 1.4 <65y: 2.0	No	Women↑
Magid et al[32]	NA	NA	NA	2.2	2.5	<65y: 2.0 ≥65y: 2.5	Age only	Women ↑ Older patients >65y↑
Carrabba et al[41]	NA	NA	NA	2.2	2.8	NA	No	Women ↑
Karlson et al[28]	NA	NA	NA	2.8	3.8	NA	No	Women ↑
O'Donnell et al[43]	NA	NA	NA	1.8	3.1	<65: 1.7 ≥65: 2.5	Yes	Women ↑ Older patients ↑
Bouma et al[14]	NA	NA	NA	1.92	2.3	35–44y: 2.0 45–54y: 1.9 55–64y: 1.8 65–74y: 2.1	Age & sex	Women ↑
Walsh et al[40]	NA	NA	NA	3.4	7.2	NA	Yes	Women ↑
Grace et al[17]	NA	NA	NA	1.5	1.8	NA	No	No age and sex differences
Dracup et al[15]	1.9±1.4	1.0±1.2	29–40y: 1.1 41–60y: 1.8 61–86y: 2.0	NA	NA	NA	No	No sex differences Older patients↑
Mckinkey et al[26]	1.9±1.3	1.8±1.2	29–60y: 1.1 41–60y:1.8 61–86y:2.0	NA	NA	NA	No	No sex differences Older patients

	Mean Delay (hours)			Median Delay (hours)				
First Author	Men (M)	Women (W)	Age groups	Men (M)	Women (W)	Age groups	Adjusted confounders	Conclusions
Mckinkey et al[26]	1.9±1.3	2.3±1.5	29–60y: 1.7 41–60y: 2.0 61–86y: 2.1	NA	NA	NA	No	No age and sex differences
Zerwic JJ et al[50]	NA	NA	NA	2	2.5	NA	No	No age and sex differences
Moser et al[25]	NA	NA	NA	3.1	3.1	≤55y: M:2.1; W:1.4 >56y: M:2.8; W:3.7	Yes	No age and sex differences Age and sex interaction
Bank et al[11,12]	NA	NA	<55y: 13.9 >55y: 13.3	3.5	4.4	<55y: 4.1 >55y: 4.1	No	No age and sex differences
Morgan et al[42]	NA	NA	NA	1.6	1.8	NA	No	NA
Rosenfeld et al[47]	NA	NA	NA	NA	4.3	NA	No	NA

NA: Not available;

* duration of patient delay

Table 3

Summary Of Selected Studies Reporting Distributions of Pre-hospital Delay According to Age and Sex

First Author	Men vs Women		Age Groups (%)	Adjusted confounders	Conclusions
Behar et al[13]	<6 hours (h): 62% vs 47%		NA	No	Women had increased delay (↑)
Sawaya et al[24]	≤3 h: 41.4% vs 27.3 % 3–6h: 9.6% vs 11.1% 6–12h: 8.1% vs 8.1 % >12h: 34.5% vs 48.5%		NA	No	Women ↑
Isaksson et al[19]	Age< 65 years (y) <2h: 41.2% vs 41.1% <4h: 20.2% vs 19.8% 4–24h: 27.7% vs 29.2% >24h: 10.9% vs 9.8%	Age≥65years 41.1% vs 40.2% 21.2% vs 20.2% 25.4% vs 27.1% 12.3% vs 12.5%	NA	No	Age<65y: no sex differences Age ≥ 65y: women ↑; Sex differences did not narrow over time
Kaplan et al[35]	<6h: 82% vs 80%		<6h: <65y: 81% >65y: 59%	No	No sex differences Age differences: marginally significant
Lovlien et al[21,22]	≤1h: 23% vs 20% 1–2h: 26% vs 27% 2–6h: 25% vs 30% >6h: 26% vs 22%		NA	No	No sex differences
Grace et al[17]	Delayed*: 84.4% vs 77.8%		NA	No	No sex differences
Lovlien et al[20]	Patient delay ≥2h: 36% vs 34% Health care delay:≥1h: 50% vs 50%		Health care delay: patients≤50 y <1h: 62%; >1h:37%	No	No sex differences
Bank et al[11]	Delayed*: 46% vs 54%		NA	No	No sex differences
King et al[49]	<1h: 26.7% vs 26.7%	<1h: mean age: 66.1y >1h: mean age: 61.2y	No		No age or sex differences
Ting et al[39]	≥12 h: 7.8% vs 10.5%	≥12 h: <60y: 71% 60–69y: 8.3% 70–79y: 10.1% >79y: 12.0%		NA	NA

NA: Not available;

* no definition of being delayed was reported

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Table 4

Summary of Studies Reporting Distribution of Age and Sex According to Different Pre-hospital Delay Cutoffs

First Author	<2 h	≥2h	2–4 h	<4h	>4h	2–6 h	<6h	≥6h	ORs (95%CI)	Adjusted confounders	Conclusions
Gibler et al[16]										Yes	Older patients
Age, means, y	60		63		63				≤40 y: 0.82(0.73–0.93) >40 y: 0.92(0.81–1.04) For 10 year ↑ of age		increased delay (↑) Women↑
Men (%)	75		69		68				W vs M: 1.08(1.05–1.11)		
Goldberg et al[7‖]										Yes	Older patients ≥65↑
Age group(%)											Women↑
<55y	33					26		25	1.00		
55–64y	24					21		20	NA		
65–74y	26					26		30	1.35(1.09–1.66)		
≥75y	17					27		25	2.16(1.69–2.77)		
Men (%)	6					71		67	M vs W: 0.79 (0.65–0.98)		
McGinn et al[10]										Yes	Older patients ≥65↑
Age group (%)											Women↑
≤65y				48	52				1.00		Sex differences
>65y				52	48				1.22(1.11–1.33)		narrowed over time
Men (%)				53	47				W vs M: 1.23(1.12–1.36)		
Ottensen et al[33]									>2h: 1.02(1.01–1.58)	Yes	Older patients ↑
Age group (%)									>6h: 1.01(1.00–1.02)		Women↑
<45y	5					4		3	For 1 year ↑ of age		
45–55y	15					11		11			
55–65y	26					22		22			
65–75y	31					34		33			
>75y	23					29		31			
Male (%)	73					67		64	M vs W >2h: 0.81 (0.70–0.93) M vs W >6h:0.85 (0.74–0.98)		
Maynard et al[34*]									Arrival 1h Women↑ Older age[†]: 0.86(0.83–0.88) M vs W: 1.26 (1.21–1.31)	Yes	Older patients↑ Women↑

First Author	<2 h	≥2h	2–4 h	<4h	>4h	2–6 h	<6h	≥6h	ORs (95%CI)	Adjusted confounders	Conclusions
Dracup et al[15]*									Arrival ≤ 1h: ≥60y: 1.00 <60y: 2.87	Yes	Older patients ↑
Sheifer et al[5]										Yes	Older patients↑
Age, means, y							75.4	76.0	1.01(1.00–1.01) For 5 year ↑ of age		Female, Blacks, diabetes interacted
Male (%)							55	51	NA		
Goldberg et al[8]										Yes	Older patients↑
Age group (%)											no sex differences
<55y	22	16					19	17	1.00		
55–64y	22	21					22	20	≥h: 1.39(1.11–1.74) ≥6h: 1.08(0.80–1.41)		
65–74y	29	29					29	30	≥2h: 1.49(1.19–1.85) ≥6h: 1.29(0.99–1.69)		
≤75y	27	34					30	33	≥2h: 2.07(1.64–2.61) ≥6h:1.55(1.17–2.05)		
Men (%)	64	59					67	61	W vs M: >2h: 1.05(0.91–1.21) W vs M: >6h: 0.90(0.76–1.07)		
Gurwitz et al[18]										Yes	No age differences
Age group (%)											Women↑
<55y							21	20	1.00		
55–64y							21	17	0.83(0.64–1.09)		
65–74y							28	26	0.95(0.74–1.22)		
75–84y							22	25	1.07(0.83–1.39)		
85y							8	12	1.40(1.00–1.95)		
Men (%)							65	57	W vs M: 1.24(1.04–1.48)		

||GRACE study included AMI and Unstable Angina (UA). Data presented in table 1 were for STEMI only, data for NSTEMI was not presented since they could not be separated from UA

†Age code: (1) ≤60y, (2)61–74; (3)≥75;

*no distribution of age and sex according to pre-hospital delay 1h was available