REVIEW ARTICLE

The Causes of Prehospital Delay in Myocardial Infarction

Cornelia Gärtner, Linda Walz, Eva Bauernschmitt, Karl-Heinz Ladwig

SUMMARY

Introduction: The elapsed time between the onset of symptoms and reperfusion is a critial determinant of the clinical course of patients with myocardial infarction. The patients' own decision time is the most important component of prehospital delay.

Methods: Selective literature review based on the references in a meta-analysis, complemented by a PubMed search on the expression "prehospital delay" in combination with "myocardial infarction," "acute coronary syndrome," "psychological factors," "gender," and "public campaign." A total of 73 papers addressing factors that influence prehospital delay were selected.

Results: The reasons for delays of more than 120 minutes in a patient with symptoms of myocardial infarction reaching the hospital are still not sufficiently elucidated. Patients' uncertainty about their symptoms, advanced age, and female sex are three factors that appear to be associated with longer delays.

Discussion: Factors influencing prehospital delay operate at the following levels: the perception of acute symptoms, the recognition of the importance of these symptoms, and the decision to call for help. Intervention trials should consider these levels in meeting the needs of clinically relevant subpopulations.

Klinik und Poliklinik für Psychosomatische Medizin und Psychotherapie des Klinikums rechts der Isar, Technische Universität München: Gärtner, Walz, Bauernschmitt, Prof. Ladwig, PhD, MD habil.

Helmholtz Zentrum München – National Research Center fro Environmental Health, Institute of Epidemiology: Prof. Ladwig, PhD, MD habil.

In acute myocardial infarction, the temporal window between the onset of symptoms and reperfusion is a critical determinant of the temporal course of treatment (e1–e3). Studies performed at the beginning of the thrombolysis era showed that the time taken up by the technical components of treatment is negligible by comparison (e4). A number of sources of delay were identified that were then dealt with individually to reduce delay times (e5). Yet the greatest part of the prehospital time (PHT) – as much as 75% of it – consists of the patient's own decision time (1, e6) (figure 1). Even when medical rescue services function perfectly at a high technical level, the subjective element of the onset of illness remains the major factor in the time expended until treatment is delivered.

Methods

The authors performed a review of the literature on the basis of the references of a current meta-analysis (e7), supplemented by a PubMed search between December 2006 and August 2007 on the on the expression "prehospital delay" in combination with "myocardial infarction," "acute coronary syndrome," "psychological factors," "gender," and "public campaign." This search revealed well over 100 articles published from 1990 to 2006 (and from 1984 for "public campaign"), which we considered with regard to the following subtopics: epidemiology, trends, sex differences, setting, previous illnesses, personality, and possibilities for prevention. The criteria for inclusion in this review were population access, population size, and the inclusion of a control group.

Results

Comparability of data

The data were rendered less comparable by variable methodology, differing segmentation of elapsed times, and differing inclusion criteria for the coronary patients (table). Patients who sustained an acute myocardial infarction (AMI) while in a state requiring acute resuscitation, or while already hospitalized, were not excluded from the analysis in all of the studies. Very short temporal windows should be viewed with some degree of skepticism, as it seems doubtful that patients' reports of the time their symptoms began will be accurate to the minute (e8).

The prevalence of prehospital delay

The patient's chance of survival is significantly higher if treatment is begun within the so-called "golden hour" after the onset of symptoms (e3, e9), but few patients actually reach the hospital within this period. In three large-scale studies (2–4), only 22% to 44% of patients arrived at a hospital within two hours of the onset of symptoms. According to data collected in the Augsburg (southern Germany) Myocardial Infarction Registry (e10), 40% of patients with acute myocardial infarction have a prehospital time longer than four hours; even if a six-hour criterion is used, 25% to 33% of patients still arrive at the hospital too late. The percentage of patients arriving more than 12 hours after the onset of symptoms has remained between 10% and 20% (1–6, e5–e11).

International studies have shown that a very wide range of prehospital times (a few minutes to several days) is a ubiquitous phenomenon (2–4, 7–11). The mean PHT in Germany is now 192 minutes (9).

The PHT in the United States, the United Kingdom, and Germany is much too high, but it is even higher in Asian countries: as reported by McKinley et al. (12), the median PHT is 3.5 hours (1.2 to 15.2 hours) in the USA and 2.5 hours (1.5 to 8.7 hours) in the United Kingdom, but 4.4 hours (1.8 to 13.3 hours) in South Korea and 4.5 hours (2.0 to 16.3 hours) in Japan.

Trends in prehospital delay times

The MITRAplus registry, which contains data on over 30 000 patients and accurately reflects the delivery of care in Germany, has shown a significant prolongation of the median prehospital time from 166 minutes in 1994 to 192 minutes in 2002 (9). The multicenter ARIC study in the USA, with data on 18 928 patients (7), showed that the PHT became no shorter over the observation period from 1987 to 2000, but the percentage of patients who called the emergency medical services increased significantly. The American NRMI-2 myocardial infarction registry, with data on 364 131 patients, also showed no change in median PHT from 1994 to 1997 (8). A similar result was obtained in the Worcester Heart Attack Study (3), which showed no improvement

FIGURE 1
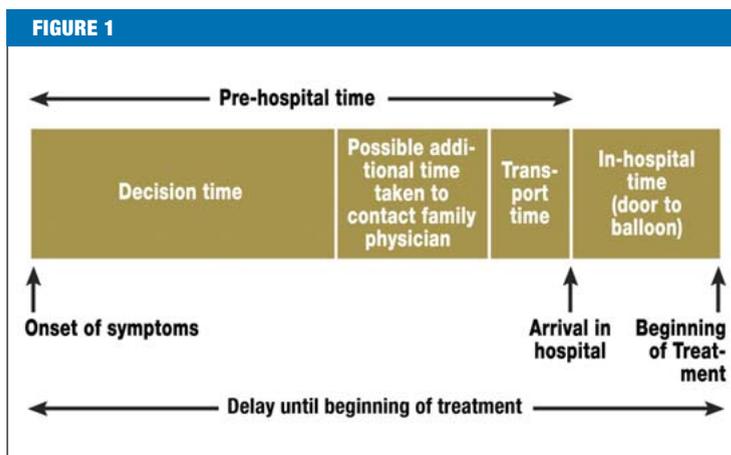
The temporal window between the onset of symptoms and the beginning of treatment in acute myocardial infarction

in the time from symptom onset to treatment in the city of Worcester, Massachusetts, from 1986 to 1997. Quite the reverse: the percentage of patients with a PHT exceeding six hours grew over this period from about 18% to more than 22% (*figure 2*).

Social and demographic factors

Age – With the exception of only a few studies including small numbers of patients (13, 14), most published studies show a significant association of older age with longer PHT; the median figure is approximately 0.5 hours (2, 3, 7–10, 15, e11, e12).

Sex – Studies on potential sex differences in the perception of symptoms of acute myocardial infarction have revealed little in the way of significant differences. Data from the Augsburg Myocardial Infarction Registry (e10) on 486 women and 1436 men showed no difference in the frequency of typical chest pain, but a significantly higher frequency of nausea, dyspnea, and fear of death among women. Cold sweats were common in both sexes without any significant difference in frequency between them, though the study of Goldberg et al. (e13) arrived at a different conclusion. A possible effect of

TABLE

Examples of varying types of study design

Study	Inclusion criteria	Latecomers	Method
NRMI-2 (1999)	Acute myocardial infarction	> 3 hours	Chart review
Sheifer et al. (2000)	Acute myocardial infarction	> 6 hours	Chart review
Ottesen et al. (2003)	Acute coronary syndrome	Not defined	Interview
McKinley et al. (2004)	Acute myocardial infarction	> 1 hour	Interview + Chart review
ARIC (2005)	Acute myocardial infarction	> 4 hours	Chart review
Taylor et al. (2005)	Undifferentiated chest pain	> 3 hours	Interview
GREECS (2006)	STEMI *1 / NSTEMI *2 / unstable angina pectoris	> 2 hours	Interview

*1 STEMI, ST-segment elevation myocardial infarction
*2 NSTEMI, non-ST-segment elevation myocardial infarction

FIGURE 2
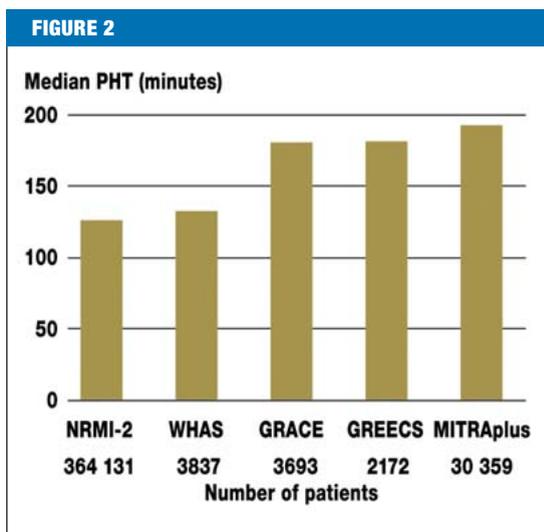
The increasing median pre-hospital time in recent population-based registry studies.
NRMI-2, National Registry of Myocardial Infarction 2, 1999; WHAS, Worcester Heart Attack Study, 2000; GRACE, Global Registry of Acute Coronary Events, 2002; GREECS, study of Pitsavos et al., Greece, 2006; MITRAplus, Maximal Individual Therapy in Acute Myocardial Infarction plus, 2006.

patient sex and symptoms on the PHT has been studied to date only by Meischke et al. (e14): although sex differences were found in the frequency of three different symptoms (women had cold sweats less frequently, but nausea and dyspnea more frequently), it was only the more frequent sweating among men that led to a shortening of the prehospital delay.

Nonetheless, most studies conclude that the PHT is significantly longer among women than among men (1–10, 15, e15). There are some indications that the difference has become smaller over the years (7). Moreover, it seems that a greater delay is often caused by the first physician contacted rather than by the patient herself (1, 7, e8). Moser et al. (16) found that age has only a minor influence on PHT in men, but a major one in women: women over age 55 had a PHT that was more than twice as long as that of younger women.

Social status – Smaller-scale studies (i.e., studies with fewer than 200 patients) have revealed no differences in PHT depending on social status (16, 17, e8), but larger studies indicate that patients with lower incomes (6, 14, e16) or with lower educational attainments (4, 7, 14, 18) have a longer PHT.

Clinical parameters and risk factors

Severity – Patients in cardiogenic shock after cardiac arrest arrive at the hospital sooner than others (2, 6, 15, 19, e15, e17). For these patients, the acute medical situation is so dramatic as to leave no room for subjective ambivalence. On the other hand, severity parameters such as the size of the infarct (15), enzyme values (13), ejection fraction, the number of occluded arteries (20), and the vital signs (16) do not seem to affect the PHT significantly.

Hypertension is associated with a longer PHT (2–5, 7, 8, 10), with a median of 2.2 hours as compared to 2.0 hours in normotensive patients (3). Three studies with smaller case numbers revealed no significant difference (1, 14, 21). One reason for this may be a less sensitive perception of pain in patients with hypertension as a risk factor for myocardial infarction (e18).

Diabetes – With a few exceptions (1, 14, 21), most studies have indicated that diabetes significantly predicts a longer PHT (2–4, 6–9). This may be due to the suppression of pain by diabetic neuropathy (e19).

Smoking – In three larger studies involving more than 2000 patients each (2, 4, 9), smokers had significantly shorter prehospital times than non-smokers. The reason for this is perhaps that the risk of myocardial infarction among smokers has been well publicized by the media (9).

The potential influence of body-mass index, hypercholesterolemia, and physical activity on prehospital times has only been investigated in the GREECS study (4); no significant effect was found for any of these factors.

Pre-existing heart disease

Angina pectoris – Patients with a prior history of angina pectoris tend to have a longer prehospital time (2, 3, 6, 19). Apparently, these patients have more difficulty identifying and attaching the proper significance to the chest pain of myocardial infarction. The ARIC study (7), however, found no effect of angina pectoris on the PHT, and the NRMI-2 study (8) and that of Kentsch et al. (18) even found that patients with prior angina pectoris arrived at the hospital earlier than others.

Previous myocardial infarction – Though one might imagine that patients who have previously sustained a myocardial infarction would arrive at the hospital more quickly in the event of reinfarction, this is by no means necessarily the case. The MITRAplus study (9) and a Swedish study with more than 2000 patients (10) showed no difference in PHT between patients with a first infarction and patients with a reinfarction. In the first study period of the Worcester Heart Attack Study (1986–1990), patients with reinfarctions actually took longer to get to a hospital (odds ratio 1.6 for a more than six-hour delay, as compared to patients with a first infarction) (22). A Danish study came to the conclusion that patients with a reinfarction have a markedly shorter PHT, while patients with a previous mechanical revascularization procedure interpreted their symptoms correctly but nevertheless had significantly longer decision times (1).

Previous revascularization or bypass operation – In most studies, these patients were found to arrive at the hospital sooner than others (2–4, 5–8, 15), perhaps because of the sensitization of their families and treating physicians by the previous events.

Contextual influences

Time of occurrence – Many studies have found no difference in PHT due to the time of day or the day of the week (11, 20–22, e20, e21), while others have found a shorter PHT at night (6, 19) or, alternatively, a longer PHT at night or on the weekend (2, 5, 9, e22).

Contact with family physician – Well under half of all patients call the emergency medical services first (5, 11, e23–e25); instead, many first contact their family physician. This prolongs the prehospital time (median, 120 minutes, compared to 74 minutes) (11, e23, e26, e27) *(box 1)*.

Home environment – Consultation of non-physicians for advice markedly prolongs the prehospital delay (18, 23); patients who do so have an odds ratio of 2.06 to 2.34 for a delay greater than one hour (11). Most patients ask their spouse for advice and 21% even speak with their children before calling a physician (e24). On the other hand, it may provide some degree of comfort to the patient to have someone else call the emergency medical team. A delegation of responsibility may be especially helpful when the patient's symptoms do not correspond to his or her own conception of a heart attack (17, e22).

According to some studies, patients who experience their first symptoms while at home tend to arrive at the hospital with a greater delay than others (1, 24, e16, e26). Other studies, however, have shown no difference (14, 16, 20, e20, e21). The presence of other persons seems not to influence the prehospital time (12, 13, 16, 20, 24, e16, e20, e21, e28). Patients that try to suppress their warning symptoms by self-medication or self-distraction (23, e24) have a roughly threefold elevation of relative risk for arriving late at the hospital (18).

The acute perception of symptoms

Pain pattern – Chest pain is the most common symptom of myocardial infarction, with a frequency of 80% to 95% (21, 24, e13, e28). Patients with the classic sudden, unexpected, and severe chest pain are the most likely to arrive at the hospital in good time (23). Radiating pain also shortens the PHT (17). The intensity of the pain has no significant effect on the PHT (1, 12, 16, 20, e16, e29, e30). The intensity of anginal pain was positively correlated with a shorter PHT only in the studies of Horne (17), Rawles (25), and Dracup (14).

Symptoms – Vague symptoms and non-specific complaints are significant predictors of a delay in the patient's decision time. Sweating occurs in about 65% to 75% of cases (24, e28) and tends to shorten the PHT (2, 14, 18, e18, e31). Excessive sweating after relatively mild physical exertion is likely to be interpreted as unusual and thus as a possible sign of serious illness (e31). Symptoms such as nausea and heartburn, which arise in 45% to 52% of patients (17, e28), lengthen the PHT (14, 24, e31). Shortness of breath, which arises in about 28% to 59% of patients (17, 21, e28), is an alarming symptom but is often misinterpreted and thus tends to prolong the PHT (2, 14, e20).

Previous knowledge – The patient's knowledge of the main symptoms of myocardial infarction, including atypical ones such as sweating, nausea, or dyspnea, leads to a shorter prehospital delay (12, 23, e20), though not in all studies (14, 24). Dracup et al. (14) found that the patient's knowledge of the possibilities for treatment shortened the PHT, but Ottesen et al. (1) found that

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BOX 1

Subjective reasons why some patients inform the family physician first about their medical emergency (myocardial infarction)

- The patient does not feel ill enough to call the emergency medical services (e24, e25)
- The patient believes the family physician is "on his or her side" (e22)
- The patient desires the family physician's permission to call the emergency medical services (e22)
- The patient believes calling the family physician first is the right thing to do, so that the family physician can then notify the emergency medical services (e22)

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knowledge about thrombolytic treatment made no difference to the PHT.

The patient's own interpretation of the symptoms – The patient's ability to interpret the symptoms correctly decisively determines his or her behavior. Patients who attribute their symptoms to a cardiac problem seek help more quickly (1, 13, 14, 16, 18, 20, 24, e30–e32). Only two smaller studies arrived at a different conclusion (e20, e28) *(box 2)*.

The complexity of interpretive behavior was made especially clear by Kentsch et al. (18) in their study of 739 patients with acute myocardial infarction. 44% of patients who realized that they were having a heart attack and were aware, at the same time, that heart attacks can be fatal, nonetheless took more than an hour to call for medical help. In a multivariate model, the following attitudes were found to contribute to these patients' delay in deciding to seek medical attention: "I wanted to wait and see first"; "I didn't take the symptoms
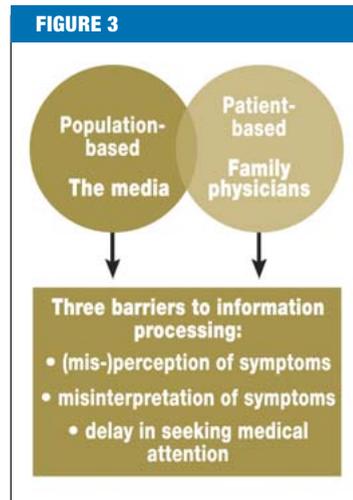

BOX 2

Delays caused by erroneous interpretation of symptoms

Some patients have symptoms of myocardial infarction, but fail to react appropriately, because they:

- do not consider the symptoms to be serious (e16, 18, 20, e23)
- have a "mismatch between symptom expectations and experience" (17)
- choose to wait and see whether the symptoms improve (12, 14, e16, 18, e23, e24, e26)
- do not want to be a burden on anyone (14, e16, 18, e22, e26, e48)
- find it unpleasant or embarrassing to seek medical help (12, 14, e16, 20, e22)
- ignore the symptoms for emotional reasons (18, e22)
- fear the consequences of obtaining help (e16, e48)

Goal-orientation in preventive strategies for the reduction of pre-hospital delay

FIGURE 3

change (e39–e44), among them the REACT study (e43) (n = 20 364), which was carried out from 1995 to 1997 in 20 American cities. Although persons living in the target areas of the public information campaigns were demonstrably better informed about the subject afterward, the PHT in the target areas was not shortened significantly in comparison to control areas. On the other hand, the previous fear that false-positive self-referrals to the hospital would become more common after such information campaigns, thereby incurring higher costs, was not substantiated (e39).

Discussion

On both the national and the international level, the pre-hospital time (PHT) is the most important factor leading to a temporal delay in the initiation of treatment for acute myocardial infarction. The studies that have been performed to date show that the most important factors influencing the PHT are the sex and age of the patient and the patient's misinterpretation of the symptoms. Empirical data on the effect of psychological mechanisms and coping strategies remain scarce at present.

One cannot yet draw a clear risk profile for "latecomers" that would be of use in everyday clinical practice and in patient education. There is still no theoretically well-founded and empirically confirmed basis for understanding patients' decisional behavior thus predicting their actions. There is a consensus, however, that general knowledge about the typical symptoms of heart attack is a necessary foundation of prevention but still does not suffice to prepare patients adequately for an acute crisis (e17).

In the future, the psychosocial and economic conditions of the population will have to be considered more closely, patients at high risk will have to receive greater individual attention, and more sex-specific patient education will have to be provided (e45). Preventive action will have to be tailored more specifically to the groups that are most at risk. It would be desirable to develop predictive algorithms for decisional behavior in groups with well-defined identifying features (e.g., age < 60; female sex; anxious-avoidant behavior style), so that individualized prevention strategies could be offered *(figure 3)*.

A further opportunity to identify patients at risk seems to be provided by observation of the prodromal phase of acute myocardial infarction. In the days preceding the acute event, many patients suffer increased irritability, depressive mood, unexplained fatigue, or anxiety (e46, e47). Physicians consulted because of such symptoms should think of the possibility of an impending myocardial infarction and take the corresponding steps to inform the patient about what to do in case this happens.

seriously"; "I didn't want to trouble anyone"; "The symptoms got better"; consumption of analgesics.

Fear of death – 35% of women and 20% of men experience the fear of death (a sensation of impending doom) during the acute infarction phase (11). In the study of Whitehead et al. (e33), 32.6% of women and 18.4% of men reported having experienced considerable worry and fear of death. Fear during the acute event significantly shortens the prehospital delay (16, 20, e28, e29).

Psychological factors

The psychological paradigms that would seem to have the greatest potential relevance to PHT are the concepts of denial and related types of operationalization, such as alexithymia (difficulty perceiving and expressing one's own feelings). Here, too, the findings are inconsistent: O'Carroll et al. (e30) found no effect of alexithymia on the prehospital delay, while Kenyon et al. (13) found that it significantly prolonged the prehospital delay. Prolongation has likewise been found to result from a hyperactive behavior style (type A behavior) (19) and from a fatalistic attitude to one's own health (e30).

In the study of Bunde and Martin (e31), which included 433 patients, a depressive mood was found to contribute significantly to a prolonged decision time. The only items that differed significantly between timely arrivers and latecomers had to do with fatigue, sleep disturbances, and exhaustion; thus, the correlation between depression and prehospital delay might reflect a difficulty mustering the energy required to call for help.

Opportunities for prevention

Most people know little about heart attacks. Many know that chest pain is an important symptom, but few can correctly name more than two further symptoms (e34). Thus, a number of studies have sought to answer the question whether prehospital delays might be shortened by public education in the media, public events, and special training. According to a review of ten studies on the influence of such efforts on the PHT (e35), four studies showed significantly shorter prehospital times than before the intervention (e36–e38), while six revealed no

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Corresponding author
Prof. Karl-Heinz Ladwig, PhD, MD habil.
Helmholtz Zentrum München
National Research Center for Environmental Health
Institute of Epidemiology
Ingolstädter Landstr. 1
85764 Neuherberg, Germany
ladwig@helmholtz-muenchen.de

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