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Pre-Hospital Delay in Older Adults with Acute Myocardial Infarction: The SILVER-AMI Study

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Abstract

Background/Objectives—Timely administration of anti-ischemic therapies improves outcomes in patients with acute myocardial infarction (AMI). Prior literature on delays in AMI care has largely focused on in-hospital delay ("door-to-balloon" time). Our objective was to identify factors associated with pre-hospital delay in a contemporary, national cohort of older AMI patients.

Design—Cross-sectional analysis from SILVER-AMI (ComprehenSIVe Evaluation of Risk Factors in Older Patients with Acute Myocardial Infarction), an observational study of older patients hospitalized for AMI.

Setting—94 U.S. academic and community hospitals.

Participants—2500 patients aged 75 or older hospitalized for AMI.

Measurements—Pre-hospital delay was defined as symptom duration ≥ 6 hours before hospital presentation and was obtained by patient/caregiver report during AMI hospitalization. Potential predictors of delay from the following domains (demographics, clinical presentation, comorbid conditions, function, and social support) were obtained through in-person assessment during the index hospitalization and medical record abstraction.

Results—Non-white race, atypical symptoms, and heart failure (HF) were significantly associated with delay (adjusted OR 1.54, p=0.002 for non-white race; adjusted OR 1.41, p=0.001 for atypical symptoms; adjusted OR 1.35, p=0.006 for HF).

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Ouellet, Chaudhry: Study concept and design. Tinetti, Chaudhry: Critical appraisal of methods and content expertise. Geda, Tsang: Acquisition of data. Ouellet, Murphy, Chaudhry: Analysis and interpretation of data. Ouellet: Drafting of manuscript. All authors: Revision for critical intellectual content and approval of manuscript.

Conclusion—In contrast with younger AMI populations, female sex and diabetes were not associated with delay in this older cohort. However, factors from multiple different domains (non-white race, atypical symptoms, and HF) were significantly associated with delay. These results can be used to tailor future public health efforts to encourage early presentation for older AMI patients.

Keywords

Risk factors; Pre-hospital delay; Myocardial infarction

Introduction

Among patients with acute myocardial infarction (AMI), longer ischemic time results in poor short- and long-term outcomes, specifically larger infarct size, increased rates of ischemic cardiomyopathy, and increased mortality.[1–6] Older adults are at increased risk for delays in revascularization after experiencing an AMI.[7–10] Many efforts to improve outcomes after AMI have targeted in-hospital treatment delays (i.e., “door-to-balloon time” strategies); however, total ischemic time also notably includes the pre-hospital period from the onset of symptoms to presentation to a healthcare setting. Unfortunately, the rates of pre-hospital delay remained relatively static through the 1990s and early 2000s.[8] Patients with pre-hospital delay are also more likely to experience in-hospital delays to effective treatments.[11] Therefore, reducing pre-hospital delay remains an important target for improving timeliness of AMI therapies such as revascularization and ultimately for improving clinical outcomes in older patients with AMI.

Previous studies identified a wide array of clinical risk factors for pre-hospital delay in AMI patients. Female sex,[7, 12–14] diabetes,[7, 8, 14, 15] and non-white race[7, 14] were associated most consistently with pre-hospital delay. These studies have largely either included a broad age spectrum without distinctly examining older patients[7, 8] or were restricted to younger populations.[12, 13, 15] This is problematic as older patients may face different challenges in timeliness of their response to symptoms than younger patients, including limitations in social support or mobility. The only large study focused on risk factors for delay in older adults, the Cooperative Cardiovascular Project, was performed over 20 years ago and included a relatively broad age range of older adults (patients were 65 or older).[14]

The objective of this study was to identify predictors of pre-hospital delay in a contemporary, national cohort of older AMI patients with rich demographic, clinical, functional, and social data. We utilized data from a cohort of 2500 patients 75 years of age and older hospitalized for AMI at 94 hospitals across the United States. The results of this study can be used to inform current efforts to improve the timeliness of older patients’ response to AMI symptoms.

Methods

The study population comprises the first 2500 patients enrolled in SILVER-AMI (ComprehenSIVe Evaluation of Risk Factors in Older Patients with Acute Myocardial Infarction), a prospective cohort study of 3000 older adults (age ≥ 75 years) hospitalized for

AMI (NIH/NHLBI R01HL115295). Details of the study's methods have been previously published.[16] Site coordinators screened hospital admission records to identify patients with AMI in accordance with the Third Universal Definition of Myocardial Infarction.[17] Exclusion criteria included initial troponin elevation > 24 hours after admission (to avoid enrolling patients with AMI secondary to in-hospital procedures), transfer from another hospital after a stay of > 24 hours (because of difficulty in reliably obtaining complete medical records from the initial hospital), death prior to enrollment, not speaking English or Spanish, and severe communication barriers (e.g., aphasia, lethargy, etc.). All study procedures were approved by the institutional review boards of Yale University and all study sites.

Analytic Sample Derivation

During the enrollment period of the first 2500 subjects, 8650 patients met inclusion criteria, i.e. age ≥75 and AMI by the Third Universal Definition of Myocardial Infarction.[17] Among those deemed ineligible due to exclusion criteria, 280 patients were excluded due to death before enrollment and 352 were excluded due to severe communication barriers. After study enrollment, only 46 patients were unable to complete the baseline assessment. Reasons for non-completion included poor clinical status, death, and post-consent refusal. For patients that did complete the baseline assessment, the mean time from admission to the baseline assessment was 3.4± 2.85 days.

Explanatory Variables

Twelve potential explanatory variables were selected a priori from the following domains: demographic characteristics, clinical presentation, comorbid conditions, pre-hospital disability, and social support. Older age, female sex, non-white race, heart failure, diabetes mellitus, and atypical symptoms were selected on the basis of prior literature suggesting associations with delay in younger cohorts[7, 8, 12–15]. Variables that we hypothesized could plausibly be associated with delay based on our experiences in clinical medicine were also included in the multivariable model. These included prior history of AMI, educational attainment and income (as measures of socioeconomic status), living alone, pre-hospital disability, and social support.

Data Collection

Local research staff conducted baseline in-person assessments during the index hospitalizations. During this baseline assessment, patients were asked a series of closed-ended questions relating to demographics, clinical presentation, social support, and self-reported pre-hospital disability. Data on medical history were captured via medical record abstraction.

Demographics

Age, sex, race, income, and educational attainment were selected as potential explanatory variables. Low income was defined specifically in the context of availability of funds to be used for healthcare, i.e., an affirmative answer to the question: "In the past year, have you

avoided obtaining any health care services because of cost?" Educational attainment was dichotomized into > 12 years versus ≤ 12 years.

Clinical Presentation

Clinical presenting symptoms were dichotomized into typical and atypical symptoms. As chest pain is by far the most recognized symptom of AMI,[18] we operationalized atypical symptoms as any constellation of symptoms which did not include chest pain or chest discomfort, consistent with previous literature.[19, 20]

Comorbid conditions

Diabetes mellitus and heart failure (HF) were selected as potential explanatory variable. As these covariates were of particular interest, summary comorbidity scores which include these diagnoses were not used to avoid potentially unstable estimates of effect.

Function

Participants were asked to recall their functional status thirty days before hospitalization. Pre-hospital disability was defined by impairment (i.e., requiring assistance) in at least one of the following basic ADLs: bathing, dressing, transferring, and short distance ambulation.

Social Support

Due to the potential importance of social support in making the decision to seek care, we selected two measures of social support: living alone and instrumental social support. Perceived support was evaluated by the shortened 5-item Medical Outcomes Study Social Support Survey.[21] Each item of the survey used the following prompt: "How often is each of the following kinds of support available to you if you need it? [Insert type of social support]. None of the time, a little of the time, some of the time, most of the time, or all of the time?". The five specific types of social supports addressed in this survey were: "someone to confide in or talk to about your problem", "someone to get together with for relaxation", "someone to help you with daily chores if you were sick", "someone to turn to for suggestions about how to deal with a personal problem", and "someone to love and make you feel wanted." We were particularly interested in the absence of support by persons who could physically be present, as this could most logically be linked with our outcome of delayed presentation. As such, low instrumental support was defined as selecting "some of the time", "a little of the time", or "none of the time".

Outcome

The primary outcome was pre-hospital delay of ≥ 6 hours from the time of symptom onset to hospital presentation. Delay was assessed by report of patient or caregiver at the time of enrollment as a categorical variable with the following categories: <1 hour, 1 to < 6 hours, 6 to < 12 hours, 12 to < 24 hours, 1 to < 3 days, 3 days to < 1 week, or 1 week or longer. The cutoff of 6 hours was chosen given evidence of increased mortality with ischemic times with this duration[2] and significant precedent in prior studies of pre-hospital delay.[14, 22–24]

Statistical Analysis

Unadjusted associations were assessed using bivariate logistic regression. Multivariable logistic regression was used to assess adjusted associations with pre-hospital delay. Model calibration was assessed with the Hosmer-Lemeshow goodness of fit test. Statistical significance was defined as a two-sided p-value < 0.05. Analyses were performed using SAS V9.3 (SAS Institute, Cary, NC).

Results

As shown in Table 1, the mean age of participants was 81.6 years, 44.7% of participants were female, and 10.7% were non-white. 659 patients (26.4%) had ST elevation myocardial infarctions (STEMI), while 1841 (73.6%) patients had non-ST elevation myocardial infarctions (NSTEMI). 42.1% (1053 of 2500 study patients) experienced the primary outcome of pre-hospital delay ≥ 6 hours. Patients with delay were more likely to be non-white, have co-morbid HF, and have atypical symptoms (Table 1).

Non-white race was associated with significantly higher odds of delay than white race, and the effect remained significant in the multivariate model (unadjusted OR 1.61, 95% CI 1.25–2.08, p<0.001; adjusted OR 1.54, 95% CI 1.17–2.01, p=0.002). Atypical symptoms and HF were also associated with delay, even when adjusted the other aforementioned covariates (unadjusted OR 1.43, 95% CI 1.18–1.73, p<0.001, adjusted OR 1.41, 95% CI 1.15–1.72, p=0.001 for atypical symptoms) (unadjusted OR 1.35, 95% CI 1.11–1.66, p=0.003; adjusted OR 1.35, 95% CI 1.09–1.68, p=0.006 for HF).

Overall, 21.4% of study patients (535 of 2500 study patients) presented with atypical symptoms, i.e. without chest pain. The five most common atypical symptoms were shortness of breath (49.1%), weakness/fatigue (31.5%), shoulder/arm pain (29.3%), indigestion (20.3%), and nausea (18.9%) (Figure 1). A significantly greater proportion of patients with typical symptoms correctly ascribed their symptoms to a cardiac etiology than those with atypical symptoms (56.4% vs. 26.6%, p <0.001).

Discussion

In this study of patients 75 and older hospitalized for AMI, pre-hospital delay was much more than common (42.1%) than in studies of younger AMI populations, in whom the reported prevalence ranges from 20% to 25%.[6–8] This highlights the importance of understanding risk factors for pre-hospital delay in older adults with AMI. Among the domains of potential risk factors assessed in our study, non-white race, atypical symptoms, and HF were independently associated with pre-hospital delay. Other factors previously found to be associated with pre-hospital delay in younger AMI populations, including female sex and diabetes mellitus were not significant predictors in this older population. These findings highlight both the continued role of racial disparities in timely presentation and the importance of atypical symptoms and common comorbid disease in older AMI patients.

This study has notable strengths in its examination of risk factors for pre-hospital delay. SILVER-AMI is a large, contemporary cohort of exclusively older adults with AMI with detailed information about both medical and non-medical characteristics. This study uniquely assesses multiple domains of potential associations with delay concomitantly (specifically demographic characteristics, clinical presentation, comorbid medical conditions, function, and social support).

There are several important issues to consider in interpreting our results. While risk factors from several domains were accounted for in the multivariable model, unmeasured confounders may have affected the study outcome. For example, information about pre-hospital cognitive status, which may have influenced delays in presentation, was unavailable. Furthermore, our results should be cautiously applied to populations that differ in key characteristics from our cohort. In this study, approximately 95% of patients lived within 30 miles of the presenting hospital and as such, our results may not generalize to populations in more geographically isolated areas. While similar in prevalence to other samples of community-dwelling older adults,[25, 26] a relatively small subset of this sample had pre-hospital disability (13.5%). For this reason, these results may not be applicable to patients with significant functional limitations, e.g. patients in nursing homes.

Our results show a strong association of non-white race with delay, even when adjusted for income and educational attainment. Previous studies have either included large age ranges[7] or were based on data from the 1990s.[14] It is notable that this association is still observed more than 20 years later despite significant public health efforts to reduce overall delays. This underscores the importance of disseminating information about the importance of timely presentation after AMI to non-white communities.

There are several potential reasons for the observed racial disparity in delays noted in our study. Prior studies have highlighted the potential role of income in changing care-seeking behavior[27] as well as disparities in health education in influencing delay.[28] In our study, however, non-white race was still a significant risk factor for delay even when adjusted for income and education. Furthermore, the observed racial disparity in our study is unlikely to be mediated by atypical symptoms, as there were no significant differences in the prevalence of atypical symptoms between white and non-white patients. Another possible explanation is that delay may be the result of distrust of the medical system by non-white patients due to historic and current inequities.[29] It appears that the underlying mechanism of the racial disparity in delay is likely multifactorial and will require a multifaceted approach to fully address.

Our study is also unique in demonstrating the association of atypical symptoms with delay in an older AMI population. Most previous studies of risk factors for pre-hospital delay did not address the role of atypical symptoms,[7, 12–14] and those that did have notable limitations. Two studies, one from the Worcester Heart Study and one from the Northern Sweden MONICA study found no role of atypical symptoms but used an extremely early definition of delay, i.e., ≥ 2 hours from symptom onset to care seeking.[8, 15] Others included only younger patients or a broad age range without assessment of age group specific effects.[30]

The only study focused on atypical symptoms exclusively in elderly patients (75 or older) did not control for demographic factors and was quite small (n=255).[31]

The association between atypical symptoms with pre-hospital delay is likely mediated in part by patients' and caregivers' understanding of the potential clinical significance of atypical symptoms. Previous studies have identified symptom misattribution as a risk factor for pre-hospital delay.[32, 33] In particular, previous studies have identified consistently better recognition of AMI by patients with chest pain.[33, 34] Our finding that 56.4% of patients with chest pain correctly identified a cardiac etiology while only 26.6% of patients with atypical symptoms did corroborates this.

The results of this study also show a significant association of HF with pre-hospital delay in older adults with AMI, similar to younger populations.[35] While HF is significantly associated with atypical AMI symptoms,[19] it was still an independent predictor when adjusted for atypical symptoms. This may be due to the increased prevalence of chronic angina in patients with HF,[36] making it difficult to differentiate AMI from chronic chest pain. This is of utmost concern as HF patients with angina experience higher risk of recurrent cardiac events.[36, 37]

In contrast with results in younger AMI populations, our study did not find a significant association between diabetes and delay. Prior studies have hypothesized that atypical symptoms account for much of the differences in delay between men and women and between diabetics and non-diabetics.[19] In our study, however, there was no difference in the prevalence of atypical symptoms between diabetics and nondiabetics and the difference between men and women was quite small (18.8% for men and 24.6% for women). It is possible that the high overall prevalence of atypical symptoms in older adults attenuates differences previously observed in younger populations based on sex and presence of diabetes.

Living alone and low instrumental social support also did not make independent contributions to the odds of delay. As many patients likely initiated emergency medical services for transportation, whether another person was physically available may have been irrelevant. Both measures of lower socio-economic status, i.e. low income and low educational attainment, also did not contribute significantly to the odds of delay. As AMI is truly a high acuity condition, cost concerns may not have played a significant role in patients' decisions to seek care. Finally, pre-hospitalization disability did not contribute to the multivariable model. Given that our study participants were overall quite functional (86.6% reported no ADL limitations), we may have been underpowered to detect an effect on delay.

Improving timeliness of presentation to care has potential to improve AMI outcomes in older patients. This study demonstrates that non-white race, atypical symptoms, and HF are associated with delays to hospital presentation in a contemporary cohort of older patients with AMI. Older patients are less likely to receive guideline-based AMI care,[38] even though evidence exists for continued benefit in higher-risk patients.[39] Importantly, pre-hospital delay has also been associated with lower likelihood of receiving reperfusion.[11] In order to

more effectively tailor our future public health efforts, we need to develop strategies to ensure timely presentation among older AMI patients, especially those experiencing atypical symptoms and those with HF. We also need to understand mediators of the observed racial disparity in timely presentation in order to tailor and improve educational messages about AMI to non-white communities. As pre-hospital delay continues to be commonplace in older AMI patients, a redoubling of public health efforts to promote timely presentation appears necessary.

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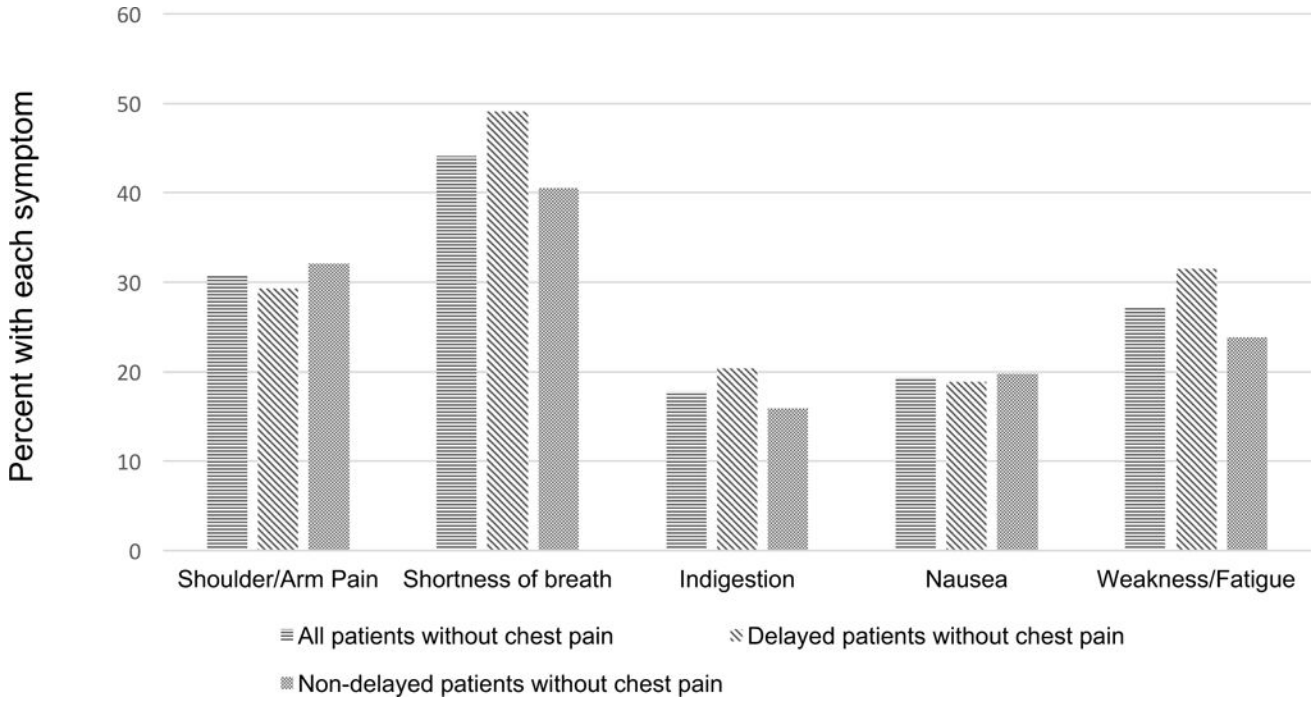

Figure 1.

Table 1

Baseline characteristics of study sample

	Pre-hospital Delay < 6 Hours N=1435	Pre-hospital Delay > 6 Hours N=1053	Total Study Population N=2500
Demographics			
Age	81.5+4.93	81.7+5.10	81.6+5.01
Female sex	44.0	46.0	44.7
Non-white race *	8.8	13.5	10.7
Low income	9.5	9.3	9.4
≤ 12 years education	56.1	59.6	57.6
Clinical Presentation			
Atypical symptoms *	18.9	25.0	21.4
Prior AMI	28.3	26.9	27.8
Comorbid Conditions			
Diabetes mellitus	35.8	37.4	36.6
Heart failure (HF) *	16.9	21.6	18.9
Function			
Pre-Hospital Disability	13.5	13.5	13.5
Social Support			
Living alone	37.0	40.1	38.2
Low instrumental social support	20.0	19.8	19.9

Values expressed are percentages for categorical values and mean with standard deviation for continuous variables.

* Indicates $p<0.05$ for difference between groups.

Table 2

Association of Predictors with Delay

	Unadjusted		Adjusted	
	Odds Ratio	**P value**	**Odds Ratio**	**P value**
Age (continuous)	1.01 (0.99–1.02)	0.368	1.01 (0.99–1.02)	0.480
Female sex	1.08 (0.92–1.27)	0.324	0.96 (0.80–1.14)	0.639
Non-white race*	1.61 (1.25–2.08)	<0.001	1.54 (1.17–2.01)	0.002
Low income	0.99 (0.75–1.30)	0.915	0.96 (0.72–1.27)	0.774
≤ 12 years education	1.15 (0.98–1.36)	0.083	1.11 (0.94–1.32)	0.938
Atypical symptoms*	1.43 (1.18–1.73)	<0.001	1.41 (1.15–1.72)	0.001
Diabetes mellitus	1.07 (0.91–1/26)	0.413	1.09 (0.91–1.30)	0.355
Heart failure (HF)*	1.35 (1.11–1.66)	0.003	1.35 (1.09–1.68)	0.006
Prior AMI	0.93 (0.78–1.11)	0.435	0.87 (0.72–1.06)	0.167
Pre-hospital Disability	1.00 (0.80–1.27)	0.972	0.92 (0.72–1.18)	0.511
Living alone	1.14 (0.97–1.34)	0.117	1.14 (0.95–1.36)	0.153
Low instrumental social support	0.99 (0.81–1.21)	0.913	0.98 (0.80–1.21)	0.876

Statistical significance denoted with*.

Calibration adequate by Hosmer-Lemeshow test: p=0.395.