Is Duration of Symptoms Predictive of Acute Myocardial Infarction?

Robert Solomon, MD, Richard Nowak, MD, Michael Hudson, MD, FACC, Michele Moyer, MS, Gordon Jacobsen, MS, and James McCord, MD, FACC

Abstract: Patient interviews regarding the duration of symptoms are commonly conducted when evaluating a patient with possible acute myocardial infarction (AMI) and are believed to distinguish between AMI and non-AMI symptoms. In a single center, 569 patients evaluated in the emergency department (ED) for possible AMI from May 2013 to April 2015 were prospectively studied. Patients in the ED were asked by trained research personnel about the duration of their predominant symptom. The final diagnosis of AMI was determined by an independent cardiologist and emergency medicine physician in accordance with the third universal definition of AMI. Disagreements were settled by a third physician (cardiologist) who reviewed the case. There were 44 (8%) AMIs and 484 (85%) patients had chest pain as their predominant symptom. In the 26 type 1 AMIs, the median symptom duration was 3.3 hours, while in the 18 type 2 AMIs it was 1.3 hours. AMI was not present if symptom duration was under 20 minutes and was more likely during the 20-59 minute period. In conclusion, clinical symptoms still play a prominent role in the evaluation of a patient with possible AMI in the ED. Duration of symptoms was not very helpful in distinguishing

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between patients with AMI and those with non-AMI, except in the time interval of 20-59 minutes. (Curr Probl Cardiol 2021;46:100555.)

Introduction

Accurate and timely recognition of acute myocardial infarction (AMI) is a major priority in the emergency department (ED). Chest pain is the most common symptom in AMI but clinical manifestations can vary, with atypical presentations leading to increased morbidity and mortality.[1] This is especially relevant in non-ST elevation myocardial infarction (non-STEMI), which comprises 67% of all patients with acute coronary syndrome.[1] Typical chest pain has been described as substernal chest pressure provoked by physical exertion, which is relieved by rest.[2]

On the other hand, various isolated atypical symptoms of AMI have also been described, including nausea (with or without emesis), dyspnea, diaphoresis, and lightheadedness among others (with most being more frequently reported by women).[3] It is commonly believed that a very short duration of chest pain is unlikely to be acute coronary syndrome, while 10-20 minutes is related to unstable angina and 20+ minutes is correlated with AMI.[4] As the previously listed atypical symptoms can be associated with a variety of different noncardiac processes, accurate and timely diagnosis in the ED is imperative in order to initiate appropriate therapy for AMI. Furthermore, the rapid exclusion of AMI is important as the evaluation of these patients can be both time consuming and costly.[5,6]

A variety of studies have reported that chest pain duration correlates with AMI size, but less is known about how presenting symptom duration relates to the presence or absence of AMI.[7] One study reported chest pain duration that exceeded 30 minutes increased the likelihood of an AMI diagnosis in women, but not in men.[8] Clinical decision-making is greatly influenced by symptom duration, with reperfusion therapy being recommended for STEMI within 12 hours of symptom onset.[9] Tools like the HEART score aid in the risk stratification of patients being evaluated for possible AMI and include clinical suspicion based on the patient's presenting symptoms.[10,11] The duration of these symptoms may be useful in distinguishing patients with AMI, from those without.[12] The goal of this study was to assess the diagnostic utility of symptom duration in those being evaluated for AMI.

Methods

This was a substudy of the REACTION-US study. The details of this study have been previously published, assessing the utility of a change in high-sensitivity cardiac troponin (hs-cTn) to rule out AMI.[13] This was a single-center, prospective diagnostic study involving 569 patients who were evaluated in the ED for AMI from May 2013 to April 2015. Inclusion criteria included age over 21 years old and clinical suspicion for AMI as evidenced by the ordering of cardiac troponin I (cTnI) by the treating ED physician. Exclusion criteria included trauma, conditions requiring immediate life-saving intervention, electrical cardioversion (within 24 hours of presentation), transfer from outside facilities, diagnosis of STEMI that led to immediate reperfusion and pregnancy or breast feeding. Patients could only be entered once into the study.

Upon presentation to the ED, trained research personnel inquired as to the approximate duration of the patient's predominant symptom while keeping in mind the variety of educational backgrounds present in an urban hospital setting. The final diagnosis of AMI and categorization as type 1 or type 2 was determined by an independent cardiologist and emergency medicine physician in accordance with the third universal definition of AMI by review of all pertinent medical records from the time of the subject's arrival, through the 30-45-day follow-up.[12] Clinical data were recorded in study-specific case report forms and disagreements between the adjudicators were settled by a third physician (cardiologist), who reviewed the case for final determination of AMI diagnosis. A necessary condition for AMI determination was at least 1 value of cTnI (Siemens Centaur System TnI Ultra assay on a Centaur XP system) greater than 40 ng/mL (99th percentile of the assay).

Follow-up was performed by study personnel via telephone call and subsequent medical record review between 30 and 45 days after hospital discharge in order to assess for major adverse cardiac events (AMI, revascularization procedure, and death). In the case where subjects or family members were unable to be reached, an electronic medical record and obituary search was done at the 12-18-month period. Patients were provided with written informed consent before enrollment. The institutional review board approved this substudy.

Statistical Analysis

The statistical software used for analysis was version 9.4 of SAS. The duration of symptoms was compared between the AMI and non-AMI patients, as well as between the types 1 and 2 AMI patients using the

Wilcoxon rank sum test. Symptom duration was cut into time intervals before being compared between the AMI and non-AMI patients using the Cochran-Armitage trend test. Patient characteristics were also compared between the AMI and non-AMI patients using the Student 2-sample *t* test for the normally distributed patient age, the chi-square test for categorical characteristics containing no expected cell counts less than 5, and the Fisher exact test for categorical characteristics containing 1 or more expected cell counts less than 5.

Fisher exact, chi-square, and Wilcoxon rank sum tests were used to further compare a variety of other symptom characteristics including symptom continuity and severity, among others. Chi-square and Fisher exact tests were utilized to compare 30-day AMI in each of the several different symptom duration groups. For all statistical data, *P* values less than 0.05 were considered significant.

Results

There were 575 patients with suspected AMI who were evaluated, with 4 subjects being excluded as they did not have cTnI measurements performed after the triage electrocardiogram and an additional 2 being excluded as they were duplicate enrollees. Thus, there were 569 patients in the final study group. Of the 569 patients, 44 (8%) were found to have an AMI with 26 (59.1%) type 1 non-STEMIs and 18 (40.9%) type 2 non-STEMIs. In those diagnosed with AMI, the median duration of symptoms was 3 hours (interquartile range 1-11.3 hours), as compared to 3.4 hours (interquartile range 1.4-11.3 hours) in the 525 non-AMI patients (P = 0.313). In the entire group, 484 (85.1%) endorsed chest pain as their predominant symptom.

Of the 44 AMI patients, 41 (93%) had chest pain as their predominant complaint and 34 (77.3%) had an elevated cTnI at baseline. While median symptom duration was 3.3 hours (interquartile range 1.7-13.5 hours) in the 26 type 1 AMI patients, it was 1.3 hours (interquartile range 0.7-4.9 hours) in the 18 type 2 AMI patients (P = 0.077), revealing no trend between the two types. Patients with AMI were more likely to have a history of prior AMI or revascularization (Table 1). Table 2 compares symptom duration (obtained a priori) in patients with and without AMI, ultimately finding AMI was not present if symptom duration was under 20 minutes and was more likely during the 20-59 minute period.

Table 1. Patient characteristics

Characteristics	Non-AMI (N = 525)	AMI (N = 44)	Comparison *P* value
Age, years (mean ± standard deviation)	55.5 ± 11.2	59.8 ± 9.3	0.015*
Black	437 (83.2)	36 (81.8)	0.809
Female	256 (48.8)	17 (38.6)	0.197
Hypertension	423 (80.6)	41 (93.2)	0.038*
Diabetes	149 (28.4)	15 (34.1)	0.422
Tobacco abuse	192 (36.6)	20 (45.5)	0.242
Congestive heart failure	126 (24)	11 (25)	0.882
Stroke/transient ischemic attack	90 (17.1)	7 (15.9)	0.834
History of AMI	144 (27.4)	24 (54.5)	<0.001*
History of revascularization (percutaneous coronary intervention, coronary artery bypass graft)	115 (21.9)	25 (56.8)	<0.001*

AMI, acute myocardial infarction.
Values are N (%).
*Denotes significance.

While chest pain was the primary symptom for 484 (85.1%) patients, other reported symptoms included shortness of breath for 50 (8.8%), palpitations for 14 (2.5%), syncope for 6 (1.1%), dizziness/lightheadedness for 6 (1.1%), epigastric/abdominal pain for 5 (0.9%), back pain for 1 (0.2%), arm/shoulder pain for 1 (0.2%), vomiting for 1 (0.2%), and weakness for 1 (0.2%). Table 3 reveals continuous primary symptoms were appreciated less often in AMI patients (P = 0.068). Out of the 569 patients, 7 (1.2%) died within 30-45 days, with 6 (1.1%) being in the group of 525 non-AMI patients and 1 (2.3%) in the group of 44 AMI patients (P = 0.433).

Table 2. Association of primary symptom duration and AMI

Primary symptom duration	AMI n = 44	Non-AMI n = 525	*P* value
0-19 minutes (N = 19)	0 (0)	19 (3.6)	0.386
20-59 minutes (N = 70)	11 (25)	59 (11.2)	0.008*
1-2.9 hours (N = 179)	11 (25)	168 (32)	0.337
3-5.9 hours (N = 95)	7 (15.9)	88 (16.8)	0.884
6+ hours (N = 206)	15 (34.1)	191 (36.4)	0.761

AMI, acute myocardial infarction.
Values are n (%).
*Denotes significance.

Table 3. Symptom comparison results for AMI vs non-AMI patients

Variable	AMI final diagnosis		Comparison *P* value
	No (N = 525)	Yes (N = 44)	
Continuous primary symptom	278 (53)	17 (38.6)	0.068
Sudden onset of the primary symptom	341 (65)	26 (59.1)	0.435
Primary symptom severity (scaled from 0 to 10)	8 (7-10)	8 (7-10)	0.686
Hours from symptom onset to presentation	8.6 (2.3-38.7)	10.9 (1.9-47.6)	0.911
Hours from start of longest symptom duration to presentation	3.4 (1.4-11.3)	3 (1-11.3)	0.313

AMI, acute myocardial infarction.
Values are n (%) or medians (interquartile range).

Discussion

It is uncertain whether a patient's description of their presenting symptoms contributes significant enough diagnostic and prognostic data to electrocardiogram and biomarker results to ultimately influence medical practice. Although one may initially be inclined to associate symptom duration with particular cardiovascular pathology, our study demonstrates that symptom duration poorly distinguishes AMI from non-AMI patients. In this cohort, short symptom duration (<20 minutes) appears to support aforementioned commonly held beliefs that such presentations are useful to exclude AMI. However, it ultimately is not significant and included only 3% of ED patients, suggesting those with short symptom durations are unlikely to even present for medical evaluation. The duration of symptoms may be of marginal diagnostic utility in those with symptom duration of 20-59 minutes, as statistically AMI was most prevalent (15.7%) in this range.

Aside from symptom duration, other features including continuous symptoms, sudden symptom onset and symptom severity were unable to differentiate AMI and non-AMI patients. Future investigations would likely benefit from further inquiry in regards to symptoms including intermittent nature, time of onset, and prodrome. "Typical" symptoms such as chest tightness, worsening pain with exertion and radiation to the arms have been associated with coronary ischemia and AMI.[14] Physicians often attribute these symptoms to a thrombotic source for myocardial

supply demand mismatch (type 1 AMI), rather than causes other than CAD (type 2 AMI). However, our findings indicate shorter symptom onset for the latter, a peculiar fact likely complicated by the multiple factors which could be the source of its etiology on any presentation (sepsis, major noncardiac surgery, vasospasm, etc.) and worthy of further investigation in future projects.[12]

Our findings largely suggest that unless a patient's description of symptom duration falls within 20-59 minutes, it is unlikely to be useful in the diagnosis of AMI. Since patient history often provides variable benefit and atypical symptoms are not always universally recognized, a broad approach is essential to identify AMI. While it is easy to assess cardiac markers in scenarios where typical symptoms are present, the decision on whether to check cTn levels in atypical cases is more difficult as it relates to efficient resource utilization to rapidly and effectively evaluate patients.[15] Many ED providers across the nation recognize the potential danger that comes with atypical presentations of AMI, including the increased morbidity and mortality that can result from a missed diagnosis, prompting them to more broadly utilize cTn (14% of all ED patients).[16]

In addition, data continue to emerge regarding hs-cTn and its utility, serving as a new potential tool for ED physicians to better manage an already diagnostically challenging population.[17] The aforementioned tools along with algorithms (HEART score, Emergency Department Assessment of Chest Pain Score, etc.) that incorporate components of the history, electrocardiogram findings, and cardiac markers are more helpful in determining the prognosis of a patient and assisting in triage decisions.[10,11] However, our results demonstrate that even with the methods mentioned above, patient's subjective histories can distort our hypotheses and ultimately may impact the accuracy of risk stratification scores.

Limitations

This investigation was a single-center study with a relatively low number of AMI patients enrolled, which can limit its ability to be extrapolated to other communities. Hs-cTn was not used to define AMI in this study, although new data continue to emerge regarding its utility in rapidly triaging potential cases of AMI, including early rule in/rule out to help eliminate the need for further risk stratification tools.[15,17] The relationship between duration of symptoms and the diagnosis of AMI may have been different if hs-cTn were used. Additionally, it is understood that patient history is both subjective and susceptible to variability (especially in

regards to symptom timeline) throughout a hospital encounter as patients are interviewed by different medical team members.

Conclusion

Clinical symptoms still play a prominent role in the evaluation of a patient with possible AMI in the ED. We found that the duration of symptoms was not very helpful in distinguishing between patients with AMI and those with non-AMI, except in the time interval of 20-59 minutes. A variety of factors, not only just symptom duration, must be taken into account to properly triage a patient suspected of having an AMI with the understanding that patient history is likely to influence risk stratification scores and therefore one's medical conclusion and treatment plan. Continued medical advancements (including more prevalent use of objective factors such as hs-cTn) will only serve to aid healthcare providers as we seek to more efficiently identify and appropriately treat clinically significant pathology.

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