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The predictive value of $CHADS_2$ risk score in post myocardial infarction arrhythmias — A Cardiac Arrhythmias and RIsk Stratification after Myocardial infArction (CARISMA) substudy☆

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ABSTRACT

Background: Previous studies have shown substantially increased risk of cardiac arrhythmias and sudden cardiac death in post-myocardial infarction (MI) patients. However it remains difficult to identify the patients who are at highest risk of arrhythmias in the post-MI setting. The purpose of this study was to investigate if $CHADS_2$ score (congestive heart failure, hypertension, age ≥75 years, diabetes and previous stroke/TCI [doubled]) can be used as a risk tool for predicting cardiac arrhythmias after MI.
Methods: The study included 297 post-MI patients from the CARISMA study with left ventricular ejection fraction (LVEF) ≤40%. All patients were implanted with an implantable cardiac monitor (ICM) within 5 to 21 days post-MI and followed every three months for two years. Atrial fibrillation, bradyarrhythmias and ventricular tachycardias were diagnosed using the ICM, pacemaker or ICD. Patients were stratified according to $CHADS_2$ score at enrollment. Congestive heart failure was defined as LVEF ≤40% and NYHA class II, III or IV.
Results: We found significantly increased risk of an arrhythmic event with increasing $CHADS_2$ score ($CHADS_2$ score = 1–2: HR = 2.1 [1.1–3.9], p = 0.021, $CHADS_2$ score ≥ 3: HR = 3.7 [1.9–7.1], p < 0.001). This pattern was identical when dividing the arrhythmias into subgroups of atrial fibrillation, ventricular tachycardias and bradyarrhythmias. $CHADS_2$ score was similarly associated with the development of major cardiovascular events defined as reinfarction, stroke, and hospitalization for heart failure or cardiovascular death.
Conclusion: In the post-MI setting, $CHADS_2$ score efficiently identifies populations at high risk for cardiac arrhythmias.

1. Introduction

The $CHADS_2$ score is a validated clinical tool used for the prediction of stroke in the presence of atrial fibrillation (AF). The score evaluates the risk of stroke through the sum of individual risk factors for stroke (congestive heart failure (CHF), hypertension, age ≥75 years, diabetes and stroke or transient ischemic attack [doubled]) [1,2]. Recently it has been shown that the $CHADS_2$ score may also be predictive for major cardiac events such as myocardial infarction (MI) and cardiovascular mortality [3–7].

Several studies have shown that post-MI patients remain at high risk of arrhythmias and sudden cardiac death [8–10], with risk of death 4 to 6 times higher than the general population [11]. The CARISMA study included post-MI patients with a left ventricular ejection fraction (LVEF) ≤40%, and was the first study to use continuous long-term monitoring of cardiac arrhythmias in the post-MI setting. The study documented unexpectedly high incidences of new-onset AF, high degree atrioventricular block, sinus bradycardia, ventricular tachycardia (VT) and ventricular fibrillation (VF) [12]. All of these arrhythmias are associated with increased mortality post-MI [13–15].

Risk stratification for arrhythmias in the post-MI setting is important [10,16] and several non-invasive methods have been used to stratify arrhythmic risk post-MI [17,18]. However, we are still in need of a simple implementable tool for arrhythmic risk stratification to correctly identify the patients at high risk for both atrial and ventricular arrhythmias in the post-MI setting. It has been questioned whether the $CHADS_2$ score can be used in the prediction of AF [19,20], but the association

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between $CHADS_2$ score and the prevalence of overall arrhythmias has not been previously investigated.

The aim of this study was to investigate the hypothesis that $CHADS_2$ score can be used as a tool for predicting both brady- and tachyarrhythmias post-MI in a population of patients with or without previous atrial fibrillation, who all presented with left ventricular dysfunction.

2. Methods

This post-hoc analysis was conducted as a substudy of the ***C***ardiac ***A***rrhythmias and ***RI***sk ***S***tratification after ***M***yocardial inf***A***rction (CARISMA) study, which have been described in detail elsewhere [18]. In summary, the study included 312 patients with LVEF ≤40% 2–5 days after experiencing a MI. The main objective of the CARISMA study was to describe incidences of malignant arrhythmias after a MI and to risk stratify fatal or near-fatal events using invasive or non-invasive electrophysiological tests performed at week 6 after enrollment.

2.1. Population

All patients who received an implantable cardiac monitor (ICM) in the CARISMA study were included (n = 297). Of these, 26 patients had a history of AF at enrollment. Implantable cardioverter defibrillators (ICDs) were implanted in 56 patients for primary (n = 45) or secondary (n = 11) prophylaxis during the study. Fifteen patients received pacemakers during the study period for symptomatic bradyarrhythmias. The ICM was explanted in these patients.

Patients were followed for 24 months with clinical visits at week 6 and thereafter every 3 months. Medical treatment was at the discretion of the responsible electrophysiologist at each center.

2.2. Implantation and programming of the ICM

The ICM (Reveal Plus, Medtronic Inc., Minneapolis, MN, USA) was implanted subcutaneously under local anesthesia in the left parasternal region 5–21 days after index MI. The ICM was programmed to document and store any tachyarrhythmias ≥125 beats per minute (bpm) with duration of at least 16 consecutive beats, any bradyarrhythmias ≤30 bpm lasting at least 4 consecutive beats and asystolic events lasting at least 4.5 s.

In the follow-up period the memory of the ICM was interrogated at 6 weeks after implantation and thereafter at 3 month intervals for the duration of 2 years. The sensitivity of the device was adjusted individually for each patient according to the amount of false positive arrhythmic events at each follow-up visit. AF, bradyarrhythmias and ventricular tachyarrhythmias were diagnosed using the ICM, pacemakers or ICDs. If an ICD or pacemaker was implanted, the device was programmed to store events at settings identical to the ICM.

2.3. $CHADS_2$ score

$CHADS_2$ score was calculated with one point given for each of the following parameters if present at enrollment; CHF, hypertension, age ≥75 years and diabetes. Two points were given for prior transient ischemic attack (TCI) or stroke, or if the patient experienced a cerebrovascular ischemic event during hospitalization for index MI. Since all patients had a LVEF ≤40%, CHF was defined as heart failure symptoms corresponding to NYHA class II, III or IV. Patients were defined as having hypertension or diabetes if they had the diagnosis at enrollment and were receiving medical treatment for these conditions.

2.4. End point

The main end point of this study was the combined end point of all included arrhythmias, i.e. a combined end point of atrial fibrillation, bradyarrhythmias, non-sustained and sustained ventricular tachycardia (VT) and ventricular fibrillation (VF). We also evaluated the risk of the specific arrhythmias (atrial fibrillation, VT/VF and bradyarrhythmia) and a combined end point of major cardiovascular events (MACE) consisting of myocardial reinfarction, stroke, hospitalization for heart failure or cardiovascular death.

Bradyarrhythmias were defined as any of the following: 2nd or 3rd degree atrioventricular block ≤30 bpm for more than 8 s, sinus arrest ≥5 s or bradycardia ≤30 bpm lasting ≥8 s. AF was defined as any irregular rhythm and the presence of an F-wave with no visible p-waves lasting more than 16 beats. Non-sustained VT was defined as self-limiting VT events lasting between 8 and 30 s, whereas sustained VT was defined as any VT event lasting ≥30 s.

2.5. Statistics

Baseline values were compared in patients with and without an arrhythmic event. Continuous variables were tested for normality using visual inspection of histogram plots. Continuous variables were compared using Students t-tests or Wilcoxon rank sum test where appropriate, categorical variables were compared using Pearson chi-square test or Fisher's exact test. Patients were divided into three groups based on $CHADS_2$ score = 0 (N = 39), $CHADS_2$ score = 1–2 (N = 186) and $CHADS_2$ score ≥3 (N = 72).

Outcomes were displayed by Kaplan–Meier plots and compared using log-rank tests. Cox-regression analyses were used to determine hazard ratios (HRs) and their 95% confidence intervals (CIs) for arrhythmias and MACE, always using $CHADS_2$ score = 0 as reference group. p-Values for differences between $CHADS_2$ groups were determined by Cox-regression analyses using $CHADS_2$ score = 1–2 as reference group. A p-value <0.05 was considered statistically significant. Patients with a history of AF were excluded from the AF analysis, whereas patients were censored at the time of pacemaker or ICD implant in the bradycardia analysis. Analyses were conducted using SAS 9.2 version for Windows 7, 64 bit (SAS Institute, CARY, NC, USA).

3. Results

3.1. Population

A total of 297 patients were included in this study; 158 patients had an arrhythmic event during a mean follow-up of 1.89 ± 0.53 years. MACE occurred in 60 patients, with the majority consisting of a myocardial reinfarction (N = 29, 48%) and less patients experiencing stroke (N = 5, 8%), hospitalization for heart failure (N = 14, 23%) or cardiovascular death (N = 12, 20%).

Baseline characteristics of patients with or without an arrhythmic event are listed in Table 1. Patients with an arrhythmic event were older, more often male, had a higher frequency of prior AF, prior MI, right bundle branch block and wide QRS complex than patients without an arrhythmic event. Furthermore, patients with an arrhythmic event

Table 1
Baseline characteristics of the study population.

Parameter	No arrhythmic event (N = 139)	Had arrhythmic event (N = 158)
Age (years)	60.8 (±11.8)	66.9 (±9.4)***
Male	100 (72%)	129 (82%)*
Smoker	47 (34%)	35 (22%)
Body mass index (kg/m^2)	27.4 (±4.2)	27.6 (±4.8)
Medical history		
Thrombolysis	52 (37%)	51 (32%)
PCI performed for index MI	58 (42%)	34 (22%)**
Left ventricular ejection fraction	32.2 (±6.1)	31.1 (±6.4)
History of atrial fibrillation	4 (3%)	22 (14%)**
Prior myocardial infarction	41 (30%)	69 (44%)*
Renal insufficiency	6 (4%)	8 (5%)
Asthma or COLD	10 (7%)	19 (12%)
Hypercholesterolemia	57 (41%)	65 (41%)
Hypertension	52 (37%)	77 (49%)*
Diabetes	23 (17%)	36 (23%)
NYHA class ≥II	94 (68%)	133 (84%)**
Prior stroke/TCI	8 (6%)	23 (15%)*
Medical treatment at enrollment		
Beta-blockers	133 (96%)	153 (97%)
ACE-I	126 (91%)	142 (90%)
Statins	117 (84%)	128 (81%)
Clopidogrel	101 (73%)	86 (54%)*
Aspirin	127 (91%)	142 (90%)
Class I antiarrhythmic drugs	0 (0%)	0 (0%)
Amiodarone	2 (1%)	3 (2%)
Calcium antagonists	13 (9%)	17 (11%)
Digoxin	10 (7%)	24 (15%)
Diuretics	45 (32%)	82 (52%)**
ECG characteristics at enrollment		
RBBB	8 (6%)	22 (14%)*
LBBB	9 (6%)	21 (13%)
QRS width (ms)	100.0 (±23.0)	108.0 (±28.6)*
Anterior myocardial infarction	85 (61%)	84 (53%)
Heart rate at enrollment (bpm)	80 (±19)	82 (±23)

PCI: percutaneous coronary intervention, COLD: chronic obstructive lung disease, ACE-I: angiotensin converting enzyme inhibitors, RBBB: right bundle branch block, LBBB: left bundle branch block, and bpm: beats per minute.
* p < 0.05.
** p < 0.001.
*** p < 0.0001.