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Lack of control of hypertension in primary cardiovascular disease prevention in Europe: Results from the EURIKA study☆

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ABSTRACT

Background: The prevalence of and factors associated with uncontrolled hypertension and apparent resistant hypertension were assessed in the European Study on Cardiovascular Risk Prevention and Management in Usual Daily Practice (EURIKA; NCT00882336).

Methods: EURIKA was a cross-sectional observational study including patients being treated for the primary prevention of cardiovascular disease in 12 European countries. Patients were assessed if they were being treated for hypertension (N = 5220). Blood pressure control was defined according to European guidelines, with sensitivity analysis taking account of patients' age and diabetes status. Associated factors were assessed using multivariate analysis.

Results: In the primary analysis, a total of 2691 patients (51.6%) had uncontrolled hypertension. Factors significantly associated with an increased risk of having uncontrolled hypertension included female sex (odds ratio [OR]: 2.29; 95% confidence interval [CI]: 1.93–2.73), body mass index (BMI; OR per kg/m^2: 1.03; 95% CI: 1.01–1.04), and geographic location. A total of 749 patients (14.3%) had apparent resistant hypertension. Factors significantly associated with an increased risk of having apparent resistant hypertension included BMI (OR per kg/m^2: 1.06; 95% CI: 1.04–1.08), diabetes (OR: 1.28; 95% CI: 1.06–1.53), use of statins (OR: 1.36; 95% CI: 1.15–1.62), serum uric acid levels (OR: 1.16; 95% CI: 1.09–1.23), and geographic location. Similar results were seen in sensitivity analyses.

Conclusions: Over 50% of patients treated for hypertension continued to have uncontrolled blood pressure and 14.3% had apparent resistant hypertension. Positive associations were seen with other cardiovascular risk factors.

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1. Introduction

Despite recent reductions in rates of mortality from cardiovascular disease (CVD) throughout Europe, CVD remains responsible for approximately 47% of all deaths across the continent each year [1]. Primary and secondary prevention of CVD, therefore, remains of great importance. Principal risk factors for having a first cardiovascular event include age, sex, smoking, arterial hypertension, dyslipidaemia, diabetes, obesity, and physical inactivity [2]. Control of modifiable risk factors remains poor: the most recent European CVD statistics report that the prevalence of elevated blood pressure in adults aged 25 years or over ranges between 33.6% (Israel) and 48.3% (Ukraine), whereas the prevalence of

Abbreviations: ACE, angiotensin-converting enzyme; BMI, body mass index; CI, confidence interval; CVD, cardiovascular disease; DBP, diastolic blood pressure; ESC, European Society of Cardiology; ESH, European Society of Hypertension; EURIKA, European Study on Cardiovascular Risk Prevention and Management in Usual Daily Practice; HbA_{1c}, glycated haemoglobin; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; OR, odds ratio; SCORE, Systematic Coronary Risk Evaluation; SBP, systolic blood pressure; SD, standard deviation.

☆ These authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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dyslipidaemia in the same population ranges between 24.0% (Tajikistan) and 69.8% (Iceland) [1].

Recently, we conducted the European Study on Cardiovascular Risk Prevention and Management in Usual Daily Practice (EURIKA; ClinicalTrials.gov identifier: NCT00882336), a study of the management of cardiovascular risk factors in primary care in 12 European countries [3]. Included patients were aged 50 years or over and had at least one risk factor for CVD but no history of cardiovascular events. As part of this study, we have previously reported that control of blood pressure among patients with hypertension in Europe is approximately 38.8%, whereas control of blood serum cholesterol levels among patients with dyslipidaemia is approximately 43.3% [4]. In the present paper, we describe in detail the prevalence of uncontrolled hypertension and of apparent resistant hypertension among patients being treated for hypertension in the EURIKA population. Factors associated with uncontrolled hypertension and with apparent resistant hypertension were also assessed.

2. Methods

2.1. Study design and participants

EURIKA was carried out in 12 European countries (Austria, Belgium, France, Germany, Greece, Norway, Russia, Spain, Sweden, Switzerland, Turkey, and the UK) [4]. Data collection started in May 2009 and ended in January 2010, with a 3-month data collection period for each country. The study protocol was approved by the appropriate clinical research ethics committees in each participating country, and all patients provided signed informed consent.

The methods for the study have been reported in detail elsewhere [3]. Briefly, the study sample was selected in a two-stage process that involved the random selection of both physicians and their patients [3,5]. In the first stage, primary care practitioners and specialists involved in CVD prevention (including cardiologists, endocrinologists, and internal medicine specialists) were randomly selected to be invited to participate using the OneKey database (Cegedim Dendrite, Boulogne-Billancourt, France) [6]. In total, 809 physicians (approximately 60 per country) agreed to participate in EURIKA, 64% of whom were primary care practitioners [5]. In the second stage, participating physicians sequentially invited patients who met the selection criteria (aged 50 years or older, free of CVD but having at least one major cardiovascular risk factor [dyslipidaemia, hypertension, smoking, diabetes mellitus, or obesity]) [4]. Approximately 600 patients were included per country, with a final population size of 7641. For the present analysis, included patients were those who were receiving an antihypertensive medication and for whom blood pressure measurements were included in the database (N = 5220).

2.2. Assessment of CVD risk factors

Demographic information and other details of participating patients were gathered from medical records and patient interviews. For each patient, a physical examination was conducted, blood pressure was measured, and a 12-h fasting blood sample was collected within 1 day of the initial outpatient consultation [3]. Blood pressure was determined in standardised conditions, using calibrated mercury sphygmomanometers or validated automated devices, and appropriate-size cuffs [2,3,7]. The mean of three readings was used for analyses.

Blood sample analysis was carried out at a central laboratory (Bio Analytical Research Corporation, Ghent, Belgium), with the exception of samples from patients in Russia (approximately 5% of the total patient population), for whom laboratory analysis was carried out locally. High-density lipoprotein cholesterol (HDL-C) concentration was measured by a modified enzymatic method, total cholesterol concentration by the CHOD-PAP method, and triglyceride concentration by the GPO-PAP method (all using the Roche Modular P chemistry analyser; Roche Diagnostics, Indianapolis, IN, USA). Low-density lipoprotein cholesterol (LDL-C) concentration was calculated by the Friedewald formula [8]. Ten-year CVD-related mortality risk for each patient was estimated using the Systematic Coronary Risk Evaluation (SCORE) algorithms for high-risk and low-risk countries, as appropriate [9].

2.3. Control of hypertension

In the primary analysis of uncontrolled hypertension, control of blood pressure was defined in all patients as systolic blood pressure (SBP) <140 mm Hg and diastolic blood pressure (DBP) <90 mm Hg, in line with the 2007 European Society of Hypertension (ESH)/European Society of Cardiology (ESC) guidelines in place at the time the study was carried out [10]. In a sensitivity analysis, this definition was altered to consider patients' age and diabetes status, in line with the 2007 ESH/ESC guidelines [7]. In this sensitivity analysis, control of blood pressure was defined as SBP <150 mm Hg and DBP <90 mm Hg for patients aged 80 years or over regardless of diabetes status, SBP <140 mm Hg and DBP <85 mm Hg for patients aged under 80 years with diabetes, and SBP <140 mm Hg and DBP <90 mm Hg for all other patients. Apparent resistant hypertension was defined as having uncontrolled hypertension (primary and sensitivity analysis definitions as given above) despite being treated with at least three antihypertensive drugs including a diuretic, or having controlled hypertension while being treated with four or more antihypertensive drugs [7].

2.4. Statistical methods

Data are presented as mean and standard deviation for continuous variables, and as frequency and percentage for categorical variables. Comparisons between groups were performed using Student's t-tests for normally distributed continuous variables, Mann–Whitney U-tests for continuous variables that were not normally distributed, and χ^2 or Fisher's exact tests for categorical variables, as appropriate.

Factors associated with uncontrolled hypertension were assessed in the subpopulation of patients receiving one or two antihypertensive medications, using univariate and subsequently multivariate logistic regression models and using both the primary and sensitivity analysis definitions of blood pressure control. Variables included in the multivariate analyses were country, age, sex, body mass index (BMI), diabetes status, tobacco use, LDL-C levels, frequency of healthcare visits, use of statins, serum uric acid level, and overall cardiovascular risk calculated according to SCORE. A stepwise selection model was used to keep only those variables statistically significantly associated at the 5% significance level in the final model. Factors associated with apparent resistant hypertension were assessed using the same methods in the overall population. Statistical analyses were carried out using SAS version 9.3 (SAS Institute Inc., Cary, NC, USA).

3. Results

3.1. Patient characteristics and factors associated with uncontrolled hypertension

Of the 7641 patients included in EURIKA, 5220 were treated for hypertension and had blood pressure measurements available in the database, and were therefore included in the analysis. The mean age was 64.5 years, and 47.9% were men (Table 1). A total of 29.3% had diabetes, and the mean BMI was 29.6 kg/m^2.

In the primary analysis, 2691 patients (51.6%) had uncontrolled hypertension (Fig. 1). In the sensitivity analysis, using different definitions of blood pressure control according to patients' age and diabetes status, the number of patients with uncontrolled hypertension increased slightly to 2721 (52.1%) (Fig. 1). In the primary analysis, the prevalence of uncontrolled hypertension varied according to country, ranging from 38.6% in Greece to 59.7% in Turkey (Supplementary Table 1). A similar

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