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Cigarette smoking and acute coronary syndromes: A multinational observational study☆

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Abstract

Purpose: To determine the impact of cigarette smoking on the presentation, treatment, and in-hospital outcomes of patients admitted with the full spectrum of acute coronary syndromes.
Methods: GRACE is a multinational observational registry involving 94 hospitals in 14 countries. This analysis is based on 19,325 patients aged at least 18 years admitted for acute coronary syndromes as a presumptive diagnosis with at least one of the following: electrocardiographic changes consistent with acute coronary syndromes, serial increases in serum biochemical markers of cardiac necrosis, and/or documentation of coronary artery disease. The main outcomes measured were mode of presentation, treatment and in-hospital death in the ST-segment elevation myocardial infarction, non-ST-segment elevation myocardial infarction, and unstable angina groups to assess the impact of smoking status.
Results: Smokers were more frequently diagnosed with ST-segment elevation myocardial infarction (46.0%) than former smokers (27.4%) and non-smokers (30.2%) ($P<0.001$). Smokers were mostly men, were younger and more aggressively treated than former smokers and non-smokers across the three acute coronary syndrome groups. Unadjusted in-hospital mortality rates were lower in smokers compared with former smokers and non-smokers in the study population (3.3%, 4.5%, and 6.9%, respectively, $P<0.001$), and in the ST-segment elevation myocardial infarction and non-ST-segment elevation myocardial infarction groups. However, by multivariate logistic analysis, the adjusted in-hospital mortality rate was similar regardless of smoking status.
Conclusions: There is no survival advantage related to current or prior cigarette smoking in patients admitted with acute coronary syndromes, regardless of presentation. In this large multinational registry, the smokers' paradox does not exist.

Keywords: Cigarette smoking; Acute coronary syndromes; Unstable angina; ST-segment elevation myocardial infarction; Non-ST-segment elevation myocardial infarction

1. Introduction

Cigarette smoking is a well-established risk factor for the development of coronary heart disease [1]. Several studies have shown lower mortality after ST-segment elevation myocardial infarction in smokers compared with non-smokers [2–4]. This is the 'smokers' paradox', where an individual who smokes is not only more likely than a non-smoker to suffer a heart attack but is also more likely to survive it. One explanation for this paradox is that smokers may have a larger thrombus burden, leading to a greater efficacy of intravenous thrombolysis [3–7]. Also, smokers tend to be younger and have more favourable baseline characteristics than non-smokers [2,8–10]. More

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recent studies suggest that smoking is not an independent prognostic factor in terms of early survival after ST-segment elevation myocardial infarction [11]. However, there are few data regarding smoking status and outcome across the whole range of acute coronary syndromes, particularly among patients with unstable angina and non-ST-segment elevation myocardial infarction. Another problem is the potential selection bias of studies performed among patients participating in randomized clinical trials, whose characteristics may not match those of patients encountered in routine care.

The Global Registry of Acute Coronary Events (GRACE) is an ongoing, multinational, observational registry of patients hospitalized with acute coronary syndromes [12]. To assess the impact of smoking status on presentation, treatment, and outcomes in acute coronary syndromes, we analysed data from 19,325 patients consecutively enrolled in GRACE.

2. Materials and methods

Full details of the GRACE rationale and methodology have been published [12]. In brief, GRACE is designed to reflect a representative population of patients with ACS, irrespective of geographic region. Currently, 94 public and private hospitals located in 14 countries (Argentina, Australia, Austria, Belgium, Brazil, Canada, France, Germany, Italy, New Zealand, Poland, Spain, United Kingdom, United States) are participating in this observational study.

2.1. Study population

Patients entered in the registry had to be at least 18 years old and alive at the time of hospital presentation, be admitted for acute coronary syndromes as a presumptive diagnosis, and have at least one of the following: electrocardiographic changes consistent with acute coronary syndromes, serial increases in serum biochemical markers of cardiac necrosis, and/or documentation of coronary artery disease. The qualifying acute coronary syndromes must not have been precipitated or accompanied by a significant non-cardiovascular comorbidity (for example trauma, or surgery). Where required, study investigators received approval from their local hospital ethics or institutional review board, and a signed consent form for follow-up contact was obtained.

2.2. Data collection

Data were collected at each site by a trained coordinator using a standardized case report form developed for the GRACE registry. Demographic characteristics, medical history, presenting symptoms, duration of prehospital delay, biochemical and electrocardiographic findings, treatment practices, and a variety of hospital outcome data were collected; in the majority of cases patients' medical records were reviewed after the patient was discharged from hospital. Standardized definitions of all patient-related variables and clinical diagnoses were used [12].

Current smokers were people who reported active cigarette smoking within 1 month before admission to hospital. Previous smokers were defined as those who reported having stopped smoking cigarettes more than 1 month before hospital admission. Other patients were considered non-smokers.

2.3. Statistical analysis

Categorical variables are expressed as frequencies and percentages, and continuous variables are expressed as medians (interquartile range) because of non-normal distributions of these variables. Differences in patient demographics and clinical characteristics and in-hospital outcomes between current smokers, former smokers, and non-smokers were assessed using Chi-square test for categorical variables and Kruskal–Wallis tests for continuous variables. Multiple logistic regression was used to examine the association between current smokers, former smokers, and non-smokers and hospital mortality, with adjustment for demographics, hospital medications, and procedures that were deemed to be clinically relevant based on the literature and current medical management, namely: geographic region, age, sex, clinical baseline characteristics (medical history: angina, myocardial infarction, percutaneous coronary intervention/coronary artery bypass grafting, hypertension, diabetes, hyperlipidaemia, chronic heart failure; Killip class; blood pressure, pulse), in-hospital procedures (catheterization, percutaneous coronary intervention, coronary artery bypass grafting), and in-hospital medications (aspirin, unfractionated heparin, low-molecular-weight heparin, glycoprotein IIb/IIIa receptor inhibitor, thrombolytic, angiotensin-converting enzyme inhibitor, beta-blocker, calcium-channel blocker, statin). BMI was not included in the model owing to the high percentage of missing values. Multivariate analysis was performed on the overall acute coronary syndrome population as well as by subgroup (ST-segment elevation myocardial infarction, non-ST-segment elevation myocardial infarction, unstable angina). Statistical analysis was performed using SAS software, version 8.1.

3. Results

3.1. Characteristics of current smokers, former smokers, and non-smokers

The study sample consisted of 19,325 patients with acute coronary syndromes admitted between April 1999 and March 2002. Of these, 5276 (27.3%) were current smokers, 5691 (29.5%) were former smokers, and 8358