

RESEARCH LETTER

# Association of Previous Myocardial Infarction and Time to Presentation With Suspected Acute Myocardial Infarction

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**A**cute myocardial infarction (AMI) remains the leading cause of death worldwide.<sup>1</sup> As “time is muscle”, major efforts were undertaken to address patient and system delays and facilitate early diagnosis and revascularization in as many patients with AMI as possible.<sup>2,3</sup> Little is known about the impact of medical factors on patient delay. As patient education and patient empowerment to appropriately react to acute chest pain suggestive of AMI are key components in post-AMI cardiac rehabilitation programs, we hypothesized that because of the impact of these educational programs on actual patient behavior, patients with prior AMI would have shorter delays when again presenting with suspected AMI compared with patients without prior AMI.<sup>4</sup>

This hypothesis was tested in a prospective, multicenter study, including patients presenting with acute chest discomfort to 12 emergency departments (EDs) in 5 countries (ClinicalTrials.gov registry, NCT00470587). The study was approved by local ethic committees. Written informed consent was obtained from all patients.<sup>2</sup> Times of chest pain onset (CPO) and chest pain maximum were prospectively assessed by study physicians. Patient delay, as quantified by time from CPO to the ED (CPO-ED) was the primary

outcome measure. Time from chest pain maximum to ED presentation was the secondary outcome measure. Time of ED presentation was the time of first vital sign documentation in the ED. Two independent cardiologists adjudicated the final diagnosis, according to the universal definition of AMI.<sup>2,3</sup> Patients on long-term dialysis were excluded, according to the study protocol. Sensitivity analyses explored the impact of a history of coronary artery disease (CAD) with or without prior AMI, the impact of sex, and the final adjudicated diagnosis underlying acute chest discomfort (AMI versus other causes). Differences between groups were assessed using Kruskal-Wallis rank-sum test for continuous variables and  $\chi^2$  or Fisher exact test for categorical variables. The 95% CIs of proportions were constructed using bootstrap. The data have not been made publicly available, but are available from the authors on reasonable request.

From April 2006 to April 2018, 6649 patients, 33% women, were eligible for this analysis. Of these patients, 1515 (23%) had a history of prior AMI, and 606 (9%) had a history of CAD, but no prior AMI.

CPO-ED was comparable in patients with and without prior AMI (median, 5.0 [interquartile range {IQR},

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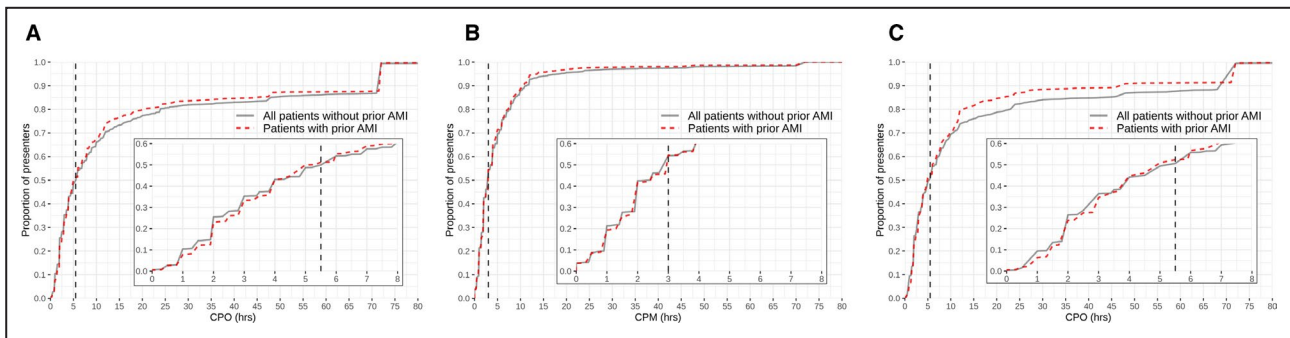
\*A complete list of the APACE Investigators can be found in the Appendix at the end of the article.

<sup>†</sup>Dr Troester and Dr Strebel contributed equally to this work and are co-first authors.

For Sources of Funding and Disclosures, see page 3.

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**Figure.** Cumulative distribution curve of patient delay of patients with vs without prior acute myocardial infarction (AMI), quantified as time from chest pain onset (CPO) to presentation to the emergency department (ED) (A), time from chest pain maximum (CPM) to presentation to the ED (B), and time from CPO to presentation to the ED in the subgroup of patients with an adjudicated final diagnosis of AMI (C).

\*Vertical line denotes the overall median.

2.5–13.0] hours versus 5.8 [IQR, 2.0–17.5] hours;  $P=0.86$ ; Figure [A]). Similarly, time from chest pain maximum to ED presentation was comparable in patients with and without prior AMI (median, 3.0 [IQR, 1.5–6.0] hours versus 3.0 [IQR, 1.5–6.0] hours;  $P=0.99$ ; Figure [B]). Also, both patient groups with and without prior AMI had comparable rates of ED admission by the ambulance (17% [95% CI, 15.0%–18.8%] versus 16% [95% CI, 14.5%–16.5%];  $P=0.23$ ). Sensitivity analysis revealed similar findings for the comparisons of patients with a history of CAD (with or without prior AMI) versus patients without CAD (eg, CPO-ED was comparable in patients with prior CAD versus patients without prior CAD (median, 5.5 [IQR, 3.0–13.0] hours versus 5.5 [IQR, 2.0–18.0] hours). Similarly, sensitivity analysis addressing the possible impact of sex (eg, CPO-ED in women with prior AMI [median, 6.0 [IQR, 3.0–14.0] hours] versus women without prior AMI [median, 6.0 [IQR, 2.0–18.0] hours]) and the final adjudicated diagnosis on CPO-ED, restricting the analysis to patients with an adjudicated diagnosis of AMI, confirmed the main findings. In this subgroup, CPO-ED was comparable in patients with prior AMI versus patients without AMI (median, 5.0 [IQR, 2.5–12.0] hours versus 5.5 [IQR, 2.0–14.0] hours; Figure [C]).

Quantifying the overall impact of an extensive list of medical factors on CPO-ED, multivariable binary logistic regression, including all univariable significant medical factors for the prediction of late presentation (defined as above the median of 5.5 hours in this study), showed low accuracy (area under the receiver-operating characteristic curve of 0.66 [95% CI, 0.65–0.67]).

These findings reject our hypothesis and have important clinical implications. The impact of post-AMI educational programs specifically, and medical factors in general, on CPO-ED during subsequent acute chest discomfort episodes seems much smaller than previously thought.<sup>4</sup> These findings also extend and support observations that many patients with prior AMI do

not perceive themselves as being at an increased risk of having another AMI. In addition, nonmedical factors, including sociodemographic aspects, seem to play an important role in the decision of seeking medical help.<sup>5</sup>

Two main consequences emerge from these findings. First, post-AMI educational programs need to intensify efforts aiming at increasing the implementation efficacy of the theoretical content of AMI symptom recognition and the “time is muscle” concept. This likely should include methods to better address symptom denial. Second, as nonmedical factors seem to be important contributors to CPO-ED, efforts aiming to explore and possibly mitigate them should be intensified.

In conclusion, patients with prior AMI do not present earlier to the ED when having a subsequent acute chest pain episode suggestive of AMI compared with patients without prior AMI, irrespective of sex and the final adjudicated diagnosis (AMI versus other diagnoses).

## APPENDIX

### APACE Investigators

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