

Prognostic value of flow-mediated dilatation following myocardial infarction

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Abstract

Background: Risk stratification for subsequent cardiovascular events following a myocardial infarction (MI) is an important area of research. Previous findings indicate flow-mediated dilatation (FMD) may be a valuable prognostic indicator. This study investigates the prognostic value of FMD in patients suffering an uncomplicated MI.

Methods: One hundred and seventy nine post-MI patients [110male/69 female, mean age: 64.8 ± 10.0 years, ejection fraction: $51.9 \pm 12.2\%$] were included in this analysis. Ultrasound images of the brachial artery were used to determine FMD following reactive hyperemia. Subjects were tracked for subsequent cardiovascular events [myocardial infarction, heart failure, additional interventions (percutaneous coronary intervention, coronary artery bypass)] following data collection via medical chart review.

Results: There were 45 subsequent cardiovascular events during a mean tracking period of 13.7 (± 9.5) months. Receiver operating characteristic (ROC) curve analysis revealed a diagnosis of diabetes (ROC area: 0.67, $p=0.001$, 95% confidence interval: 0.58–0.77) and percent change in arterial diameter (ROC area: 0.63, $p=0.01$, 95% confidence interval: 0.53–0.73, optimal threshold: $\leq/\geq 4.5\%$) were prognostically significant. Kaplan–Meier analysis revealed the event-free survival rate for subjects without diabetes and an arterial diameter change $>4.5\%$, without diabetes and percent change in arterial diameter $\leq 4.5\%$, with diabetes and percent change in arterial diameter $>4.5\%$ and with diabetes and percent change in arterial diameter $\leq 4.5\%$ was 88.7%, 78.4%, 67.7% and 38.5%, respectively (Log-rank: 24.9, $p<0.0001$).

Conclusions: Non-invasive FMD is a potential risk factor after MI and may add information to conventional risk stratification. This will need to be tested in further studies.

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Keywords: Risk factors; Brachial artery; Ultrasound

1. Introduction

Individuals suffering a myocardial infarction (MI) are at variable risk for subsequent cardiovascular events. Tradi-

tional risk factors, such as hypertension, dyslipidemia and diabetes, assist in partially explaining the level of risk for future cardiovascular events in post-MI patients [1]. While prognostically important, traditional risk factors do not explain all of the variance for risk of future events. The search for other easily obtainable prognostic markers is therefore an important area of study.

Endothelial function is an important component of cardiovascular health that can be influenced by several factors including oxidative stress and a reduced availability of nitric

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oxide [2]. The most common assessment of endothelial function is through flow mediated dilation (FMD) in a peripheral artery via ultrasound [3,4]. Several previous investigations have found peripheral FMD to reflect coronary arterial function [5] and be prognostically valuable [6,7]. To date, FMD has been shown to predict cardiac events in a heterogeneous group of subjects with cardiovascular disease (coronary artery disease, cardiomyopathy, valvular disease, etc.) [6] and peripheral artery disease [7]. A lower FMD has also been shown to predict in-stent restenosis in patients who have undergone a percutaneous coronary intervention [8–10] and carotid plaque in individuals with no prior history of cardiovascular disease [11]. The present investigation expands upon this area of research by examining the added prognostic value of FMD to traditional cardiovascular risk factors in a group of patients who have suffered an uncomplicated MI.

2. Methods

This is a prospective analysis of consecutive post-MI patients who were followed until the study closing date (June 2006) or three years after enrollment. One hundred and seventy-nine consecutive subjects (110 male/69 female, mean age: 64.8 ± 10.0 years, ejection fraction: $51.9 \pm 12.2\%$) participated in this analysis. All subjects had suffered an uncomplicated MI (20% STEMI/80% NONSTEMI, no hemodynamic or arrhythmic complications) and were studied within 5 days post-event and prior to discharge from San Paolo hospital in Milan, Italy. All subjects underwent successful revascularization following their initial uncomplicated MI. Subjects were tracked for subsequent cardiovascular events [myocardial infarction, heart failure, additional interventions (percutaneous coronary intervention, coronary artery bypass)] following data collection via medical chart review. Subject outcome was assessed by hospital follow-up. In subjects suffering a subsequent cardiovascular event, only time to the first event was considered for this analysis. All subjects gave written informed consent prior to participation in this study. The ethical review board at San Paolo hospital approved the study protocol.

3. Vascular endothelial FMD assessment

FMD studies were performed as described previously [12]. In brief, brachial diameter and flow velocity were determined in the control state, during arrest of forearm circulation, and during reactive hyperemia (Q Lab Software; Philips Medical Systems; The Netherlands). Measurements were started after the patient had remained relaxed for at least 15 min on the table, until heart rate varied by no greater than three beats per minute in different minutes. Then, the cuff was inflated for 5 min and a second scan was taken for 90 s after cuff deflation with measurements taken 15, 30, 45, 60 and 90 s following deflation. Maximal increase in arterial diameter occurred 30 s after release of the occluding cuff,

and was taken as FMD. Images were stored on a video format and were then analyzed with image analysis software.

4. Echocardiography

Transthoracic two-dimensional echocardiography was performed by current methods. Left atrial dimensions, left ventricular end-systolic and end-diastolic chamber dimensions and left ventricular volumes, by the area-length method (to measure ejection fraction), were quantitated by standard techniques [13].

5. Statistical analysis

Unpaired *t*-testing and chi-square analysis assessed differences in continuous and categorical variables of interest between subjects who were event free and those who suffered a cardiovascular event during the tracking period. Receiver operating characteristic (ROC) curve analysis was used to assess the prognostic characteristics of age, ejection fraction, blood flow mediated vasodilation, percent arterial diameter change, diagnosis of hypertension, systolic blood pressure, diastolic blood pressure, diagnosis of diabetes, total cholesterol, blood glucose concentration and pharmacologic interventions. Variables having significant prognostic classification schemes were further assessed using univariate and multivariate Cox regression and Kaplan–Meier analyses. For the multivariate Cox regression, the forward stepwise method was employed with entry and removal values set at 0.5 and 0.10, respectively. Statistical tests with a *p*-value < 0.05 were considered significant. A statistical software package was used for all analyses (SPSS 14.0, Chicago, IL).

6. Results

None of the patients were lost during follow-up. There were 45 subsequent cardiovascular events during a mean tracking period of $13.7 (\pm 9.5)$ months. The annual event rate was 18.6%. Twenty subjects suffered another myocardial infarction, 10 underwent a subsequent revascularization procedure (4 coronary bypass grafts/6 percutaneous coronary interventions), seven subjects suffered a cerebral vascular event and seven were admitted for decompensated heart failure. Unpaired *t*-test and chi-square test results are presented in Table 1. Of the continuous variables, subjects suffering a cardiac event during follow-up had significantly higher fasting blood glucose level compared to subjects who remained event-free. With respect to categorical variables, a significantly higher percentage of subjects suffering a cardiovascular event during follow-up were previously diagnosed with diabetes and hypertension. Furthermore, a significantly higher percentage of subjects suffering a cardiovascular event were prescribed an ACE inhibitor.

Receiver operating characteristic curve analyses revealed a diagnosis of diabetes and percent arterial diameter change

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