

Secondary prevention of coronary heart disease in elderly population of Turkey: A subgroup analysis of ELDERTURK study

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Abstract

Background: Secondary prevention plays an important role after acute coronary event due to high risk of adverse events in elderly. In present study we aimed to evaluate the lifestyle, management of risk factors and medical treatment for secondary protection in elderly patients with known coronary heart disease (CHD).

Methods: ELDERTURK is a non-interventional, multi-centered, observational study, which included total of 5694 elderly patients (> 65 years) from 50 centers in Turkey. In this study elderly patients from the ELDERTURK population with known CHD were evaluated for cardiovascular risk factors, comorbidities and medication usage.

Results: A total of 2976 (52.3% of study) out of 5694 patients included in the ELDERTURK study were evaluated. All had known CHD with a mean age of 73.4 ± 6.2 years and 60.3% were male. 13.0% of patients were smokers, 42.4% were overweight and 21.1% were obese. Only 23.6% of patients reported to do regular exercise, 73.4% had history of hypertension, 47.4% had dyslipidemia and 33.9% had diabetes mellitus. The rate of patients with systolic blood pressure > 140 mmHg were 31.1% and only 13.9% of patients had a recommended ≤ 70 mg/dL level of low-density lipoprotein cholesterol. Anti-platelet, statin, beta-blocker and angiotensin-converting enzyme inhibitor/angiotensin receptor blocker usage was limited to 27.3%.

Conclusions: The ELDERTURK study shows that many patients with CHD have a high prevalence of modifiable risk factors and unhealthy lifestyle. Apart from this, many patients are not receiving therapeutic intervention and as a consequence most were not achieving the recommended goals. (Cardiol J 2019; 26, 1: 13–19)

Key words: coronary disease, prevention, aging, drugs, treatment, epidemiology

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Introduction

The elderly population is rapidly increasing in Turkey as in all industrialized countries. The rate of population aged ≥ 65 is expected to reach 10.2% in 2023, 20.8% in 2050 [1]. In several studies, increasing age is a powerful predictor of both short-term and long-term mortality following acute myocardial infarction [2–4]. The prevalence and incidence of coronary heart diseases (CHD) are significantly increased in the elderly population due to increase of traditional risk factors and prevalence which is associated with aging due to increases of inflammation, endothelial dysfunction and atherosclerosis [3]. The presence of obstructive coronary artery disease at autopsy is 50% in elderly women and 70% to 80% in elderly men [5]. Secondary prevention is as important as acute treatment in patients with CHD. There is clear guidance for secondary protection with lifestyle changes, management of risk factors and appropriate drug therapy advice. However, guideline recommendations may not apply exactly in practical living. Especially recommendations which could be applied less in elderly patients due to polypharmacy, drug interactions and side effect concerns associated with difficulties in changing long-term habits [6].

In the present study the aim was to evaluate lifestyle, management of risk factors and medical treatment for secondary prevention in elderly patients with known CHD enrolled in the ELDER-TURK study.

Methods

The design, conduct, and main results of the ELDERTURK (Frequency of cardiovascular diseases and drug use in the elderly Turkish population was followed up at cardiology clinics) in this study have been presented previously [7]. In brief, the ELDERTURK study was a non-interventional, multi-centered, observational study to provide national epidemiological data for the incidence of cardiovascular diseases, risk factors, comorbid diseases and drug usage among an elderly group (> 65 years of age) in Turkey. This study was performed with the Institutional Review Board protocol approval date 11/03/2015 and number 700 between March 2015 and December 2015. All patients 65 years and older who admitted to the inpatient and outpatient cardiology clinics with symptoms were enrolled in the study.

Study inclusion criteria were as follows:

- 65 years and older age;

- admitted to an outpatient clinic and were able to provide a medical history;
- gave written consent.

Study exclusion criteria were as followed:

- below 65 years old;
- not available to give a reliable medical history because of concomitant diseases;
- refusal to give written consent.

A total of 5694 patients from 73 centers around different parts of Turkey were included. In this study elderly patients from the ELDERTURK population with known CHD ($n = 2976$; 52.3% of study) were included to evaluate cardiovascular risk factors, comorbidities and medication usage. CHD was defined as having a previous history of a coronary artery bypass graft (CABG) operation, percutaneous trans-luminal coronary angioplasty or stent, myocardial infarction, and stable coronary artery disease. Demographic information of the patients were recorded. The smoking habit was described as being an active smoker defined inclusion to the study. Participants who exercised were grouped as doing exercise less than 150 min or more than this per week. Patients who were newly diagnosed with diabetes mellitus (DM) or were already on anti-diabetic therapy were identified as diabetic. Hypertension was defined as taking anti-hypertensive therapy, diagnosed with hypertension or having a systolic blood pressure (SBP) ≥ 140 mmHg and diastolic blood pressure (DBP) ≥ 90 mmHg without diagnosis. The value of SBP < 140 mmHg was the target value for blood pressure control as recommended by European Society of Cardiology (ESC) hypertension guidelines in patients with CHD [8]. Body mass index (BMI) was calculated by using weight [kg]/height [m²] formula. Subjects were divided into four groups based on BMI: underweight < 18.5 kg/m²; normal 18.5–24.9 kg/m²; overweight 25–29.9 kg/m² and obese ≥ 30 kg/m² [9]. Total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglyceride and fasting blood glucose levels were recorded for each patient. Target values recommended by the ESC dyslipidemia guideline is LDL-C ≤ 70 mg/dL or a $\geq 50\%$ reduction from baseline LDL-C in patients with known CHD [10]. In this study target LDL-C level was < 70 mg/dL.

Statistical analysis

All data were analyzed with SPSS (Statistical Package for the Social Sciences) software for Windows version 20.0. Continuous and quantitative data were summarized using descriptive statistics

Table 1. Baseline characteristic features of patients.

Features	N	Mean \pm SD or %
Age [years]	2976	73.4 \pm 6.2
\geq 80 years	541	18.2
Male	1794	60.3
CABG	837	28.1
PTCA/stent	1290	43.3
Heart failure	1128	37.9
HF _r EF	681	22.9
HF _p EF	447	15.0
Dysrhythmia	810	27.2
Pacemaker	116	3.9
Prosthetic valve	91	3.1
Cigarette smoking	388	13.0
Exerciser	704	23.6
Exercise < 150 min/week	357	12.0
Exerciser > 150 min/week	347	11.7
Hypertension	2184	73.4
Hyperlipidemia	1412	47.4
Diabetes mellitus	1008	33.9
Anemia	508	17.1
Pulmonary hypertension:	508	17.1
Primary	8	0.3
Secondary	500	16.8
Respiratory system disease	596	20.0

CABG — coronary artery bypass graft; HF_rEF — heart failure with reduced ejection fraction; HF_pEF — heart failure with preserved ejection fraction; PTCA — percutaneous transluminal coronary angioplasty; SD — standard deviation

including mean, standard deviations, medians (min–max), frequency distributions and percentages. Normality of data distribution was verified by Kolmogorov-Smirnov/Shapiro-Wilk test. Homogeneity of variance was assessed by Levene's test. Quantitative variables were compared with Student t test or Mann-Whitney U test. P-values of < 0.05 were considered statistically significant.

Results

Among 2976 patients with CHD, 60.3% were male, mean age was 73.4 \pm 6.2 (65–94) years and 18.2% of patients (n = 541) were > 80 years old. Characteristic features of the patients are summarized in Table 1. 43.3% (n = 1290) of patients had a history of percutaneous transluminal coronary angioplasty/stent and 28.1% (n = 837) CABG. The number of patients diagnosed with heart failure was 1128 (37.9%) and heart failure with reduced ejection

Table 2. Laboratory values of study population.

Feature	Median (min.–max.)
BMI [kg/m ²]	27.2 (14.6–58.8)
Overweight (BMI 25–29.9 kg/m ²) (n = 1261)	42.4%
Obese (BMI \geq 30 kg/m ²) (n = 628)	21.1%
SBP [mmHg] (n = 2636)	130 (70–220)
DBP [mmHg] (n = 2636)	80 (25–122)
SBP > 140 mmHg (n = 819)	31.1%
Heart rate [bpm]	75 (32–169)
Hemoglobin	13 (7–19)
eGFR	67.2 (1–176)
Fasting blood glucose [mg/dL] (n = 2158)	105 (35–502)
Total cholesterol (n = 2203)	181 (76–514)
LDL-C (n = 2288)	106 (10–422)
LDL-C < 70 mg/dL (n = 318)	13.9%
Triglycerides [mg/dL] (n = 2275)	132 (27–906)
LDL-C < 70 mg/dL, SBP < 140 mmHg (n = 219)	9.6%

BMI — body mass index; DBP — diastolic blood pressure; eGFR — estimated glomerular filtration rate; LDC-C — low density lipoprotein cholesterol; SBP — systolic blood pressure

fraction (22.9 %, n = 681) was more frequent. Patients who had a history of arrhythmia were reported at 27.2% (n = 810) and the most frequent arrhythmia was atrial fibrillation/flutter (80%, n = 649). 13.0% (n = 387) of patients were smokers and the ratio of male smokers (19%, n = 334) was significantly higher than in the female smokers (4.5%, n = 53) (p < 0.001). Hypertension (73.4%, n = 2184) was the most frequent risk factor followed by hyperlipidemia (47.4%, n = 1412) and diabetes mellitus (33.9%, n = 1008). The mean BMI was 27.6 \pm 4.4 kg/m² (median 27.2, 14.6–58.8) and 42.4% (n = 1261) were overweight and 21.1% (n = 628) were obese (Table 2). Seven hundred and four (n = 704, 23.6%) patients reported that they did regular exercise, but only a limited 11.7% (n = 347) exercised more than 150 min or more per week. Median systolic and diastolic blood pressures were 130 (70–220) and 80 (25–122), respectively in patients whose blood pressures were recorded (n = 2636, 88.5% of study population). The rate of patients with SBP > 140 mmHg were 31.1% (n = 819) among patients whose blood pressure was recorded (Table 2).

Additionally, among patients who had hypertension (n = 2184, 73.4% of study population) the rate of patients with SBP > 140 mmHg were re-

Table 3. Pharmacological treatment.

Drug treatment	N = 2976	%
Anti-platelet	2360	79.3
Anti-platelet-PPI	1120	37.6
DAPT	559	18.8
DAPT-PPI	336	11.3
Anticoagulant	473	15.9
Statin	1485	49.9
Beta-blocker	2106	70.8
ACEI/ARB	2026	68.1
PPI	1368	46.0
Anti-platelet–statin	1331	44.7
Anti-platelet–statin–beta-blocker	1045	35.1
Anti-platelet–statin–beta-blocker–ACE/ARB	812	27.3

ACEI — angiotensin-converting enzyme inhibitor; ARB — angiotensin receptor blocker; DAPT — dual anti-platelet treatment; PPI — proton pump inhibitor

Table 4. Distribution of anti-platelet therapy.

Medication	N	%
Acetylsalicylic acid	1501	63.6
Clopidogrel	290	12.2
Acetylsalicylic acid: clopidogrel	506	21.4
Acetylsalicylic acid: ticagrelor	48	2.0
Acetylsalicylic acid: prasugrel	5	0.2
Prasugrel	3	0.1
Ticagrelor	7	0.3
Total	2360	100

ported as 33.9% (n = 739) and almost all (n = 716, 98.1%) were receiving at least one anti-hypertensive agent. Similarly, the rate of hypertensive patients with at least one antihypertensive therapy was high at 97.5% (n = 2129). The median LDL-C value was 106 (10–422) mg/dL in patients whose LDL-C was recorded (2288 patients; 76.9%). Only 13.9% (n = 318) of patients had a LDL-C value of recommended ≤ 70 mg/dL level (Table 2). The recommendation level was reached in only 15.2% (n = 165) of patients with known hyperlipidemia similar to the entire population. Median LDL-C level was higher in patients with hyperlipidemia than non-hyperlipidemia or unknown patients (108 [30–422] mg/dL, 105 [10–281]; p = 0.002, respectively). The rate of statin use was 81.5% (n = 1151) in patients with a history hyperlipi-

demia and 49.9% (n = 1485) in all patients. The rate of patients who met the recommendations of secondary prevention guidelines regarding both LDL-C level and SBP were 9.6% (n = 219). The rate of medication use in patients with known CHD are summarized in Table 3. 79.3% of patients (n = 2360) were on anti-platelet treatment (Table 4). Approximately half of patients who were on anti-platelet treatment had concomitant use of proton pump inhibitors (PPI). This rate was slightly higher in patients who were receiving dual anti-platelet treatment. Concomitant use of anti-platelet and statin was limited to 44.7% (n = 1331) and combined anti-platelet, statin, beta-blocker usage was 35.1% (n = 1045) anti-platelet, statin, beta-blocker and angiotensin-converting enzyme inhibitor/angiotensin receptor blocker (ACEI/ARB) combination was used in 27.3% (n = 812).

Discussion

The assessment of elderly patients with CHD from the national epidemiologic study ELDER-TURK has shown that most patients had hypertension, half had hyperlipidemia and one-third had DM. Almost half of the patients were overweight and one fifth of all patients were obese and only one-quarter of patients did regular exercise. The number of patients with target SBP reduction and LDL-C reduction was low, elderly patients with known CHD were far from receiving appropriate secondary prevention.

The purpose of secondary prevention is to protect patients from major clinical events such as myocardial infarction and to reduce the progression of coronary heart disease. As in all developed economies the importance of secondary prevention in cardiovascular disease, which is increasing in Turkey and as well as in other elderly populations. In recent years, several randomized controlled studies, which demonstrate the importance of hypertension, hyperlipidemia, smoking, DM and antithrombotic treatment, have been published in secondary protection. Though it has been observed that a large part of elderly populations do not receive proven treatments in clinical practice [6].

Smoking is one of the major preventable risk factors for death [11, 12]. The EURIKA study in the Turkey group had an active smoking rate of 23.7%, was close to 21.3% which is Europe’s average rate [13]. The EUROASPIRE II study has been shown that at the time of the index event 87.7% of patient were smoking and at the interview 21% of patients continued to smoke [14]. In

EUROASPIRE III study during index event 69.7% of all patients included and 73.1% of patients from Turkey were smokers [15]. Interviews after the index event, 23% of patients from Turkey and 17% of all patients continued smoking [16]. In the present study smoking rates were lower compared to EUROASPIRE II, III and EURIKA studies. This could be explained by patients age differences included in this study and by older patients who smoked less than younger patients. In the EUROASPIRE II 44% of patients were over 60 years old, this rate was 58.6% in the EUROASPIRE III study.

A sedentary life is the main cause of many chronic diseases, CHD being one of the first. Similarly, an increase in physical activity, independent from age, gender and ethnicity increases quality of life [17]. Though, the rate of regular exercise among older patients is known to be very low [11]. In the EUROASPIRE III study, 59.1% of patients in the Europe group and 48.6% of patients in the Turkey group increased physical exercise, but only 7.4% of the Turkish group reported intense physical activity (3–4 times a week for at least 20 min) [16]. In the present study results are similar to the EUROASPIRE III study. It is believed that the reason for the major part of the patients not doing physical activity or only light physical activity is due to being old and having comorbidities. Overweight, one of the major problems of the modern world is one of the leading causes of CHD. In the EURIKA study the obesity rate of the Turkish group was 36.2% and 43.5% for all patients included [13]. This study shows that even after a serious event like CHD, life style changes such as regular exercise and losing weight is not easily achieved.

Hypertension is a risk factor that could affect all age groups as well as the elderly. Elderly populations have a high rate of hypertension and the Framingham study showed that lifelong risk is 90% [2, 18, 19]. In the EURIKA study, rate of hypertension was 66.5% in the Turkey group, whereas it was 72.7% in the whole study group. Ninety-four percent of all patients were under treatment for hypertension and only 38.8% reached target blood pressure levels [13]. In EUROASPIRE II, EUROASPIRE III and EUROASPIRE III the Turkey group, rate of patients with hypertension was 89.9%, 81.4% and 75.2%, respectively and after the index event. Interviews showed that 50%, 56% and 55.2% respectively did not reach target blood pressure levels [14–16]. In the present study the rate of hypertension is similar to that of other studies. However, the rate of patients that achieved target blood pressure level were higher than in previous

studies. The reason for high rates of target blood pressure level achievement may be due to regular medical treatment and frequent follow-up.

The relationship between LDL-C level and cardiovascular events continue in elderly people, despite a reduction in total and LDL-C levels with age, especially after the seventh decade [20, 21]. Although effectiveness of statins in elderly patients is demonstrated with published data, it is well known that a large number of patients do not receive this treatment at both discharge or at follow-up periods [20–22]. In the EURIKA study, the rate of dyslipidemia in Europe was 57.7% whereas in Turkey it was significantly lower (34.5%) and had the lowest rates of all countries. Though, 30.4% of dyslipidemic patients treated in Turkey group reached target LDL-C levels, this was lower than the 41.2% observed in Europe [13]. In the EUROASPIRE III study lowering total cholesterol level rate was 51.7% in the Turkey group and 48.9% in Europe [15]. Yet again, the use of statin rate after an index event was 65% in the Turkey group and 78.1% in Europe [16]. When compared to this study, both the rate of statin use and the number of patients that reached the target LDL-C levels were significantly lower than in this study. This could be explained by avoiding optimal drug use in the elderly by doctors due to polypharmacy, drug interactions and side effects. Also, in some patients the LDL-C level over 70 mg/dL might have reduced $\geq 50\%$ from baseline, but if the baseline LDL-C level is not known it might have affected the number of patients reaching the target level proposed by ESC guidelines.

Diabetes is among the most important cardiovascular risk factors. In the EURIKA study, the rate of diabetes in the Turkey group was 31.4% and 24.4% in Europe [13]. In EUROASPIRE III study, the rate of diabetes in Turkish subjects was similar to all patients included (33.6% and 34.8%, respectively). In this study 34.7% of patients had diabetes, this result correlates with prior studies. Both in this study and in previous studies, an average of 1 in 3 patients with CHD or cardiovascular risk factors has DM.

The continuity of treatment during both at the acute stage and long-term is vitally important in CHD [2, 8]. The EUROASPIRE II, III and Turkey group of EUROASPIRE III survey have reported that 85.9%, 90.5%, and 91.4% of patients respectively received an anti-platelet drug, 62.9%, 79.8%, and 73.8% of patients respectively received a beta-blocker, 38%, 70.9%, and 69% of patients respectively received ACEIs after discharge. In this study

79.3% of patients received an anti-platelet drug, 70.8% received a beta-blocker and 68.1% received ACEI/ARB. A less significant use of anti-platelet drugs may be due to concerns about bleeding in elderly patients. Despite the proven effectiveness of beta-blocker and ACEI/ARB in treatment, usage rate was slightly different than in published data. The use of PPI with anti-platelet drug therapy is recommended in patients with high risk of bleeding and with the elderly. Approximately half of the present patients were not receiving PPI therapy. Refusing medication in the elderly, avoidance of polypharmacy and various concerns physicians may have caused not initiating this efficient treatment for this patient group.

Limitations of the study

The most important limitation of the present study is that there is no comparison group. For this reason the data was compared with previous studies in Turkey and multicentre studies including Turkish patients. Due to being a cross-sectional study, some baseline laboratory values were not known and the discharge treatment is another limitation. When baseline laboratory values were not known for LDL-C level of reduction could not be assessed. The patients were elderly and may have provided incomplete information.

Conclusions

In conclusion, according to available literature this is the first study to evaluate the lifestyle, management of risk factors and medical treatment for secondary prevention among elderly patients in Turkey. Elder Turk study has shown that many patients with CHD have high prevalence of modifiable risk factors and unhealthy lifestyle. In addition, many patients are not receiving therapeutic intervention and as a consequence most are not achieving the recommended goals. There is wide gap in implementation of evidence-based medicine in practice.

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