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Gender- and age-related differences in clinical presentation and management of outpatients with stable coronary artery disease

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ABSTRACT

Introduction: Contemporary generalizable data on the demographics and management of outpatients with stable coronary artery disease (CAD) in routine clinical practice are sparse. Using the data from the CLARIFY registry we describe gender- and age-related differences in baseline characteristics and management of these patients across broad geographic regions.
Methods: This international, prospective, observational, longitudinal registry enrolled stable CAD outpatients from 45 countries in Africa, Asia, Australia, Europe, the Middle East, and North, Central, and South America.
Results: Baseline data were available for 33 280 patients. Mean (SD) age was 64 (10.5) years and 22.5% of patients were female. The prevalence of CAD risk factors was generally higher in women than in men. Women were older (66.6 vs 63.4 years), more frequently diagnosed with diabetes (33% vs 28%), hypertension (79% vs 69%), and higher resting heart rate (69 vs 67 bpm), and were less physically active. Smoking and a history of myocardial infarction were more common in men. Women were more likely to have angina (28% vs 20%), but less likely to have undergone revascularization procedures. CAD was more likely to be asymptomatic in older patients perhaps because of reduced levels of physical activity. Prescription of evidence-based medication for secondary prevention varied with age, with patients ≥75 years treated less often with beta blockers, aspirin and angiotensin-converting enzyme inhibitors than patients <65 years.
Conclusions: Important gender-related differences in clinical characteristics and management continue to exist in all age groups of outpatients with stable CAD.

1. Introduction

Average life expectancy has increased by 10 years in the last 30 years with improvements in the field of cardiology contributing to at least 7 years [1]. Despite such success, coronary artery disease (CAD) remains the leading cause of mortality and morbidity in the world [2–4]. It follows that the cardiovascular community has not solved the problem, but has delayed the occurrence of CAD-related mortality and changed the demographics of patients with CAD, with a shift of disease burden toward older patients, in both men and women [5,6].

Aging has been associated with a reduced likelihood of receiving effective cardiac therapies [7–10]. Furthermore, the prevention and treatment of CAD may not be as effective in women as in men [11–18], suggesting that for optimal treatment of CAD it is necessary to recognize the impact of age and gender differences on the outcomes of care.

Surprisingly, there is a paucity of contemporary data regarding the clinical characteristics and management of outpatients with stable CAD. The majority of data are restricted to a particular manifestation of disease such as angina or acute coronary syndrome [6,14,19–24] and are limited to a specific country or a geographic area. Furthermore, gender and age are usually analyzed separately [21,22,24–26].

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Our goal is to describe the gender- and age-based differences in baseline characteristics and management of outpatients with stable CAD using a large contemporary database from 45 countries.

2. Methods

2.1. Study design

CLARIFY is an ongoing international, prospective, observational, longitudinal cohort study in stable CAD outpatients with a 5-year follow-up [27]. Patients were enrolled in 45 countries in Africa, Asia, Australia, Europe, the Middle East, and North, Central, and South America. They were treated according to usual clinical practice at each institution, with no specific tests or therapies defined in the study protocol. CLARIFY is registered in the ISRCTN registry of clinical trials with the number ISRCTN43070564 and approved by local ethical committees. All subjects provided written informed consent in accordance with national and local guidelines.

2.2. Study population

Outpatients with stable CAD had to meet at least one of the following criteria to be eligible for enrollment [27]: documented myocardial infarction >3 months previously; at least one angiographically proved >50% diameter coronary artery stenosis; chest pain with myocardial ischemia proven by stress echocardiography and electrocardiography (ECG), or myocardial imaging; and history of coronary artery bypass graft (CABG) or percutaneous coronary intervention (PCI) carried out >3 months previously. Patients were not eligible if they had been hospitalized for cardiovascular disease (CVD) within the last 3 months (including revascularization), or had planned revascularization, or had conditions hampering participation or 5-year follow-up such as limited cooperation or legal capacity, advanced heart failure, severe valve disease, history of valve repair/replacement, or serious non-cardiovascular disease limiting life expectancy (cancer, drug abuse, etc.).

Patients were recruited between November 2009 and July 2010. To ensure a balanced representation of participating countries, a general target enrollment for any participating country was 25 patients per million inhabitants (range 12.5–50). A broad range of physicians were involved in the selection of patients including cardiologists, general practitioners and internists. Each physician recruited a maximum of 15 outpatients with stable CAD as defined by the protocol. Patients were enrolled in each practice over a brief period of time to provide near, if not consecutive, patient enrollment.

2.3. Baseline data collection and data management

Data regarding patient demographics, medical history, risk factors, employment status, physical examination, heart rate (determined by both pulse palpation and 12-lead electrocardiography) using the most recent ECG within 6 months in clinically stable patients, laboratory values (if available), and current chronic medical treatments were collected by the participating physician using an electronic case report form. A number of procedures were set up to ensure data quality control. All case report forms were sent to the data management center, where data were checked for completeness, internal consistency, and accuracy. Data quality control was performed onsite in 5% of sites chosen at random in each country. At each of these sites, 100% of case report forms for patients enrolled at that site were monitored for source documentation and accuracy.

2.4. Statistical analysis

Data were collected and analyzed by an independent statistics center, the Robertson Center for Biostatistics, University of Glasgow, UK. Continuous variables are presented as means and standard deviations (SDs) in the case of normal distribution, or medians and interquartile ranges (IQRs) and ranges in the case of non-normal distribution. Categorical data are presented as counts and percentages.

3. Results

The CLARIFY registry screened a total of 33 432 patients from 45 countries. Baseline data were available for 33 280; 47 patients did not meet the inclusion criteria and 105 did not provide consent. Of these 33 280 patients, age and gender were recorded for 33 214 (gender was not recorded in 46 patients and age was not recorded in 20).

The mean (SD) age of the population surveyed was 64 (10.5) years. Women represented 22.5% of the population overall and were slightly older than the men, with a mean age of 66.6 (10.0) years compared with 63.4 (10.5) years in men. A total of 17 206 patients were <65 years old, 10 812 were aged 65–74 years, and 5196 were aged ≥75 years.

3.1. Gender differences in the presentation and clinical management of outpatients with CAD

The baseline data for men and women are presented in Tables 1 and 2. A number of important differences in clinical characteristics and management were identified. Compared with men, women were on average 3.1 years older and had higher resting heart rates (69.6 versus 67.9 bpm, pulse palpation) and systolic blood pressure (133.3 versus 130.3 mm Hg). Women were less physically active, with 23.4% performing no physical activity compared with 14.3% of men. Only 9.6% of women performed at least 20 min of vigorous physical activity at least three times per week compared with 17.3% of men, and only 11.9% of women versus 18.2% of men performed vigorous activity once or twice per week.

In terms of cardiovascular history, women had a shorter duration of CAD (4 years versus 5 years, P<0.0001) and were more frequently diagnosed with diabetes, hypertension, stroke, and transient ischemic attack. Smoking, a history of myocardial infarction, and peripheral arterial disease (PAD) were more common in men. Women presented with angina more often than men (28% versus 20%) and this was true for all angina classes defined by the Canadian Cardiovascular Society grading scale (Fig. 1). In contrast, women were less likely to have undergone PCI (54.9% versus 59.8%) or CABG (17.8% versus 25.0%) (Fig. 2).

Women were less likely to have undergone cardiac investigations. Coronary angiography was performed in 79.9% of women versus 87.0% of men. Non-invasive tests for myocardial ischemia were done in 58.3% of women compared with 62.9% of men. In those patients with data from non-invasive testing, evidence for myocardial ischemia was observed more often in women than men (17.3% versus 15.9%).

Women were prescribed angiotensin-converting enzyme (ACE) inhibitors and lipid-lowering drugs significantly less frequently than men, but received antianginal agents, antidiabetes drugs, non-steroidal anti-inflammatories, proton pump inhibitors, and thyroid hormone replacements more often than men (Fig. 2). There was no significant difference in the use of beta-blockers between the sexes.

3.2. Age-related differences in the presentation and clinical management of outpatients with CAD

Table 1 demonstrates that concomitant conditions were widely prevalent among the study population. The proportion of those with atrial fibrillation, transient ischemic attack, hospitalization for congestive heart failure, asthma/chronic obstructive pulmonary disease (COPD), PAD, dyslipidemia, hypertension, and diabetes increased progressively with age. Tobacco and alcohol use decreased relative to age.

There were significant age-related differences among both men and women (Table 1). Compared with those aged <65 years, patients aged ≥75 years had higher systolic blood pressure (129.0 versus 132.5 mm Hg in men and 131.2 versus 136.0 in women), lower body mass index (BMI) values (26.1 versus 27.9 kg/m^2 in women and 26.5 versus 27.6 kg/m^2 in men) and were less likely to be current smokers (2.3% versus 11.5% in women and 4.5% versus 19.6% in men). Patients ≥75 years had lower resting heart rates measured by pulse palpation (69.2 versus 70.4 bpm in women and 66.8 versus 68.8 bpm in men) or by ECG (68.7 versus 69.8 bpm in women and 65.7 versus 67.4 bpm in men).

Older patients were more often asymptomatic, with angina present in 20.7% of women and 17.1% of men aged ≥75 years compared with 32.7% of women and 22.9% of men aged <65 years (P<0.0001). This may be due to reduced physical activity below the ischemic threshold, sedentary lifestyle, or locomotor disability. Nearly one third of women (31.3%) and 21.9% of men aged ≥75 years performed