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The use of different evidence-based medications and 5-year survival after an acute coronary syndrome: An observational study

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Abstract

Background: The use of different evidence-based medications (EBM medications) in-hospital survivors of acute coronary syndrome (ACS) may be associated with different long-term survival.
Methods: In 1025 consecutive survivors receiving aspirin, we analysed the associations between statins (prescribed in 59.5%), beta-blockers (76.8%) and ACE-inhibitors/angiotensin receptor blockers (54.1%) and all-cause mortality up to 5 years as the endpoint, adjusting to the baseline risk using the GRACE hospital discharge risk score.
Results: The use of beta-blockers and statins was associated with reduced mortality. Significant reduction was observed from 6 months for statins, and from 2 years for beta-blockers. Results were similar after further adjustment for concomitant use of other EBM medications. When interaction terms between different EBM medications were tested, the only significant interaction was between statins and beta-blockers ($P=0.010$). This interaction persisted ($P=0.018$) when the 1025 patients were sub-grouped *regardless* of the use of ACE-inhibitors/angiotensin receptor blockers. The use of beta-blockers was associated with reduced mortality for patients not discharged on statins (hazard ratio of 0.46, 95% C.I. 0.30–0.69), but this was not true for patients discharged on statins (hazard ratio of 1.19, 95% C.I. 0.62–2.30).
Conclusions: Different EBM medications after an ACS may be associated with different long-term survival and statins may be more important than others in patients already taking aspirin.

Keywords: Statins; Beta-blockers; Acute coronary syndrome

1. Introduction

In 1358 consecutive patients presenting with acute coronary syndrome (ACS), Mukherjee et al. reported an increasing mortality benefit over 6 months from the use of more evidence-based medications (EBM medications) including aspirin, statins, ACE-inhibitors/angiotensin receptor blockers and beta-blockers at hospital discharge [1]. In the Guideline Applied in Practice (GAP) Projects, a comparison of 2 cohorts of patients with acute myocardial infarction (including 1368 patients in the year before and 1489 patients in the first 4 months of GAP implementation) revealed that GAP implementation resulted in higher use of EBM medications and lower mortality up to 1 year [2].

The most recent 2006 update of the AHA/ACC guidelines for secondary prevention for coronary disease includes a class 1 recommendation for the use of aspirin, statins, beta-blockers and ACE-inhibitors/angiotensin receptor blockers [3]. However, there is no information as to whether the benefit of one EBM medication is comparable to another, whether different EBM medication combinations confer different benefit, and whether higher-risk patients benefit more than lower-risk patients. The relative lack of longer term studies in "real world" patients have made these questions even more pertinent in daily practice.

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We previously established the use of the GRACE hospital discharge risk score [4] in predicting mortality up to 4 years for unselected hospital survivors with ACS [5]. The current study analysed in the same cohort [5] the benefits from individual EBM medication or combinations of EBM medications prescribed at hospital discharge over a follow-up period of up to 5 years adjusting for their baseline risk as measured by the GRACE score.

2. Methods

This is a retrospective study including consecutive patients with ACS admitted into 2 related centers in New Zealand, including the tertiary teaching hospital in Dunedin, Otago and the regional hospital in Invercargill, Southland from the years 2000 to 2002 [5,6]. Patients having ACS precipitated by significant non-cardiac co-morbidity, trauma or surgery were excluded. This study protocol was in accordance with the local hospital research guidelines [5,6].

All clinical data were collected by a research physician, including both the use of EBM medications (aspirin, beta-blockers, statins and ACE-inhibitors/angiotensin receptor blockers) at hospital discharge and details of the hospitalisation [5,6]. The latter included, among other data fields [5,6], age, sex, cardiac risk factors, history of ischemic heart disease, history of stroke, peripheral vascular disease, smoking; presenting heart rate, blood pressure, killip class; episodes of cardiac arrest on arrival and cardiogenic shock; initial ECG characteristics (degree of ST-deviation and T-waves changes), troponin I levels, creatinine level; left ventricular function; in-hospital therapy (medications in the first 24-hour, reperfusion and revascularisation therapy).

All-cause mortality was used as the study endpoint, over an up to 5-year follow-up period. Information on the deaths (until 1st April 2005) was obtained from medical records and the New Zealand national death registry.

Patients with ACS were classified into 3 categories: ST elevation myocardial infarction if they had ST elevation ≥ 1 mm in two contiguous leads (or ≥ 2 mm in V_1 to V_3 leads) or new left bundle branch block together with chest pain for >30 min and/or evidence of myonecrosis with elevated troponin I (Abbott AxSYM assay) ≥ 2.0 μg/L; non-ST elevation myocardial infarction if they had no ST elevation despite elevated troponin I and chest pain for more than 30 min; or unstable angina if they had ischemic chest pain lasting more than 30 min with no evidence of myonecrosis or ST elevation [5,6].

Parameters in the GRACE hospital discharge risk score include age, history of congestive heart failure, history of myocardial infarction, elevated heart rate and low systolic blood pressure on arrival, ST segment depression, elevated initial serum creatinine, elevated cardiac enzymes and not having in-hospital percutaneous coronary intervention [4]. In the current cohort of patients, the GRACE score discriminated survivors from non-survivors with a high C-index in all 3 categories of ACS, and higher score was associated with higher mortality [5].

3. Statistical analysis

Baseline characteristics were summarized by using frequencies and percentages for categorical variables, and means and standard deviations for continuous variables.

A multivariable Cox proportional hazard analysis was performed to test if the use of each EBM medication was associated with mortality (versus the non-use of that particular EBM medication) over the whole follow-up period, and at specific time points of 6 months, 1 year, 2 years, 3 years and 4 years. In these models, adjustments were made for the GRACE score (as a continuous variable) and for the use or non-use of other EBM medications. Using patients with aspirin plus only beta-blockers as reference, further modelling was performed to compare mortality outcome for patients on aspirin plus other EBM medications.

Interaction terms between the different EBM medications themselves and between the EBM medications and GRACE score were tested in the Cox models.

4. Results

Of 1143 consecutive patients with ACS, including 446 with STEMI, 450 with NSTEMI and 247 with unstable angina, 1057 survived hospitalisation and formed the cohort for the current study. All reached 2-year, 82% reached 3-year and 54% reached 4-year follow-up time point for survival status (median follow-up time 43 months, interquartile range 32–53 months). Table 1 shows the baseline characteristics.

Table 1
Baseline characteristics of the 1057 hospital survivors with ACS

Demographics	
Age [a]	64.9 (12.6)
Men	666 (63.0%)
Medical history	
History of ischemic heart disease	493 (46.6%)
History of hypertension	515 (48.7%)
Diabetes mellitus	175 (16.6%)
Dyslipidaemia	678 (64.2%)
Coronary artery bypass graft	88 (8.3%)
Family history of coronary disease	278 (26.3%)
History of smoking	579 (54.8%)
Clinical signs at presentation	
Heart rate, beats/min [a]	77 (20)
Systolic blood pressure (SBP), mm Hg [a]	139 (28)
Diastolic blood pressure (DBP), mm Hg [a]	78 (18)
Killip class	
I	868 (83.5%)
II	141 (13.6%)
III	30 (2.9%)
IV	1 (0.1%)
Cardiac arrest	77 (7.4%)
Initial creatinine level, mmol/L [a]	0.104 (0.042)

[a] Continuous data expressed as mean (SD).