Medicinski podmladak

Medical Youth

Review article

CARDIOVASCULAR RISK FACTORS FOR STROKE AMONG THE ELDERLY

KARDIOVASKULARNI FAKTORI RIZIKA ZA MOŽDANI UDAR KOD STARIH OSOBA

Nataša Stojanovski[1], Aleksandra Tomić[2,3], Aleksandra Radojičić[2,3], Milija Mijajlović[2,3]

[1] Univerzitet u Beogradu, Medicinski fakultet, Institut za humanu genetiku, Beograd, Srbija
[2] Univerzitet u Beogradu, Medicinski fakultet, Beograd, Srbija
[3] Univerzitetski klinički centar Srbije, Klinika za neurologiju, Beograd, Srbija

Correspondence: milijamijajlovic@yahoo.com

Abstract

By the year 2050 there will be around 426 million people over 80 years of age. As lifespan is extended, cardiovascular risk factors are becoming one of many challenges. Cardiovascular diseases are the leading cause of death at the age over 65. Stroke is also one of the leading causes of disability and mortality. It is estimated that 75% of strokes occur in people over 65 years of age. Understanding how to manage modifiable risk factors for stroke and recognizing the influence of non-modifiable risk factors is crucial. Age is a leading factor in a non-modifiable group of stroke risk factors. Gender is also highlighted due to socioeconomic and biological differences between men and women. Modifiable risk factors for stroke are diabetes mellitus (DM), obesity, psychosocial factors, dyslipidemia, smoking, physical inactivity, diet, alcohol intake, high blood pressure and other cardiovascular diseases like atrial fibrillation (AF), with hypertension being one of the most important risk factors in the group of elderly patients. Knowing more about the associations of these risk factors with stroke in different age groups can help with better management and stroke prevention.

Keywords:
cardiovascular risk factors,
stroke risk factors,
elderly

The authors declare no conflicts of interest.

doi:10.5937/mp75-51625
Editorial board: podmladak.med.bg@gmail.com
e-ISSN: 2466-5525

Sažetak

Do 2050. godine biće oko 426 miliona ljudi preko 80 godina starosti. Pošto je životni vek sve duži, kardiovaskularni faktori rizika postaju sve veći izazov. Kardiovaskularne bolesti su vodeći uzrok smrti kod osoba preko 65 godina. Moždani udar je, takođe, na jednom od vodećih mesta među uzrocima mortaliteta i invaliditeta. Procenjuje se da se 75% moždanih udara javlja kod ljudi starijih od 65 godina. Važno je znati kako se može uticati i koliko na promenljive faktore rizika za moždani udar, a kako oni faktori rizika koji se ne mogu menjati utiču na rizik od pojave moždanog udara. Godine života su vodeći faktor rizika među nepromenljivim faktorima rizika za moždani udar. Kao važan se takođe može izdvojiti pol zato što postoje socioekonomske i biološke razlike između muškaraca i žena. U one faktore rizika koji su promenljivi spadaju: dijabetes, gojaznost, psihosocijalni faktori, dislipidemija, pušenje, fizička neaktivnost, ishrana, prekomerni unos alkohola, visok krvni pritisak i druga kardiovaskularna oboljenja, poput atrijalne fibrilacije (AF), pri čemu je hipertenzija možda i najvažniji faktor iz ove grupe kod starijih osoba. Bolje poznavanje povezanosti ovih faktora rizika sa moždanim udarom u različitim starosnim grupama može pomoći u boljoj kontroli i prevenciji moždanog udara.

Ključne reči:
kardiovaskularni faktori rizika, faktori rizika za moždani udar, starije osobe

Introduction

The World Health Organization predicts that by the year 2030, 1 out of 6 people in the world will be over 60 years old. The number of individuals over 80 years of life by 2050 will triple, so that number will be around 426 million. In the EU population in 2020, 20.6% of people were 65 and over, and it's estimated to be 40.6% by the year 2050 (1). One of the numerous challenges in the elderly is cardiovascular risk factors that can lead to stroke. In people over the age of 65, cardiovascular diseases are the leading cause of death and it is estimated that 75% of strokes occur in people older than 65 years (1-3). Mortality due to cardiovascular diseases decreased in high-income countries during recent decades, whilst there is an increase in low-income countries (4). The American Heart Association data between 2017 and 2020 showed that 127.9 million American adults had at least one cardiovascular disease, and stroke took the 5th place as a cause of death (2, 5). In Brazil, stroke is the leading cause of mortality (6). It was shown that having 65 years or more was associated with a 3-fold risk of stroke (7). The stroke is a global cause of immobility, lower quality of life and mortality. The elderly population has more hospitalization days and higher post-stroke mortality (2). For example, in the United Kingdom, over 25 billion pounds per year are spent on the management of stroke-related disability and patients care (8). The risk factors for stroke are divided into groups of non-modifiable risk factors such as: age, sex, race/ethnicity, genetics and modifiable risk factors: high blood pressure, diabetes mellitus (DM), abdominal obesity, psychosocial factors, apolipoproteins levels, smoking, physical inactivity, diet, alcohol intake and cardiac causes (9). The question about stroke risk factors has been asked for decades. In 1992, Zeiler et al. indicated that the relevance of stroke risk factors varied with age and that hypertension, DM and high serum levels of cholesterol and triglycerides were often found in older patients (10). Age represents a prevailing factor in a non-modifiable group of risk factors for stroke (6, 11).

Stroke-heart syndrome is a term that came into use last few years, and it was shown that there was a risk for poststroke major adverse cardiovascular events, with older age being significantly associated with that risk (12, 13). Furthermore, ischemic stroke was independently associated with an increased risk of major adverse cardiovascular events like myocardial infarction, unstable angina, congestive heart failure, coronary artery disease (CAD), coronary artery revascularization or cardiovascular death (13). Therefore, we can say that managing cardiovascular risk factors not only prevents cerebrovascular insults, but also cardiac complications after stroke.

Gender

It is considered to be a disease with a higher prevalence in men, but there may be a predominance of women with stroke in the population over 80. One of the reasons could be higher life expectancy in women than men (14). Differences in stroke epidemiology between sexes can be due to the poorer socioeconomic status of women and also biological differences (6, 11). The Framingham Heart Study included women over 60 years of age without stroke history who did not use estrogen before menopause. The association between age at natural menopause before the age of 42 and increased risk for ischemic stroke was shown (14). A more recent study corroborated these findings, indicating that women who experience earlier age at natural menopause have a higher risk of ischemic stroke (15). It is estimated that 4 - 5% of strokes in all women can be attributed to the fact of early natural menopause. Other risk factors for stroke that are specific for women include pregnancy, oral contraceptive pill use and hormone replacement therapy. Estrogen was considered to have a cardioprotective effect in premenopausal women (11, 14, 16). The recent data of the UK Biobank and EPIC-CVD (European Prospective Investigation into Cancer and Nutrition-Cardiovascular Diseases) study also confirmed the association between stroke and earlier age at natural menopause but with

inconsistency in stroke subtypes and without clear causality. Understanding the connection between gender differences and stroke will provide critical insights into the distinct pathophysiological mechanisms underlying cerebrovascular events in men and women (16).

Physical activity

Physical activity exerts beneficial effects on health through the modulation of inflammation, enhancement of endothelial function, and improvement of vascular reactivity. Its protective effect against ischemic stroke, however, may also be mediated through its influence on conventional stroke risk factors (17). In a multiethnic study of older, urban-dwelling and stroke-free individuals, with an average age of 69.2 ± 10.3 years, it was found that greater exercise intensity is associated with lower stroke risk, but only in men. This gender-specific protective effect may be due to the fact that women were more likely to be physically inactive and less likely to engage in moderate to high-intensity physical activities (17).

Smoking

Smoking is an important risk factor for stroke. It was found that active smoking influenced the age at which acute stroke occurs, making it an important modifiable risk factor, particularly in young people. Furthermore, quitting smoking was shown to rapidly reduce the risk of stroke, emphasizing the critical role of smoking cessation in stroke prevention (9). In line with this, alcohol abuse, physical inactivity and obesity were associated with an increased risk of having an acute cerebrovascular event before the age of 75 (9). There are maybe fewer smokers in the older group of patients, but that can be due to other fatal diseases related to smoking, such as cancer (6). In the study of Harmsen et al, which included a 28-year follow-up of middle-aged men, smoking was identified as a significant risk factor for stroke during the first 21 years of the study. However, in the last seven years of the follow-up period, this significant association was no longer observed. It is important to note that the number of smokers decreased over time, which may obscure the true influence of smoking on stroke risk in the later years of the study (18). Furthermore, the prevalence of smoking declined over time, from above 50% to 6%, thus having less impact as a risk factor for cardiovascular disease (19).

Hyperlipidemia

It was suggested that dyslipidemia had less influence as a risk factor for stroke than in cardiac diseases, with a low incidence of dyslipidemia in patients with stroke, especially in patients over the age of 65 (6). The LDL cholesterol is a strong risk factor both for myocardial infarction (MI) and stroke. The benefit of using statins in primary prevention of stroke should be considered. However, the use of statin as secondary prevention of stroke in elderly patients is recommended, together with blood pressure lowering, cessation of smoking, diet modification and antithrombotic treatment (6, 19, 20).

A study from Sweden found a strong association between total serum cholesterol and coronary artery disease (CAD) but not with stroke (21). Furthermore, some other studies reported an inverse association between total serum cholesterol and stroke, while most epidemiological studies failed to find a direct relationship (21). It is known that HDL have protecting effect against atherosclerosis through several mechanisms (22). However, an association between elevated HDL levels and stroke severity was described in a group of older patients, possibly because acute ischemic stroke (AIS) increases the proportion of dysfunctional HDL with a stressful effect on endothelial cells (23). Some previous studies showed an association between higher serum HDL and reduced stroke severity in patients under the age of 50 (24). Relationship between HDL and its subclasses and stroke is complicated and further research is needed to better understand the potential role of HDL in stroke prevention (23, 25).

Diabetes mellitus

Diabetes mellitus is another very well-known risk factor for heart disease, as well as for stroke. In younger patients, DM represents a higher risk for heart failure than in older ones (26). It is a significant predictor for lacunar stroke. However, it was shown that the frequency of lacunar stroke associated with DM is lower in patients over 85 years of age compared to those younger than 85 (27). A study from Japan showed an association between DM and a higher risk of stroke in a group of older patients between 60 and 74 years, but not in older than 75 years (28). This lack of a strong association between DM and stroke risk in the elderly might be due to the occurrence of fatal cardiovascular events at younger ages. Individuals with DM often have other cardiovascular risk factors like dyslipidemia and hypertension, which can lead to fatal outcomes earlier in life (28).

Asymptomatic carotid artery stenosis

Asymptomatic carotid artery stenosis (ACAS) is a complication of atherosclerotic cardiovascular disease (29). The annual stroke rate in patients with ACAS is 1 - 3% (30). ACAS is defined as ≥ 50% carotid stenosis without previous transient ischemic attack (TIA) or stroke in the territory of ACAS. Some evidence showed that 40 - 50% of older patients with ACAS may have cognitive dysfunction due to cerebral hypoperfusion (29). ACAS with ≥ 50% diameter reduction occurs in about 10% of people over 65 years of age. Patients with over 70% of diameter reduction are at higher risk of cardiovascular events (29). Howard et al. found that the stroke risk in cohort studies was highly dependent on the degree of ACAS (31). In the same study patients with 50 - 99% ACAS had a mean age of 77.5 and the risk of stroke was less than 5% in patients with medical

therapy for moderate stenosis and around 15% in ones with severe stenosis (31).

Hypertension

Hypertension is a well-recognized stroke risk factor. Hypertension is an important risk factor for both ischemic and hemorrhagic stroke (27). It is particularly significant for lacunar and atherothrombotic ischemic stroke. However, the influence of hypertension as a risk factor for stroke diminishes in some older age groups. Specifically, its direct effect appears to be less pronounced in stroke patients over 80 years of age (6,32). Giang et al. described that only high systolic blood pressure (SBP) was a major individual risk factor for stroke among 7174 middle-aged men, after 35 years of follow-up, but also SBP along with age, serum cholesterol and smoking had a cumulative effect with more impact on CAD. A study from Japan showed that individuals over 75 years of age have a high risk for stroke, and it was found that those within this age group with a history of high blood pressure were at an increased risk of stroke (9,28). Another study found no association between traditional risk factors and stroke in patients over 75 years of age except for high blood pressure (9). The REGARDS study described a significantly smaller association of hypertension, DM, and heart disease with stroke in older patients compared to younger individuals (33). A Spanish study found that among 303 patients with ischemic stroke at the age of 85 years and older, the most common risk factors were hypertension (44.9%) and AF (42.6%), followed by DM (16.2%), congestive heart failure (15.5%), ischemic heart disease (11.9%), transient ischemic attack (11.2%), previous cerebral infarction (9.6%), and hyperlipidemia (9.2%). In the same study when compared with patients younger than 85, a history of hypertension along with DM, heavy smoking and hyperlipidemia were less frequent in patients older than 85 years (27). One of the explanations could be that individuals with these comorbidities often die before reaching the age of 85. Brazilian retrospective study showed an increased proportion of patients with hypertension in the elderly (over 65) with stroke, but no difference between groups younger and older than 80 years was found (6).

Atrial fibrillation

Atrial fibrillation is a well-known risk factor for acute stroke, particularly ischemic stroke. Some studies have shown that the impact of AF on stroke risk increases with aging, although its prevalence decreases after the age of 70 - 80 (32). Notably, after the age of 80, AF is more prevalent in women (32). Newly diagnosed AF has been found to result in a 2-fold increase in the risk of stroke in older ages (34). Furthermore, the occurrence of paroxysmal AF in patients with acute stroke is more often than we think, because it can be underdiagnosed (35). In the well-known CHADS2 scoring system for stroke risk assessment in AF, increased age is included as a risk factor for stroke (1). It has to be noted that an important cause of hemorrhagic stroke in the elderly is, besides cerebral amyloid angiopathy, the use of anticoagulant therapy. Bleeding risk should always be assessed and then therapy should be administered accordingly (20,36). A Brazilian study that included a group of patients diagnosed with stroke revealed varying prevalence rates of AF across different age groups. The study found that AF was diagnosed in 12% of patients aged 65 to 79, in 26% of patients over the age 80, and 5% of younger patients (6). It is a leading risk factor for cardioembolic stroke, which is associated with larger strokes, higher mortality and poorer outcome (11,37).

Heart failure

Heart failure (HF) and age are important risk factors for acute ischemic stroke (38). It increases the risk of ischemic stroke recurrence 2 to 3 times (6). Individually, hypertension, hypercholesterolemia and diabetes are significantly associated with HF in older adults, and all these risk factors together with smoking increase this risk up to 20 times (39). Coronary artery disease is the main cause of HF, whereas severe HF is a source of cerebral emboli (6). In individuals over 75 years of age who suffered an AIS and had HF, an elevated heart rate was associated with higher stroke severity (38).

Coronary artery disease

Age is an important non-modifiable risk factor for CAD, while CAD is associated with a higher risk of stroke. Pieri et al. detected a significant increase in the prevalence of CAD in people with stroke over the age of 65, while there was no difference between the ones below and over the age of 80 (6). CAD could indicate that the patient has generalized atherosclerosis, so if an ischemic stroke occurs, there is a high probability that the cause is atherothrombotic (27).

Peripheral vascular disease

Peripheral vascular disease (PVD) was associated with higher stroke severity in a group of AIS patients between 65 and 74 years, as well as in the group of AIS with HF patients over 75 (38). It is an independent predictor of poor outcomes in AIS patients (38).

Myocardial infarction

Age over 65 is a predictive risk for cerebrovascular events after MI (5). It is important to think about stroke after MI, particularly in older patients. Lichtman et al. identified 20% of older people who had a higher risk of stroke within 6 months after being released from the hospital after MI, based on the presence of clinical factors (AF, diabetes, hypertension etc.) (40). In a high-risk group of patients, 1 of 12 that had acute myocardial infarction will have a stroke within a year (40).

Table 1. The risk factors for stroke in elderly.

Author(s), publication year	Risk factors for stroke	Results
Pieri et al, 2008	Gender	Predominance of women with stroke after 80 years
Roy-O'Reilly et al, 2018 Lisabeth et al, 2018		Gender related risk factors: earlier menopause, pregnancy, OCP use, HRT
Willey et al, 2009	Physical activity	Greater exercise intensity associated with lower stroke risk in men at the age 70
Soto et al, 2020	Smoking	Less influence of smoking as a risk factor in elderly (over 75 years)
Pieri et al, 2008	Dyslipidemia	Low incidence of dyslipidemia in patients with stroke, especially in patients over the age of 65
Arboix et al, 2006	Diabetes mellitus	Frequency of lacunar stroke associated with DM lower in patients over 85 years
Murakami et al, 2017		Association between DM and higher risk of stroke in patients between 60 and 74 years
Soto et al, 2020 Murakami et al, 2017	Hypertension	Less important for groups over 80 years, but most common risk factor for stroke over the age of 75
Pieri et al, 2008 Giang et al, 2013		SBP is a major individual risk factor for stroke in the middle aged men
Andersen et al, 2010	Atrial fibrillation	AF increases risk for stroke with aging, but prevalence is lowering after the age of 70-80
Morseth et al, 2021		AF results in a 2-fold increase for stroke risk in elderly (over 70 years)
Ribeito et al, 2024	Heart failure	Hypertension, hypercholesterolemia, diabetes and smoking increase risk of heart failure up to 20 times in older adults (average age 70.4 years)
Pieri et al, 2008	Coronary artery disease	Increase in prevalence of CAD in people with stroke over age of 65
Edrissi et al, 2022	Peripheral vascular disease	PVD is associated with greater stroke severity in patients with AIS between 65 and 74 years, and in patients with AIS and HF over 75 years
Singer et al, 2019.	Myocardial infarction	Age over 65 is a risk factor for CVE after MI

Abbreviations: OCP - Oral contraceptive pill; HRT - Hormone replacement therapy; DM - Diabetes mellitus; SBP - Systolic blood pressure; AF - Atrial fibrillation; CAD - Coronary artery disease; PVD - Peripheral vascular disease; AIS - Acute ischemic stroke; HF - Heart failure; CVE - Cerebrovascular event; MI - Myocardial infarction.

Conclusion

Given the increase in average life expectancy, it is crucial to identify modifiable risk factors for heart disease and stroke. Understanding the most prominent risk factors in different age groups, how these factors change over time, their interactions, and their short- and long-term impact on stroke risk is essential for effective primary prevention and overall quality of life, particularly in older.

Literature

1. Gado K SA, Markovics D, Virag A. Most common cardiovascular diseases of the elderly– A review article. DHS. 2021; 4(2):27-32.
2. Tsao CW, Aday AW, Almarzooq ZI, Anderson CAM, Arora P, Avery CL, et al. Heart Disease and Stroke Statistics-2023 Update: A Report From the American Heart Association. Circulation. 2023; 147(8):e93-e621.
3. Benjamin EJ, Blaha MJ, Chiuve SE, Cushman M, Das SR, Deo R, et al. Heart Disease and Stroke Statistics-2017 Update: A Report From the American Heart Association. Circulation. 2017; 135(10):e146-e603.
4. Ruan Y, Guo Y, Zheng Y, Huang Z, Sun S, Kowal P, et al. Cardiovascular disease (CVD) and associated risk factors among older adults in six low-and middle-income countries: results from SAGE Wave 1. BMC Public Health. 2018; 18(1):778.
5. Singer J, Gustafson D, Cummings C, Egelko A, Mlabasati J, Conigliaro A, et al. Independent ischemic stroke risk factors in older Americans: a systematic review. Aging. 2019; 11(10):3392-407.
6. Pieri A, Spitz M, Lopes TO, de Barros CG, Faulhaber MW, Gabbai AA, et al. Prevalence of cardiovascular risk factors among elderly Brazilians over eighty with ischemic stroke. Arq Neuropsiquiatr. 2008; 66(3A):454-7.
7. Marinigh R, Lip GY, Fiotti N, Giansante C, Lane DA. Age as a risk factor for stroke in atrial fibrillation patients: implications for thromboprophylaxis. J Am Coll Cardiol. 2010; 56(11):827-37.
8. Ahmed A, Pinto Pereira SM, Lennon L, Papacosta O, Whincup P, Wannamethee G. Cardiovascular Health and Stroke in Older British Men: Prospective Findings From the British Regional

Heart Study. Stroke. 2020; 51(11):3286-94.
9. Soto-Cámara R, González-Bernal JJ, González-Santos J, Aguilar-Parra JM, Trigueros R, López-Liria R. Age-Related Risk Factors at the First Stroke Event. J Clin Med. 2020; 9(7):2233.
10. Zeiler K, Siostrzonek P, Lang W, Gossinger H, Oder W, Ciciyasvilli H, et al. Different risk factor profiles in young and elderly stroke patients with special reference to cardiac disorders. J Clin Epidemiol. 1992; 45(12):1383-9.
11. Roy-O'Reilly M, McCullough LD. Age and Sex Are Critical Factors in Ischemic Stroke Pathology. Endocrinology. 2018; 159(8):3120-31.
12. Scheitz JF, Sposato LA, Schulz-Menger J, Nolte CH, Backs J, Endres M. Stroke-Heart Syndrome: Recent Advances and Challenges. J Am Heart Assoc. 2022; 11(17):e026528.
13. Sposato LA, Lam M, Allen B, Richard L, Shariff SZ, Saposnik G. First-ever ischemic stroke and increased risk of incident heart disease in older adults. Neurology. 2020; 94(15):e1559-e70.
14. Lisabeth LD, Beiser AS, Brown DL, Murabito JM, Kelly-Hayes M, Wolf PA. Age at natural menopause and risk of ischemic stroke: the Framingham heart study. Stroke. 2009; 40(4):1044-9.
15. Zhu D, Chung HF, Dobson AJ, Pandeya N, Giles GG, Bruinsma F, et al. Age at natural menopause and risk of incident cardiovascular disease: a pooled analysis of individual patient data. Lancet Public Health. 2019; 4(11):e553-e64.
16. Tschiderer L, Peters SAE, Van der Schouw YT, van Westing AC, Tong TYN, Willeit P, et al. Age at Menopause and the Risk of Stroke: Observational and Mendelian Randomization Analysis in 204 244 Postmenopausal Women. J Am Heart Assoc. 2023; 12(18):e030280.
17. Willey JZ, Moon YP, Paik MC, Boden-Albala B, Sacco RL, Elkind MS. Physical activity and risk of ischemic stroke in the Northern Manhattan Study. Neurology. 2009; 73(21):1774-9.
18. Harmsen P, Lappas G, Rosengren A, Wilhelmsen L. Long-term risk factors for stroke: twenty-eight years of follow-up of 7457 middle-aged men in Goteborg, Sweden. Stroke. 2006; 37(7):1663-7.
19. Lind L, Sundstrom J, Arnlov J, Lampa E. Impact of Aging on the Strength of Cardiovascular Risk Factors: A Longitudinal Study Over 40 Years. J Am Heart Assoc. 2018; 7(1):e007061.
20. Lindley RI. Stroke Prevention in the Very Elderly. Stroke. 2018; 49(3):796-802.
21. Giang KW, Bjorck L, Novak M, Lappas G, Wilhelmsen L, Toren K, et al. Stroke and coronary heart disease: predictive power of standard risk factors into old age--long-term cumulative risk study among men in Gothenburg, Sweden. Eur Heart J. 2013; 34(14):1068-74.
22. Sanossian N, Saver JL, Navab M, Ovbiagele B. High-density lipoprotein cholesterol: an emerging target for stroke treatment. Stroke. 2007; 38(3):1104-9.
23. Simmons CA, Poupore N, Nathaniel TI. Age Stratification and Stroke Severity in the Telestroke Network. J Clin Med. 2023; 12(4):1519.
24. Sanossian N, Saver JL, Kim D, Razinia T, Ovbiagele B. Do high-density lipoprotein cholesterol levels influence stroke severity? JJ Stroke Cerebrovasc Dis. 2006; 15(5):187-9.
25. Tian F, Chen L, Qian ZM, Xia H, Zhang Z, Zhang J, et al. Ranking age-specific modifiable risk factors for cardiovascular disease and mortality: evidence from a population-based longitudinal study. EClinicalMedicine. 2023; 64:102230.
26. Tromp J, Paniagua SMA, Lau ES, Allen NB, Blaha MJ, Gansevoort RT, et al. Age dependent associations of risk factors with heart failure: pooled population based cohort study. BMJ. 2021; 372:n461.
27. Arboix A, Miguel M, Ciscar E, Garcia-Eroles L, Massons J, Balcells M. Cardiovascular risk factors in patients aged 85 or older with ischemic stroke. Clin Neurol Neurosurg. 2006; 108(7):638-43.
28. Murakami K, Asayama K, Satoh M, Inoue R, Tsubota-Utsugi M, Hosaka M, et al. Risk Factors for Stroke among Young-Old and Old-Old Community-Dwelling Adults in Japan: The Ohasama Study. J Atheroscler Thromb. 2017; 24(3):290-300.
29. Gray VL, Goldberg AP, Rogers MW, Anthony L, Terrin ML, Guralnik JM, et al. Asymptomatic carotid stenosis is associated with mobility and cognitive dysfunction and heightens falls in older adults. J Vasc Surg. 2020; 71(6):1930-7.
30. Den Hartog AG, Achterberg S, Moll FL, Kappelle LJ, Visseren FL, Van der Graaf Y, et al. Asymptomatic carotid artery stenosis and the risk of ischemic stroke according to subtype in patients with clinical manifest arterial disease. Stroke. 2013; 44(4):1002-7.
31. Howard DPJ, Gaziano L, Rothwell PM, Oxford Vascular S. Risk of stroke in relation to degree of asymptomatic carotid stenosis: a population-based cohort study, systematic review, and meta-analysis. Lancet Neurol. 2021; 20(3):193-202.
32. Andersen KK, Andersen ZJ, Olsen TS. Age- and gender-specific prevalence of cardiovascular risk factors in 40,102 patients with first-ever ischemic stroke: a Nationwide Danish Study. Stroke. 2010; 41(12):2768-74.
33. Howard G, Banach M, Kissela B, Cushman M, Muntner P, Judd SE, et al. Age-Related Differences in the Role of Risk Factors for Ischemic Stroke. Neurology. 2023; 100(14):e1444-e53.
34. Morseth B, Geelhoed B, Linneberg A, Johansson L, Kuulasmaa K, Salomaa V, et al. Age-specific atrial fibrillation incidence, attributable risk factors and risk of stroke and mortality: results from the MORGAM Consortium. Open heart. 2021; 8(2):e001624.
35. Flint AC, Banki NM, Ren X, Rao VA, Go AS. Detection of paroxysmal atrial fibrillation by 30-day event monitoring in cryptogenic ischemic stroke: the Stroke and Monitoring for PAF in Real Time (SMART) Registry. Stroke. 2012; 43(10):2788-90.
36. Kodani E, Inoue H, Atarashi H, Okumura K, Yamashita T, Origasa H, et al. Characteristics and outcomes in elderly patients with non-valvular atrial fibrillation and high bleeding risk: subanalysis of the J-RHYTHM Registry. Heart Vessels. 2024; 39(4):330-9.
37. Schumacher K, Kornej J, Shantsila E, Lip GYH. Heart Failure and Stroke. Current heart failure reports. 2018; 15(5):287-96.
38. Edrissi C, Rathfoot C, Knisely K, Sanders CB, Goodwin R, Nathaniel SI, et al. Age Stratification in Acute Ischemic Stroke Patients with Heart Failure. J Clin Med. 2022; 12(1):38.
39. Ribeiro GJS, Moriguchi EH, Pinto AA. Clustering of Cardiovascular Risk Factors and Heart Failure in Older Adults from the Brazilian Far North. Healthcare (Basel). 2024; 12(9):951.
40. Lichtman JH, Krumholz HM, Wang Y, Radford MJ, Brass LM. Risk and predictors of stroke after myocardial infarction among the elderly: results from the Cooperative Cardiovascular Project. Circulation. 2002; 105(9):1082-7.