



## RESEARCH

# FREQUENCY OF CARDIOVASCULAR DISEASES AND DRUG USE IN TURKISH ELDERLY POPULATION FOLLOWED UP AT CARDIOLOGY CLINICS: THE ELDELTURK STUDY

## ABSTRACT

**Introduction:** In Turkey, there is a lack of data on the frequency of cardiovascular diseases, risk factors, co-morbid diseases, and drug usage among the elderly population. We aimed to compile a data of frequency of cardiovascular diseases, cardiovascular risk factors, concomitant diseases, and drug usage among elderly patients visiting cardiology clinics in Turkey.

**Materials and Method:** This non-interventional, multicenter study evaluated 5694 patients aged 65 years or older and who were followed up at cardiology clinics. Cardiovascular diseases, risk factors, co-morbidities, and medication use were surveyed.

**Results:** Mean age of patients was 73.5±6.3 years (males: 49.8%). The frequency rates were 73% for hypertension, 28.8% for diabetes mellitus, 35% for hyperlipidemia, 50% for previous myocardial infarction, 27.3% for atrial fibrillation, and 11.5% for chronic renal failure. The body mass index of participants was 27.7±4.4 kg/m<sup>2</sup>, systolic blood pressure was 130±18 mmHg, diastolic blood pressure was 77.1±11 mmHg, and resting heart rate was 76±14 bpm, 66.3% of the study population used beta blockers, 71.7% angiotensin system inhibitors, 59.6% diuretics, 7.9% digoxin, 30.5% calcium channel blockers, 34% lipid-lowering agents, 71.5% acetylsalicylic acid, and 25.9% oral anticoagulants. The most common non-cardiovascular medications were vitamins (12.3%) and nonsteroidal anti-inflammatory drugs (11.2%).

**Conclusion:** Valuable data of Turkey's elderly population at cardiology clinics, pertaining to cardiovascular and co-morbid diseases was collected. The identification of risk factors for cardiovascular diseases as well as concomitant diseases, and medication use in elderly patients may lead to interventions that could improve the health of elderly in the general population.

**Keywords:** aged, cardiovascular disease, risk factors

Turkish Journal of Geriatrics  
2017;20 (2):73-81

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Received: 26/02/2017  
Accepted: 24/05/2017

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## ARAŞTIRMA

# KARDİYOLOJİ KLİNİKLERİNDE TAKİP EDİLEN YAŞLI TÜRK NÜFUSUNDA KARDİOVASKÜLER HASTALIK SIKLIĞI VE İLAÇ KULLANIMI: ELDELTURK ÇALIŞMASI

## Öz

**Giriş:** Türkiye'deki yaşlı popülasyonda kardiyovasküler hastalık sıklığı, risk faktörleri, ko-morbid hastalıklar ve ilaç kullanımına ait bir veri yoktur. Amacımız, Türkiye'de kardiyoloji kliniklerince takipli yaşlı nüfusta kardiyovasküler hastalık sıklığı, kardiyovasküler risk faktörleri, eşlik eden hastalıklar ve ilaç kullanımları ile ilgili bir veri oluşturmaktır.

**Gereç ve Yöntem:** Çalışmamız müdahalesiz ve çok merkezli bir çalışmadır. Kardiyoloji kliniklerince takip edilen 65 yaş ve üzeri 5694 hasta çalışmaya dahil edilmiştir. Kardiyovasküler hastalıklar, risk faktörleri, eşlik eden hastalıklar ve ilaç kullanımları sorgulanarak kaydedilmiştir.

**Bulgular:** Çalışma popülasyonunda ortalama yaş 73.5±6.3 idi (erkek oranı %49,8). Hipertansiyon %73, diyabet %28,8, hiperlipidemi %35, geçirilmiş miyokard enfarktüsü %50, atrial fibrilasyon %27,3 ve kronik böbrek hastalığı %11,5 oranında görülmekteydi. Çalışmaya katılanların ortalama vücut kitle indeksi 27.7±4.4 kg/m<sup>2</sup>, sistolik kan basıncı 130±18 mmHg, diyastolik kan basıncı 77.1±11 mmHg ve istirahat kalp hızı 76±14 vuru/dakika idi. Çalışma popülasyonunun %66,3'ü beta bloker, %71,7'si anjiyotensin sistem inhibitörleri, %59,6'sı diüretik, %7,9'u digoksin, %30,5'i kalsiyum kanal blokeri, %34'ü lipid düşürücü ajanlar, %71,5'i asetil salisilik asit ve %25,9'u oral antikoagülan kullanmaktaydı. En sık kullanılan kardiyovasküler sistem dışı ilaçlar vitaminler (%12,3) ve non-steroid anti-inflamatuar ilaçlardı (%11,2).

**Sonuç:** Gözlemsel çok merkezli çalışmamızda, yaşlı Türk popülasyonundaki kardiyovasküler ve ko-morbid hastalıklarla ilgili değerli veriler elde ettik. Yaşlı hastalardaki kardiyovasküler hastalıklar için risk faktörlerinin belirlenmesi, eşlik eden hastalıklar ve kullanılan ilaçların tanımlanması, tüm yaşlı nüfusun sağlığı için uygun ve gerekli girişimlerin yapılmasına yardımcı olabilir.

**Anahtar kelimeler:** yaşlı, kardiyovasküler hastalık, risk faktörleri

## INTRODUCTION

There is a remarkable increase in the elderly population aged over 65 years worldwide. In Turkey, which is known to have a predominantly young population, the 8% elderly population recorded in 2014 is anticipated to grow to approximately 10.3% in 2023 (1). Aging, not only leads to an increase in socioeconomic problems, but also is an independent risk factor for cardiovascular diseases. Cardiovascular diseases are specifically most dominant in this age group, and the disease profile differs among the different population groups across the world. Turkey is a developing country and has seen rapid changes in life-style, and consequently in disease prevalence. Region-specific data are markedly important for preventing and controlling the pathogenesis of cardiovascular diseases and risk factors. However, in Turkey, there is no data on the frequency of cardiovascular diseases, risk factors, comorbid diseases, and drug usage, especially among the elderly population. Cardiovascular diseases are the leading cause of death among elderly people in the country, accounting for a mortality rate of 46.8% (1), which is greater than the rate in Europe, 42% (2).

The elderly population with cardiovascular diseases comprises a group that needs special interest and care. In particular, comorbid diseases and polypharmacy in this group deserve attention. Cardiovascular drugs account for more than one third of the total adverse drug interactions in the elderly (3). Today, there are no age-specific guidelines for the treatment of cardiovascular diseases and the goals are mainly the same as for the middle-aged population. Suitable profiling of this specific group to define areas of focus for prevention and treatment is required.

Our primary aim was to create a data on the frequency of cardiovascular diseases, risk factors, co-morbid diseases, and drug usage in the elderly population visiting cardiology clinics. We believe, our study reflected a valuable data of the specific elderly group with multiple co-morbidities and risk factors, though this data can not be generalized to

the whole elderly population. To provide a better and specific health-care system for this age group, we need to know more about the population profile and determine the priorities of the national elderly health-care program.

## MATERIALS AND METHOD

### Study population

This non-interventional, multicentric, observational trial evaluated the cross-sectional data of patients older than 65 years of age who were followed up at cardiology clinics, after they had provided written informed consent for study participation. Both inpatient and outpatient cardiology clinics were included for patient enrollment. There was no specific treatment protocol, because this was an observational study; patients were treated according to the local clinical practice of the center. At least 2500 patients followed up at cardiology clinics were the target for inclusion in this study conducted over a 10-month period. No follow-up protocol was defined for this study. Cardiovascular disease profile, coexisting risk factors, comorbidities and drug usage of the patients were evaluated and recorded.

Patient enrollment commenced in March and ended in December 2015. Inclusion criteria were being older than 65 years of age, follow-up at cardiology clinics, and provision of informed consent for study participation. Our study was approved by the local ethics committee of Ankara Kecioren Training and Research Hospital (date: 11/March/2015, number: ISM.4.06.68.49) and we followed the principles of the Declaration of Helsinki (as revised in Brazil, 2013).

Demographic information of patients, such as date of birth, sex, weight, height, body mass index (BMI), and current tobacco use were recorded. Validated digital office scale was used for weight measurements and BMI was calculated by the formula recommended by World Health Organisation (kilograms/meter<sup>2</sup>). Physical activity



level was recorded, and patients performing at least 30 minutes of moderate exercise at least 3 days a week were recorded as regular exercisers. Patients were considered hypertensive if they were on antihypertensive medications or had high blood pressure on examinations ( $>140/90$  mmHg), performed twice for confirmation. Blood pressure measurements were done as office measurements with validated digital sphygmomanometer. Patients were deemed diabetic if they were using antidiabetic medication or insulin, or had a fasting blood glucose higher than 126 mg/dL. Hyperlipidemia was diagnosed in patients on lipid lowering drugs or who were newly prescribed for their lipid levels according to the lipid guidelines of the European Society of Cardiology (4). Anemia was diagnosed according to recommendation of World Health Organisation (hemoglobin level  $<12$  g/dL in women and  $<13$  g/dL in men). History of cardiovascular interventions, such as percutaneous coronary interventions or bypass grafting; history of myocardial infarction, dysrhythmia, peripheral arterial disease, valvular disease (patients with moderate or severe valvular disease); co-morbidities such as cerebrovascular diseases, pulmonary, hepatic, renal, thyroid diseases, musculoskeletal disorders, malignancies; outpatient or emergency department visits, and medication history (including over-the-counter drugs) were questioned and recorded after searching the medical records of study subjects. On physical examination, heart rate and blood pressure were recorded and the patient was questioned about hypotensive episodes, defined as symptomatic episodes with blood pressure lower than usual. Electrocardiography of each patient was evaluated by the cardiologist and arrhythmias with clinical significance were reported as dysrhythmia. For the laboratory data, patient's most recent blood biochemistry and complete blood count values studied at the clinic were recorded. There were no invasive interventions or pharmacological drug usage during the trial. During the study, patient data were recorded on electronic case report forms, with

each center having password-controlled access to the data of only their own patients.

### Statistical analysis

Study centers were designed to represent the 12 territorial units of Turkey, accepted by the National Statistics Unit. All statistical analysis were conducted using SPSS, version 16 (SPSS Inc., Chicago, IL, USA) for Windows XP. Summary of data analysis was planned to be shared as tables. Because it was an observational, non-interventional study, there were no specific hypotheses to be tested, no comparisons and no end points. Continuous variables were presented as mean  $\pm$  standard deviation and data on frequency were presented as percentage (%).

## RESULTS

### Clinical characteristics

We enrolled 5694 patients from 73 centers in Turkey between March and December 2015. The mean age of the patient group was  $73.5 \pm 6.6$  years, and 41.5% were older than 75 years. Male/female ratio was almost 1, because the percentage of males was 49.8%. Mean value for BMI was  $27.4 \pm 4.4$ , and mean resting heart rate was  $76 \pm 14$  bpm. The proportion of regular exercisers was 21.7%. Mean systolic and diastolic blood pressure were  $130 \pm 18$  and  $77.1 \pm 11$  mmHg, respectively, and 4.6% of subjects reported hypotensive episodes. Levels of LDL cholesterol, creatinine and fasting blood glucose were  $117 \pm 38$ ,  $1.2 \pm 0.5$ , and  $117 \pm 43$  mg/dL, respectively. Mean value of estimated glomerular filtration rate (eGFR, calculated by the MDRD equation) was  $68.7 \pm 23$  mL/min/1.73 m<sup>2</sup>. In the study population, 16.3% had anemia, 6.2% had hypothyroidism, and 4% had malignancy. Cardiovascular risk factors of hypertension, diabetes mellitus, and hyperlipidemia were detected in 73%, 28.8%, and 35% of subjects, respectively. Current smokers comprised 11.3% of the study population. Details of cardiovascular disease and comorbidities are presented in Table 1.

**Table 1.** Cardiovascular and comorbid diseases

Disease	Frequency (%)
Prior MI	50
History of PCI	49.2
History of CABG	66.9
History of stroke	18.7
Atrial fibrillation*	27.3
Non-ischemic cardiomyopathy	3.6
Chronic kidney disease**	11.5
Prosthetic heart valve	5
Pacemaker	4
Anemia	16.3
Hypothyroidism	6.2
Alzheimer	1.6
COPD or asthma	15
Anemia	16.3
Malignancy	4

Values are given as frequencies.

\*All types of atrial fibrillation (paroxysmal, permanent, persistent) were recorded.

\*\*Patients with GFR<60 mL/min for at least 3 months were recorded as chronic kidney disease.

CABG: Coronary artery by-pass grafting, COPD: Chronic obstructive pulmonary disease, MI: Myocardial infarction, PCI: Percutaneous coronary intervention.

### Cardiovascular medications

In the study population, 66.3% were using beta-blockers, 38.6% angiotensin-converting enzyme inhibitors, 33.1% angiotensin receptor blockers, 59.6% diuretics, 7.9% digoxin, 30.5% calcium channel blockers, 34% lipid-lowering agents (statins and non-statins), 25.9% oral antidiabetic drugs, 3% insulin, 71.5% acetylsalicylic acid (100 mg), and 25.9% oral anticoagulants (61% warfarin). Fenofibrates, alone or in combination with statins, were 5.2% of the lipid-lowering agents used. Cardiovascular medications used by the patients and their frequency of use are listed in Table 2. Most common noncardiovascular

medications included vitamins (excluding oral iron and calcium; 12.3%), nonsteroidal anti-inflammatories (11.2%), and antidepressants (10.3%). Herbal products were used by only 1% of our study population. Four or more prescription medications were used by 25% of the overall study population.

**Table 2.** Cardiovascular medications

Drugs	Frequency (%)
Beta blockers	66.3
Diuretics	59.6
ACE inhibitors	38.6
ARBs	33.1
Calcium channel blockers	30.5
Lipid lowering agents	34
Asetyl salicylic acid	71.5
Oral anticoagulants (OAC)	25.9
Warfarin use among the OACs	61
Digoxin	7.9

Values are given as frequencies ACE: Angiotensin converting enzyme, ARB: Angiotensin receptor blocker.

Emergency room visits in the preceding year were recorded as 19%, and 73% of them were treated at cardiology inpatient wards. Visits to outpatient clinic more than 10 times a year was recorded as 18.9% in the study population.

### DISCUSSION

This observational multicenter study collected valuable data from Turkey's elderly population, comprising patients who were followed up at cardiology clinics. Patient profile was outlined by demographic data, cardiovascular and comorbid diseases, and medication use.

In developing countries such as Turkey, rapid socioeconomic growth leads to an increase in cardiovascular risk factors. The prevalence of



hypertension (>140/90 mmHg) was reported to be 77% in women and 60.9% in men among the population aged over 70 years in the TEKHARF cardiovascular risk survey (5). The Patent study reported that more than 70% of the population aged over 80 years were hypertensive (6). Recently, Ozkara et al. showed that 75.4% of the population aged over 60 years was hypertensive based on a cross-sectional survey (7). Our finding of 73% hypertensive patients was similar to the rate reported for the general elderly population. The prevalence of diabetes mellitus was reported to be 13.7% in the general Turkish population in the TURDEP study (8). Among the elderly population of Turkey, the prevalence of diabetes was shown to be 27.4% (7). The rate of hyperlipidemia in our population aged over 50 years was reported to be 32% (5). Our study, which was comprised of elderly at cardiology clinics, revealed the diabetes rate as 28.8% and hyperlipidemia rate as 35%. According to the National Institute of Health, obesity is defined as BMI > 30 kg/m<sup>2</sup> (9). In Turkey, the overall prevalence of obesity was approximately 32% among the adult population (8), and among the elderly, it was reported to be 27.2% (7). Mean BMI in our study population was 27.4±4.4. More than one quarter of the study population had atrial fibrillation, which increases the risk of stroke fivefold, and the stroke frequency in our study was 18.7%. In a study conducted in the United States (US), stroke prevalence in adults was 2.3% and more than three quarters of subjects were aged over 65 years (10). The high rate of cerebrovascular disease in our study could be attributed to the high risk profile of the study population of cardiology clinics, but this alarming profile should also make us consider and question the effectiveness of the risk scoring and anticoagulation undertaken in the country.

Turkey is a country with a poor reputation for cigarette smoking. Among the adult population, the rate of regular smokers was 23.2%, and among the elderly, the rate was 8.4% (1). In our study, the current smoker rate was 11.3%. We found that at least one out of ten patients being followed at cardiology clinics were current smokers, and it should

be noted that 50% of the study population had a history of myocardial infarction. This remarkable data implied the insufficiency of educational programs against smoking, especially at the cardiology clinics. Smoking cessation rehabilitative programs need to be intensified and should receive further focus.

Cardiovascular drugs are the most commonly used drugs in the elderly population. Jörgensen et al. reported that 47.2% of the population aged over 65 years used cardiovascular drugs, particularly diuretics (11). There is an increase in the use of medicines among the elderly and when compared to past, the elderly are being more intensely treated according to the guidelines (12). Among all cardiovascular drugs, the most commonly used drugs were the angiotensin system inhibitors, both receptor blockers and enzyme inhibitors (used in 71.7% of the patient population). According to the latest guidelines for hypertension, this drug group is recommended as first-line therapy in hypertensive patients (13). Beta-blockers and diuretics were used by 66.3% and 59.6% of the patient group, respectively. These high frequencies were owing to the cardiovascular disease profile of our patient population. However, these numbers should generate caution about the high rate of probable side effects from these drug groups. In our study, 4.6% of the patient population reported hypotensive episodes, which could lead to falls and fractures that could be fatal in this age group. Another important fact to be considered is that old people have multiple medical conditions, which expose them to the risks of polypharmacy. In the literature, polypharmacy is usually defined as inappropriate drug use or taking five or more pills per day (excluding over-the-counter drugs) (14, 15). Jörgensen et al. found the average number of drugs per subject to be 4.3 in the elderly population (11). Bushart et al. reported a rate of six or more pill usage in the US general elderly population as being 29.4% (14). In a study from Spain, the rate of polypharmacy in patients older than 70 years in cardiology clinics was reported to be 84.5% (15). In our study, we

found that 25% of the study population was using four or more prescription medications. This was a lower rate than expected. We believe there could have been missed data due to these details having been recorded at only one visit; this is a limitation of our study.

The most commonly used noncardiovascular medication was NSAIDs, used by nearly one out of ten patients. When the dominance of oral anticoagulants and antiplatelet medications in this population is considered, much more care should be taken to question the use and necessity of NSAIDs. Drug drug interactions can lead to lethal results, especially in the elderly. Cardiovascular drugs accounted for more than one third of the adverse drug interactions among elderly people in a study by Tipping et al. (3). Concomitant use of prescription drugs and dietary supplements such as vitamins and herbal products can be much more frequent than estimated. The rate of concomitant use was reported to be 13% in the elderly in the US (16, 17), but the Ginkgo Evaluation of Memory study cohort found the rate to be 83% in people aged over 75 years (18). In our study we did not research concomitant use, but the most commonly used dietary supplements were vitamins, used by 12.3% of the study population. This drug group also has a potential risk for adverse drug interactions, and should be particularly considered during anticoagulant use and increased risk of bleeding (19).

Geriatric patients represent a special population for emergency services. It has been reported that the rate of emergency room visits of elderly patients was 13%-23% (20-22). Emergency admissions increase proportionally with increasing age. In our study, the rate of emergency room visits in the recent year was recorded as 19%. In another study, cardiac problems were the most common reason for admission to the emergency room among older patients (23). In our study, the annual rate of more than 10 visits to the cardiology outpatient clinic was 18.9%, which was really high. We considered INR monitoring for warfarin therapy to be a contributor to the high rate in our study population.

## CONCLUSION

This study was conducted to define the general profile of elderly patients in Turkey's cardiology clinics. This cross-sectional frequency data may potentially facilitate further concentration on the specific needs and problems of this group of patients. One of the limitations of our study is that our data does not reflect the profile of the entire elderly population because only subjects being from cardiology clinics were included. However, we believe these results can enlighten the problems requiring focused attention, and as clinicians, we may notice some specific details that we have not considered earlier. By identifying and improving the needs of this specific group, we may generalize the benefits to the entire elderly population.

**Acknowledgement:** Our trial was supported by 'Turkish Society of Cardiology'.

**Author disclosure statement:** No conflict of interest.

**Financial disclosure:** No specific funding.

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