Can family history of premature coronary artery disease be a risk factor for clinical outcomes in patients with acute myocardial infarction?

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Survivors of acute myocardial infarction (AMI) face a substantial excess risk of further cardiovascular events, including increased mortality. The prognosis varies markedly according to the presence of adverse risk factors. Risk stratification of patients with AMI begins upon presentation and is a continuous process to predict those who are at high risk for further ischemic events and who are at increased risk after discharge. Several risk scores have been developed over the past decade to assess short- and long-term outcomes after AMI. The most widely used is the Thrombolysis in Myocardial Infarction (TIMI) risk score to predict 14- to 30-day mortality [1]. The Global Registry of Acute Coronary Events (GRACE) risk score is an alternative model that can be used to estimate in-hospital and 6-month mortality following acute coronary syndrome (ACS) which may have a slightly higher predictive value than that of the TIMI score [2]. In particular, the GRACE 6-month postdischarge model (age, history of heart failure, history of myocardial infarction, heart rate, systolic blood pressure, ST segment depression, initial serum creatinine, elevated cardiac enzymes, no percutaneous coronary intervention [PCI]) is a robust tool for predicting long-term clinical outcomes in patients with ACS and has been demonstrated to predict mortality for up to 4 years with good accuracy [3]. These risk factors could be very useful for guiding postdischarge care such as optimal medical therapy.

Family history of premature coronary heart disease (<55 years in first-degree male relatives and <65 years in female relatives) is a traditional risk factor for future coronary artery disease (CAD) [4]. Depending on the definition used, family history confers a relative risk for developing CAD that ranges from two to 12 times that in the general population. However, there is a lack of evidence as to whether a family history of CAD has prognostic implications for the family history of patients with AMI [5,6].

In concert with these studies, Kim et al. [7] in this issue of The Korean Journal of Internal Medicine reports the impact of family history of premature CAD on clinical outcome in patients with AMI. A cohort of 11,612 consecutive patients (male 8,132 [70%], 62.7 ± 12.6 years old) with AMI from the Korea Acute Myocardial Infarction Registry (KAMIR) conducted during November 2005 to 2008 was analyzed.
KAMIR, launched in November 2005, is a Korean prospective multicenter data collection registry that reflects real world treatment practices and outcomes in Asian patients presenting with AMI. The registry consists of 50 community and teaching hospitals with facilities for primary PCI and on-site cardiac surgery. In the study, 727 patients with a family history of premature CAD were compared to 12,885 controls. The patients with a family history were younger and included more male patients. Male patients with a family history included more current smokers and individuals with poor lipid profiles. During about 1 year of clinical follow-up (median, 341 days; interquartile range, 36 to 388 days), 75 patients had composite major adverse cardiac events (MACEs), resulting in 22 cardiac deaths. Using multivariate analysis, family history was related to the risk of MACEs (hazard ratio [HR], 1.41; \( p = 0.009 \)) and cardiac death (HR, 1.56; \( p = 0.080 \)). In a subgroup analysis, family history had negative prognostic implications for females (composite MACEs, \( p = 0.057 \)) and a low-risk subset group (cardiac death, \( p = 0.008 \)). Therefore, the authors concluded that family history might be an independent prognostic predictor in females and in a low-risk subset of patients with AMI.

However, there are some limitations and unanswered questions in the study. First, a 6.3% family history reporting rate is relatively low compared to other studies (Western 15%, other Asian ethnic 15.6%) [8,9]. This could reflect a truly low incidence of a family history of CAD or could be related to ignorance of the implications of a family history of premature CAD. Second, the authors did not include known risk factors that affect the clinical outcome of patients with AMI in the multivariate analyses. The clinical outcome after AMI is worse in patients with larger infarct size and more comorbidities and mainly affects the appropriate reperfusion strategy as well as the adjunctive use of multiple medical therapies. Although epidemiological factors (age, sex, body mass index, hypertension, diabetes mellitus, dyslipidemia, and current smoking), ejection fraction, and estimated glomerular filtration rate were used, the authors did not include several important clinical and angiographic factors in the multivariate analyses. For example, KAMIR risk score (age, Killip class, serum creatinine, performance of PCI, left ventricular ejection fraction, and admission glucose) was used to assess clinical outcomes of patients with AMI in the KAMIR [10]. These risk factors were not included in the multivariate analyses of the study. Third, the authors did not describe the reason for negative prognostic implications between family history of premature CAD and long-term clinical outcome of AMI.

Despite the aforementioned limitations, this report provides useful information on the significance of family history as a risk factor in the setting of secondary prevention. The study emphasizes the fact that family history may be a prognostic predictor for patients with AMI, particularly females and the low-risk subset group. This conclusion might be helpful when assessing individual risk strategies for treating AMI survivors with a family history. Further study might be helpful to reveal the prognostic implications of a family history in a variable risk stratification system.

Conflict of interest
No potential conflict of interest relevant to this article is reported.

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