Aspirin Use in Patients Aged 80 years and over in Turkey: Snapshot of Results from the ASSOS Study

Kadriye Memiç Sancar,[1] Oğuzhan Çelik,[2] Cem Çil,[2] Özcan Başaran,[2]
Erkan Demirci,[3] Veysel Ozan Tanık,[4] Mücahit Yetim,[5] Osman Karaarslan,[5]
Lütfü Bekar,[5] Tolga Doğan,[6] Mubariz Murat Resulzade,[7] Çağlar Kaya,[8]
Volkan Doğan,[2] Murat Biteker[2]

[1]Department of Cardiology, Mehmet Akif Ersoy Cardiothoracic and Vascular Surgery Training and Research Hospital, Istanbul, Turkey
[2]Department of Cardiology, Mugla Sitki Kocman University Training and Research Hospital, Mugla, Turkey
[3]Department of Cardiology, Kayseri City Hospital, Kayseri, Turkey
[4]Department of Cardiology, Ankara Dıskapı Yıldırım Beyazıd Training and Research Hospital, Ankara, Turkey
[5]Department of Cardiology, Hitit University Corum Erol Olcok Training and Research Hospital, Corum, Turkey
[6]Department of Cardiology, Bursa Ihtisas Training and Research Hospital, Bursa, Turkey
[7]Department of Cardiology, Private Hospital Park Darica Hospital, Kocaeli, Turkey
[8]Department of Cardiology, Edirne Trakya University, Faculty of Medicine, Edirne, Turkey

ABSTRACT

Objectives: Acetylsalicylic acid (aspirin) is commonly used with various indications, especially in the elderly population. This study aims to evaluate the prevalence of polypharmacy and aspirin use in patients aged ≥80 years.

Methods: The ASSOS trial is a cross-sectional, national registry study. This nonrandomized study was conducted by 30 cardiologists in 14 cities on the elderly (over the age of 80 years) who used aspirin (80–325 mg). Polypharmacy is described as an intake of five or more medicines daily.

Results: A total of 309 patients were included in the study, and 146 (47.2%) of them were females. Aspirin treatment for primary prevention (PP) was reported to be given to 101 (32.7%) patients, and polypharmacy was detected in 198 (64.1%) patients. Major gastrointestinal bleeding was reported in 7 (3.5%) patients in the polypharmacy group and 0 (0.0%) patients in the without polypharmacy group (p=0.043). Minor bleeding was reported in 58 (29.3%) patients in the polypharmacy group and in 8 (7.2%) patients in the group without polypharmacy (p<0.001).

Conclusion: Aspirin was reported to be used commonly among patients aged ≥80 years for PP although the current guidelines do not recommend aspirin for PP in Turkey. Polypharmacy is still critical in the very elderly population and should be carefully considered in terms of complications.

Keywords: Aged, aspirin, polypharmacy

INTRODUCTION

Today, average life expectancy has increased with the prevention and/or early detection of diseases.[1] In accordance with the increase in the elderly population, an increase was also reported in the prevalence of chronic diseases and the medication taken by the elderly for the treatment of these diseases.[2] Ninety percent of elderly patients aged ≥65 years have at least one chronic disease.[3]

Polypharmacy is the concurrent use of many different medicines.[4] The definition of polypharmacy varies between the concomitant use of 2 or more and 5 or more medications. However, most of the studies regard polypharmacy as the simultaneous use of more than 5 or more medicines. The need for long-term drug use due to chronic diseases results in concurrent use of some medicines, and unwanted side effects occur easily with both drug–drug interactions.[5,6]

Cardiovascular (CV) diseases are very common in the elderly population, and many of these patients use acetylsalicylic acid (aspirin).[7] Studies have shown that CV risk doubles for each decade of life independently of the traditional risk factors. In CV diseases, aspirin use in secondary prevention (SP) is uncontroversial; however, it is still being prescribed for primary prevention (PP) although current guidelines do not suggest it. There is no consensus regarding who is supposed to be on aspirin treatment.[8] American College of Cardiology/American Heart Association (ACC/AHA) 2019 guideline on the PP of CV disease does not recommend the use of aspirin for PP in adults aged 70 years and over because the risk for major bleeding is higher than the potential benefits of reducing CV events.

This study aimed to evaluate the prevalence of polypharmacy and aspirin use in patients aged ≥80 years.

METHOD

The present study was conducted with data derived from the project entitled "The Appropriateness of Aspirin Use in Medical Outpatients: A Multicenter, Observational Study (ASSOS)." ASSOS trial is a national, multicentered trial investigating indications for aspirin use, appropriate use, and prescribing patterns of aspirin in Turkey.[9] This trial is a nonrandomized, cross-sectional, national registry study conducted with 5007 patients living in 7 geographical regions of Turkey and performed by 30 cardiologists from 14 different cities. The data were assembled from consecutive patients who had been prescribed aspirin during their regular visits to the outpatient cardiology clinics between March 1, 2018, and June 31, 2018, and they were included in the study disregarding the indications for aspirin use. No diagnostic or treatment procedure was obligatory in the study.

The indications for aspirin use were evaluated in accordance with the 2016 European Society of Cardiology (ESC) guideline, 2016 United States Preventative Services Task Force (USPSTF) guideline, and 2019 ACC/AHA guideline on the PP of CV disease guideline.[8,10,11]

In the present study, the patients aged ≥80 years on aspirin therapy were evaluated in terms of sociodemographic factors such as age, gender, place of residence, level of education, clinical characteristics, CV risks factors, and their medications regarding gastrointestinal (GI) side effects and bleeding complications. The initial dose determined by the clinicians, the duration, and the reason for aspirin use were evaluated. Polypharmacy was determined according to how many different drugs the patients take per day, and a daily drug intake of 5 and over was considered polypharmacy.[4]

The risk for bleeding was determined by the HAS-BLED [hypertension (HT), abnormal renal/liver function, stroke, bleeding history or anemia, labile international normalized ratio, elderly (≥65 years), drugs (aspirin, nonsteroidal anti-inflammatory drugs (NSAIDs)] score and other clinical parameters.[12] Major bleeding was defined as any bleeding (major GI bleeding, intracranial hemorrhage, etc.) that required a hospital stay, and minor bleedings included gingival bleeding, nose bleeding, ecchymosis, and hematuria.

Statistical analysis was made using the computer software Statistical Package for Social Sciences (IBM SPSS Statistics for Windows, Version 21.0 software, IBM Corp., Armonk, New York, USA). Normal distribution analysis was performed using the Kolmogorov–Smirnov test. The data were expressed as frequency, percentage, mean, median, standard deviation, and 25th–75th percentiles. The Mann–Whitney U test was used for comparing quantitative variables without normal distribution, and Student's t-test was used for comparing the means between two groups with normal distribution. Pearson's Chi-squared analysis was performed for categorical variables. A value of $p<0.05$ was considered statistically significant.

RESULTS

Of 309 patients who were over 80 years of age, 146 (47.3%) were females and 198 (64.1%) were reported to have polypharmacy. Sociodemographic and clinical characteristics of patients according to polypharmacy status were summarized in Table 1.

Aspirin treatment for PP was reported to be given to 101 (32.7%) patients aged 80 years and over. Aspirin use for SP was found to be higher in the polypharmacy group when compared with the group without polypharmacy [146 (73.8%) vs 62 (55.9%), p=0.001]. Aspirin use according to polypharmacy status was summarized in Table 2.

Dyspepsia complaints in patients aged ≥80 years were higher in the polypharmacy group than in the group without polypharmacy [76 (38.4%) vs 28 (25.2%), p=0.019].

Table 1. Sociodemographic and clinical characteristics of patients according to polypharmacy status

	Polypharmacy		p
	Absent (n=111)	Present (n=198)	
Age (years)	82.0±3.0	83.0±4.0	0.584*
Gender			
Female	41 (36.9)	105 (53.0)	0.007†
Male	70 (63.1)	93 (47.0)	
Educational status			
Illiterate	32 (28.8)	96 (48.5)	0.001†
Primary school	53 (47.7)	76 (38.4)	
Middle school	13 (11.8)	11 (5.5)	
High school	11 (9.9)	12 (6.1)	
University	2 (1.8)	3 (1.5)	
Place of residence			
Rural	26 (23.4)	65 (32.8)	0.082†
Urban	85 (76.6)	133 (67.2)	
Current smoker	50 (45.0)	81 (40.9)	0.480†
Alcohol use	8 (7.2)	9 (4.5)	0.325†
BMI (kg/m^2)	25.7 (24.1-29.0)	26.5 (24.4-29.3)	0.488‡
Systolic blood pressure (mmHg)	130.0 (120.0-140.0)	130.0 (120.0-140.0)	0.723‡
Diastolic blood pressure (mmHg)	80.0 (70.0-80.0)	78.0 (70.0-80.0)	0.013‡
Heart rate (bpm)	71.0 (66.0-82.0)	75.0 (68.0-82.0)	0.345‡
Comorbidity§			
Atrial fibrillation	16 (14.4)	26 (13.1)	0.752†
Heart failure	13 (11.7)	48 (24.2)	0.008†
HT	80 (72.1)	178 (89.9)	<0.001†
Diabetes mellitus	8 (7.2)	62 (31.3)	<0.001†
Chronic renal failure	5 (4.5)	29 (14.6)	0.006†
Hyperlipidemia	27 (24.3)	98 (49.5)	<0.001†
COPD	6 (5.4)	36 (18.2)	0.002†
Prior MI	19 (17.1)	82 (41.4)	<0.001†
Coronary artery disease	52 (46.8)	136 (68.7)	<0.001†
Prior CABG surgery	25 (22.5)	40 (20.2)	0.631†
Prior PCI	10 (9.0)	73 (36.9)	<0.001†
Lower extremity PAD	6 (5.4)	4 (2.0)	0.103†
Upper extremity PAD	0 (0.0)	1 (0.5)	0.641†
Carotid artery disease	4 (3.6)	14 (7.1)	0.212†
Prior CVE	11 (9.9)	24 (12.1)	0.556†
Prior pace-maker implantation	4 (3.6)	3 (1.5)	0.213†
Bioprosthetic valve replacement	0 (0.0)	0 (0.0)	–
Mechanical valve replacement	1 (0.9)	0 (0.0)	0.359†
Liver dysfunction	0 (0.0)	3 (1.5)	0.262†

BMI: Body mass index; bpm: Beats per minute; CABG: Coronary artery bypass graft; COPD: Chronic obstructive pulmonary disease; CVE: Cerebrovascular event; HT: Hypertension; MI: Myocardial infarction; PAD: Peripheral artery disease; PCI: Percutaneous coronary intervention.

Data are presented as n (%), mean±standard deviation and median (25th–75th percentiles).

*Student t-test, †Pearson's Chi-squared test., ‡Mann Whitney U test.

§There may be more than one disease.

Table 2. Aspirin use according to polypharmacy status

	Polypharmacy		p
	Absent (n=111)	**Present (n=198)**	
Aspirin dosage			
80–100 mg	99.0 (89.2)	178.0 (89.9)	0.344*
150 mg	11.0 (9.9)	14.0 (7.1)	
300 mg	1.0 (0.9)	6.0 (3.0)	
Duration of aspirin use (months)	23.0 (7.0–72.0)	48.0 (12.0–120.0)	0.019†
Prevention			
Primary prevention	49.0 (44.1)	52.0 (26.3)	0.001*
Secondary prevention	62.0 (55.9)	146.0 (73.7)	
Physician administering aspirin			
Cardiology	82.0 (73.9)	164.0 (82.8)	0.061*
Neurology	13.0 (11.7)	16.0 (8.1)	
Internal medicine	4.0 (3.6)	14.0 (7.1)	
Cardiovascular surgery	3.0 (2.7)	2.0 (1.0)	
Family physician	6.0 (5.4)	2.0 (1.0)	
Patient preference	2.0 (1.8)	0 (0.0)	
Others	1.0 (0.9)	0 (0.0)	

Data are presented as n (%) and median (25th–75th percentiles).
*Pearson's Chi-squared test, †Mann–Whitney U test.

HAS-BLED scores were higher in the polypharmacy group when compared with the group without polypharmacy [3.0 (2.0–3.0) vs 2.0 (1.0–2.0), p<0.001]. The frequency of major GI bleeding [7 (3.5%) vs 0 (0.0%), p=0.043] and minor bleeding [58 (29.3%) vs 8 (7.2%), p<0.001] were found to be higher in the polypharmacy group than in the group without polypharmacy.

The use of the following medications was found to be significantly higher in polypharmacy group than in the group without polypharmacy according to angiotensin-converting-enzyme inhibitors [88 (44.4%) vs 18 (16.2%), p<0.001], angiotensin receptor blockers [74 (37.4%) vs 29 (26.1%), p=0.044], beta blockers [146 (73.7%) vs 43 (38.7%), p<0.001], mineralocorticoid receptor antagonists [17 (8.6%) vs 0 (0.0%), p=0.001], statins [81 (40.9%) vs 15 (13.5%), p<0.001], furosemide [51 (25.8%) vs 10 (9.0%), p<0.001], hydrochlorothiazide [57 (28.8%) vs 16 (14.4%), p=0.004], isosorbide mononitrate [28 (14.1%) vs 1 (0.9%), p<0.001], and NSAIDs [37 (18.7%) vs 11 (9.9%), p=0.041]. Moreover, the use of proton pump inhibitors (PPIs) [95 (48.0%) vs 23 (20.7%), p<0.001] and H2 receptor blockers [9 (4.5%) vs 0 (0.0%), p=0.017] was found to be higher in polypharmacy group than in the group without polypharmacy.

DISCUSSION

In this study, ASSOS Study data were used to evaluate aspirin and polypharmacy in patients aged ≥80 years. Aspirin treatment for PP was reported to be given to 32.6% of patients aged 80 years and over, and polypharmacy was detected at a prevalence of 64.0%. Females in the polypharmacy group have a higher frequency than the non-polypharmacy group. In addition, CV risk factors (such as diabetes mellitus, HT, and hyperlipidemia), coronary artery disease, and heart failure were more prevalent in the polypharmacy group than in the group without polypharmacy. The prevalence of major and minor bleeding was found to be significantly higher in the polypharmacy group than in the group without polypharmacy. However, the study results are contradictory for aspirin use in PP. In the ESC guidelines, aspirin is not recommended to be used for PP in individuals without clinically manifest CV disease. The USPSTF guideline recommends using low-dose aspirin in individuals between the ages of 40 and 70 years who are at a higher risk of CV disease events but not at high risk of bleeding.[10,11] It should not be routinely recommended for aspirin therapy for individuals aged ≥70 years. Due to these recommendations, clinicians can prescribe aspirin even to patients without a known CV disease according to their own experiences. Being a

frequently used and easily accessible drug, aspirin is considered to be harmless. However, the risk of bleeding increases with age, and major extracranial bleeding doubles each decade independent of aspirin use.[13] Therefore, it is vital to be aware of the harm–benefit balance. In the Effect of Aspirin on Cardiovascular Events and Bleeding in the Healthy Elderly (ASPREE) Trial, low-dose (80–100 mg) aspirin was shown not to reduce the CV risks in healthy adults aged 70 years and over, and it also critically increased major bleeding events.[1] In the subanalysis of the ASPREE study, aspirin was reported to increase the risk of bleeding by nearly 60% in individuals aged 70 years and over. In our study, the frequency of major GI bleeding and minor bleeding were found to be higher in the polypharmacy group than in the group without polypharmacy.

Studies show an increase in the prevalence of prescriptions as age increases.[14] In a study by Husson et al., the prevalence of four or more drug use among individuals aged 60 years and over was 29.9%, Niclós et al. reported the prevalence of polypharmacy as 15.5%.[15,16] In a study conducted in Turkey by Savran and Asci, the prevalence of five or more drug use among patients staying in nursing homes was 39.3%. Taskin Sayir et al. found the prevalence of three or more drugs usage to be 91% in patients aged 65 years and over.[4,17] Arslan et al. reported that the prevalence of five or more drug use was 17.3% in their study conducted among 1944 nursing home residents in 23 provinces in Turkey, and CV system drugs were found to be the most used drugs in the study.[18] In our study, 64% of all individuals aged ≥80 years took a total of five drugs daily.

Studies show a higher prevalence of polypharmacy in females.[17] In a study, females aged 65 years and over had the highest incidence of multiple drug use, and 1 in every 5 female patients used at least 5 medications.[19] In a study conducted among patients aged >65 years by Ozturk and Ugras, polypharmacy was found to be higher and the frequency of illiteracy lower in females than in males.[20] In our study, the prevalence of polypharmacy was reported to be higher in both females and illiterates.

Polypharmacy-related GI complaints and GI bleedings have been commonly reported in the literature.[19–21] In our study, dyspeptic complaints were significantly higher in the polypharmacy group than in the group without polypharmacy. In a study conducted in our country by Discigil et al., the prevalence of PPI use was 26.1% among the elderly living in nursing homes and 12.1% among those who consulted a polyclinic.[21] In our study, PPI use was 48% in the polypharmacy group. In the subanalysis of the ASPREE study and the recent well-conducted stud-

ies, concomitant use of prophylactic PPI with aspirin and oral anticoagulants has been shown not to reduce bleeding.[22,23]

The limitation of the study was not specially designed to evaluate very elderly patients; for that matter, the rational use of aspirin and polypharmacy might not have been thoroughly evaluated for general practice and might have been overestimated considering the study results. A final limitation is the exclusion of mental diseases such as Parkinson's, dementia, and Alzheimer's from the study.

CONCLUSION

Our study results have shown that health professionals will become more aware of patients and treatment management, especially about PP for CV diseases. Polypharmacy is a critical matter for patients of advanced age, and the prevalence of polypharmacy in individuals ≥80 years of age is 64%. Additionally, minor bleeding was reported in one of every 4 patients ≥80 years of age with polypharmacy. This study may affect the daily practice of aspirin use, polypharmacy, and the approach to bleeding in people over 80 years of age.

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