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PRACA POGLĄDOWA
REVIEW

The burden of atherosclerotic cardiovascular disease in an aging population: A comprehensive review of risk factors, risk assessment, and prevention

Obciążenie chorobami układu sercowo-naczyniowego związanymi z miażdżycą w starzejącej się populacji – kompleksowy przegląd czynników ryzyka, oceny ryzyka i profilaktyki

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ABSTRACT

Aging is a key risk factor for atherosclerotic cardiovascular diseases (ASCVDs), leading to high morbidity and mortality among older adults. As the population ages and medical advances prolong survival, more individuals live with ASCVD, necessitating personalized management that addresses complex medical, social, and functional challenges. Besides traditional risk factors, geriatric syndromes and non-cardiovascular comorbidities – commonly referred to as competing risks – significantly impact outcomes. Although assessment tools exist, their clinical use is limited by complexity and patient diversity. Early prevention of geriatric conditions such as frailty, sarcopenia, malnutrition, and multimorbidity is essential to reduce adverse events and cardiovascular risk.

KEYWORDS

ASCVD in the elderly, SCORE2-OP, QRISK3, malnutrition, polypharmacy, sarcopenia, frailty, multimorbidity

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STRESZCZENIE

Starzenie się jest istotnym czynnikiem ryzyka miażdżycowych chorób układu sercowo-naczyniowego (*atherosclerotic cardiovascular diseases* – ASCVDs), powodujących wysoką zachorowalność i śmiertelność w populacji osób starszych. Wraz ze starzeniem się społeczeństwa oraz postępem medycyny, wydłużającym przeżycie, rośnie liczba osób żyjących z ASCVD, co wymaga spersonalizowanego leczenia, uwzględniającego złożone problemy medyczne, społeczne i funkcjonalne. Poza tradycyjnymi czynnikami ryzyka na wyniki kliniczne istotny wpływ mają także zespoły geriatryczne oraz współistniejące schorzenia niezwiązane z układem sercowo-naczyniowym, określane jako ryzyka konkurencyjne. Pomimo dostępności narzędzi oceny tych stanów ich zastosowanie w praktyce klinicznej jest ograniczone ze względu na ich złożoność, a także heterogenność pacjentów. Wczesne działania prewencyjne ukierunkowane na zespoły geriatryczne, takie jak sarkopenia, zespół kruchości, niedożywienie i wielochorobowość, są kluczowe w redukcji zdarzeń niepożądanych oraz ryzyka sercowo-naczyniowego.

SŁOWA KLUCZOWE

ASCVD u osób starszych, SCORE2-OP, QRISK3, niedożywienie, polipragmazja, sarkopenia, zespół kruchości, wielochorobowość

Introduction

ASCVD and its significance in the elderly population

Atherosclerotic cardiovascular disease (ASCVD) arises from the accumulation of plaque along the walls of arteries and encompasses various conditions, including:

- coronary artery disease (CAD), which includes acute coronary syndrome (ACS) and chronic coronary syndrome (CCS)
- peripheral artery disease (PAD), which encompasses conditions affecting the carotid, renal, and lower-extremity arteries due to atherosclerosis
- aortic conditions, including atheromatous disease of the aorta and aortic aneurysms [1,2].

Despite age serving as a strong risk factor for cardiovascular problems and mortality, older adults are less frequently prescribed therapy that aligns with clinical guidelines for ASCVD [3]. Several pertinent questions emerge: What are the underlying causes of this phenomenon? What consequences does it entail? What therapeutic challenges does it present? Firstly, the exclusion or insufficient representation of older individuals in numerous clinical trials significantly restricts the evidence base for this demographic [4]. Secondly, the presence of multiple health conditions in older adults often leads to intricate interactions between medications and various diseases. Furthermore, the processes of drug metabolism and response are influenced by aging, which is associated with diminished kidney function, changes in body composition, and variations in medication tolerability. This issue holds particular significance due to the prevalence of polypharmacy among older populations [5]. Another critical consideration is the challenges of compliance, since physical limitations such as difficulties with coordination and vision can impede adherence to prescribed therapies. Moreover, treatment costs are considerable in this population and should not be underestimated. Likewise, effective treatment of medical disorders in the elderly necessitates a holistic approach that considers various risks, including frailty, accidental falls, and mental impairment, alongside the evidence underpinning treatment recommendations [6]. Taking into account these issues related to seniors and the global demographic shift towards an aging population, the clinical management of ASCVD in older patients requires a comprehensive understanding of these complexities to ensure both effective and safe treatment.

Demographics of older adults

In 2020, the global population of individuals aged 60 and older exceeded that of children under 5 years old. Research suggests that by 2030, one in six people around the world will be at least 60 years old and the elderly population will reach 1.4 billion [7]. In Europe, over 20% of the population was aged 60 or older in 2017, and this figure is expected to rise to 35% by 2050 [8]. Due to the rise in life expectancy, the primary objective of doctors is not just to extend the number of healthy years lived, but also to enhance the quality of life during those years. Moreover, older adults need medical care more often and more frequently undergo outpatient procedures or hospitalization. The elderly make up a significant portion of the healthcare system's users, with individuals over 65 years accounting for about 40% of patients discharged from hospitals [9]. Key factors influencing healthcare costs include not just age, but also the presence of comorbidities.

Healthy aging

The process of aging is a fundamental aspect of the life cycle inherent to all living organisms, unfolding progressively over an extended period. Despite various efforts to identify, characterize, and categorize the aging process in humans, a unified and comprehensive definition remains elusive [10]. According to the new definition adopted by the World Health Organization (WHO) in 2016, "healthy aging is more than just the absence of disease; it is the

process of developing and maintaining the functional ability that enables well-being in older age" [11]. This definition encompasses two critical components: intrinsic capacity and environmental elements. The former represents a synthesis of all personal, somatic, and cognitive capabilities. The latter pertains to environmental factors that evolve over time and are significantly influenced by governance structures, financial systems, societal beliefs, and resource availability. The dynamic interplay between two of these crucial conditions ultimately contributes to functional ability in older adults (Figure 1) [12].

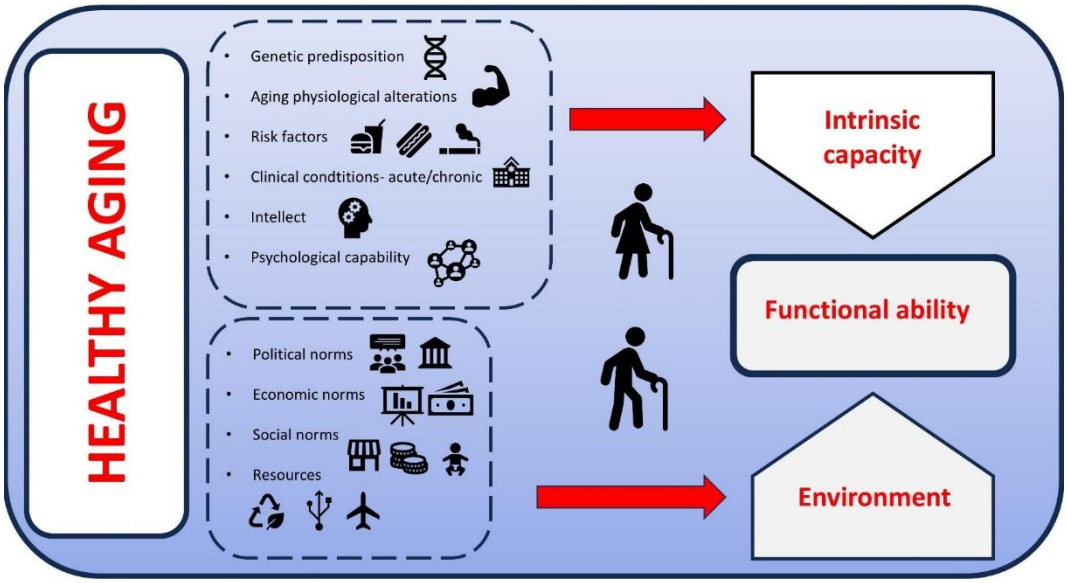

Fig. 1. Definition of healthy aging

In the initial phases of life, intrinsic capacity and functional ability follow the same course. As individuals reach middle age, though, these routes start to diverge, primarily due to the cumulative impact of health-related factors on intrinsic capacity. Although environmental factors can partially offset this decline, inadequate environmental support in later stages of life may result in a rising need for support, reduced capability, and overall deterioration [12].

Epidemiology

Prevalence of ASCVD and mortality among older adults

ASCVD is a major cause of mortality and greatly contributes to a decreased quality of life, particularly in older adults [13,14]. According to the Global Burden of Disease Study 2019 [15], in the year 2019 there were 21.17 million new cases of cardiovascular disease (CVD) globally among individuals aged over 70 years, alongside 12.17 million deaths attributed to this condition. Additionally, the total prevalence reached 195.9 million cases, resulting in 162.4 million disability-adjusted life years (DALYs) lost. Notably, since 1990, there has been a significant reduction in the global incidence, prevalence, DALYs lost, and mortality rate associated with elderly CVD [15,16]. Furthermore, the highest incidence, prevalence, DALYs lost, and mortality rates were found in individuals aged ≥95 years, while the lowest figures were observed in those aged 70 to 74 years [16]. Over the past 30 years, the burden of CVD has decreased in high-income regions, while remaining substantial in low-income areas (Figure 2) [17,18].

Globally, nearly twice as many deaths occur due to CVD compared to cancer [13]. Ischemic heart disease, followed by stroke and PAD, was the predominant type of ASCVD among the elderly; it was the leading cause of mortality and DALYs lost in older patients with CVD across both genders worldwide [19].

Fig. 2. Global burden of elderly cardiovascular disease in 2019 and its annualized changes from 1990 to 2019

Coronary artery disease

CAD is a pathological condition defined by the buildup of atherosclerotic plaque in the epicardial arteries, which can be classified as either obstructive or non-obstructive [20]. Given its dynamic characteristics, CAD manifests in a variety of clinical syndromes, which can be classified into ACS – encompassing ST-segment elevation myocardial infarction (STEMI), non-ST-segment elevation myocardial infarction (NSTEMI), and unstable angina [21] – and CCS [22]. CAD constitutes the most significant disease burden among all types of CVD worldwide. In 2019, the global prevalence of CAD reached approximately 197.2 million cases, resulting in 9.14 million deaths and accounting for 182.03 million DALYs lost. Although these figures have shown an upward trend since 1990, the age--standardized rates for these metrics have exhibited a decline over the same period [23]. Moreover, across all age groups, the global mortality rate from CAD was higher in men than in women, with the highest rates found in the oldest age category. Up to the age group of 75–79 years, the total number of deaths was greater in men than in women, peaking in the 80––84 age group for both genders [24]. The age-specific analysis reveals that while men experience the highest burden of CAD at a relatively younger age (60––64 years), women tend to experience a delayed onset of severe disease, with peak DALY rates occurring later in life (80–84 years) [24]. In 2019, the incidence and prevalence of CAD were highest in settings with a low to middle sociodemographic index (SDI), while high-SDI regions exhibited the lowest rates. Conversely, the lowest mortality rates and fewest DALYs lost were also observed in high-SDI regions; however, the highest occurred in high to middle SDI settings [16].

Stroke

Stroke is recognized as the second most common cause of mortality worldwide and is regarded as one of the most incapacitating illnesses among older adults [15]. Strokes can be categorized into two primary types: ischemic and hemorrhagic. The former accounts

for about 85% of all stroke cases, while the latter occurs less frequently but tends to cause more severe damage than ischemic strokes [25]. According to the GBD 2019 Stroke Collaborators [26], the distribution of new stroke cases in 2019 revealed that ischemic strokes represented 62.4%, while intracerebral hemorrhages accounted for 27.9% and subarachnoid hemorrhages 9.7%. Notably, from 1990 to 2019, reductions in age-standardized rates were more significant for both intracerebral and subarachnoid hemorrhages than for ischemic strokes. In accordance with Li et al. [27], the prevalence of ischemic stroke in 2021, as indicated by age-standardized rates, exhibited a steady rise among older adults, reaching its highest point in individuals aged 80 to 95 years. In the various age categories examined, it was consistently observed that men demonstrated higher age--standardized prevalence when compared to their female counterparts [28]. This trend indicates a significant disparity in the prevalence of the condition between genders but within the same age group. Similarly, the incidence of ischemic stroke also demonstrated a gradual rise with age in 2021, peaking among older adults who are ≥95 years. Although the incidence in older men progressively exceeded that of women, the gender gap narrowed for those over 85 years of age [29]. The age-standardized mortality rates for ischemic stroke in 2021 decreased for both sexes in comparison with data from 1990, although these rates continued to rise with age. Men experienced higher age-standardized mortality rates than women across most age groups [27]. Approximately 75% of all stroke-related fatalities occurred in low- and middle-income countries, whereas high-SDI settings exhibited the lowest mortality rates and fewest DALYs lost [16]. Additionally, lost DALYs reflected a downward trend in 2021 compared to 1990 [27].

Peripheral artery disease

PAD is increasingly recognized as a significant public health issue, primarily due to its escalating prevalence across the globe. Despite this rise, it frequently goes undiagnosed and inadequately treated [30,31]. According to the GBD 2019 Peripheral Artery Disease Collaborators [18], in 1990, the estimated global number of individuals with PAD was 65.7 million. By 2019, this figure had increased by 72.5%, reaching a total of 113.4 million people affected by PAD. Over the 29-year period, the global population had increased by 45%, while the population of those aged 65 and older had risen significantly (by 122%), highlighting the contrast with this finding [26]. Moreover, according to Eid et al. [32], age-adjusted prevalence decreased by 22% from 1990 to 2019, while the total lost DALYs doubled during the same period (Figure 2). The worldwide prevalence of PAD is greater among older adults, with the highest rate being in the oldest group: 20.7% (95% confidence interval [17.58–24.18]) of individuals aged 90 to 94 years [31,32]. Interestingly, the incidence of PAD diminishes with advancing age after 75 to 79 years [16].

The impact of ASCVD on men and women varies significantly. Following menopause, the likelihood of cardiovascular issues in women increases markedly [33,34]. The prevalence of PAD varies significantly across different regions categorized by SDI. Specifically, regions with low SDI exhibited the lowest prevalence, while those with high SDI reported the highest prevalence for both overall and age--standardized measures [34]. Based on a 29-year follow-up period, a two-fold increase in mortality related to PAD was observed; however, the age--standardized mortality rate associated with PAD remained stable at an estimated 1 per 100,000 individuals [28]. Remarkably, between 1990 and 2019, DALY rates associated with ischemic stroke and ischemic heart disease exhibited a nearly 30% reduction, whereas the change in lost DALYs related to PAD was minimal [35,36].

Aortic aneurysm

An aortic aneurysm is defined as a localized increase in the size of the aorta where the diameter exceeds normative values by at least 50% for individuals of similar age and sex [37]. Studies have demonstrated a significant relationship between patient age and the adjusted death rate for aortic aneurysms. The most pronounced increase occurs in individuals older than 65 years, with the highest rate reaching a 12.3-fold rise in the oldest age cohort (older than 95) [38]. Worldwide, aortic aneurysms resulted in an 82.1% rise in mortality from 1990 to 2019, increasing from 94,700 to 172,400 deaths. In contrast, the age-adjusted mortality rate for aortic aneurysms decreased by 17.9% over the same timeframe [39]. In seniors, the highest increase in the age-adjusted death rate for aortic aneurysm was observed in high-SDI areas [15]. Furthermore, the age-adjusted DALY rate increased significantly among individuals older than 55, with the highest values being in the oldest group (over 85 years) [38]. In the Global Burden of Disease 2019 analysis [15], the major risk factors associated with aortic aneurysm include smoking, high blood pressure, a high-sodium diet, and lead contamination. Moreover, according to Roth et al. [35], records regarding the prevalence and incidence of aortic aneurysm were lacking. Nonetheless, prior research indicates that the prevalence of abdominal aortic aneurysm among men aged 65 and older is declining in developed countries, primarily attributed to smoking withdrawal.

Pathophysiology

Mechanisms of atherosclerosis – vascular aging and inflammation

Vascular aging is a critical element in the pathophysiology of atherosclerosis, but the precise mechanisms driving this connection remain insufficiently understood [36,40]. This process represents a complex interplay between biological and cellular aging, together with the progression of atherosclerosis (Figure 3).

The responses of the human system are modulated by a range of physiological changes associated with aging, such as reactive oxygen species (ROS), angiotensin II, lipid levels, mechanical stress, glycemia, impaired insulin response, and the inflammatory process, which involves mechanisms essential to vascular aging [36,40,41]. Aging is attributed to a persistent, mild inflammatory condition affecting the whole body [42]. All the factors mentioned above affect inflammatory mediators, including tumor necrosis factor alpha (TNF-α), C-reactive protein (CRP), nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB), interleukin 6 (IL-6), interleukin 18 (IL-18), and fibrinogen, which may cause an elevated procoagulant state, generate ROS, and release pro-inflammatory cytokines [36]. Moreover, these determinants collectively contribute to the remodeling of the blood vessel layers (primarily the tunica intima and the tunica media), along with the dilation of the lumen [40,43]. Additionally, the accumulation of deteriorating cells may also play a crucial role in vascular aging, which causes disruptions in cellular regulation, alterations in secretory activity, and modifications to the epigenetic landscape [36,40,41].

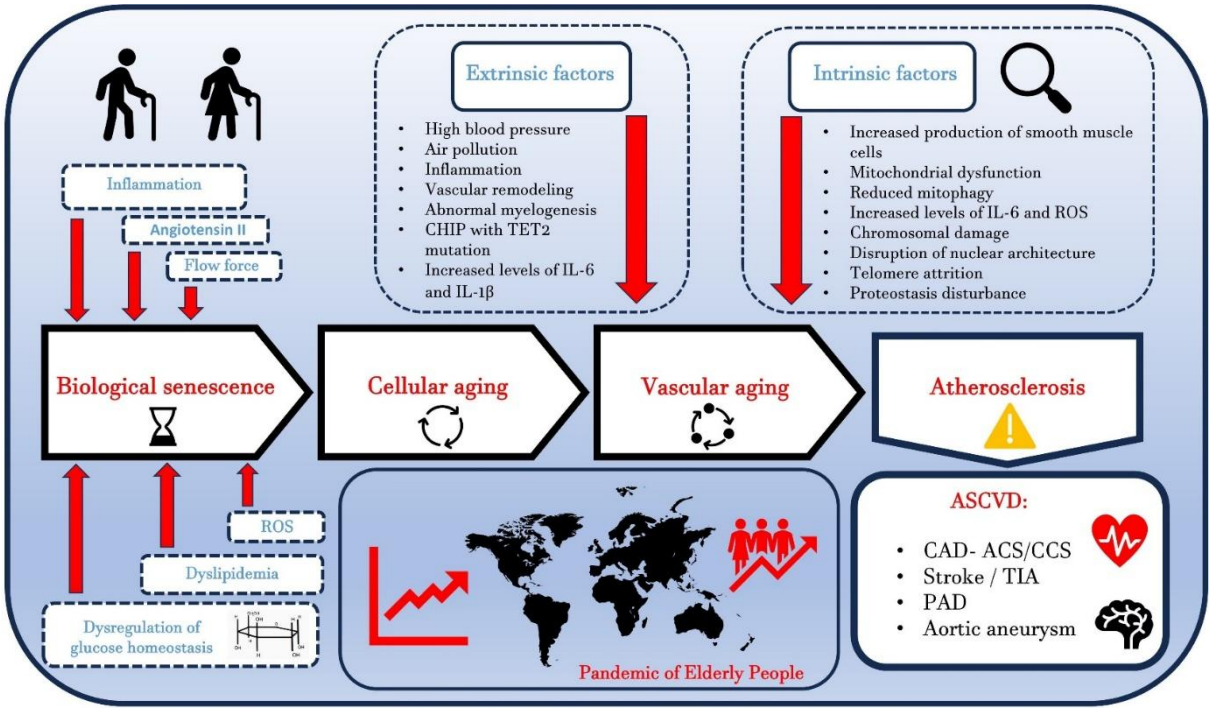

Fig. 3. Vascular aging and atherosclerosis

Intrinsic and extrinsic factors influencing disease progression

There are two primary ways in which aging contributes to the development of atherosclerosis: through intrinsic and extrinsic mechanisms (Figure 3). Internal changes are driven by several factors, such as mitochondrial malfunction, impairment of proteostasis, disruption of nuclear architecture, chromosomal injury, telomere attrition, and epigenetic alterations [40]. Conversely, external elements caused by global, regional, national, and local environmental factors – such as high blood pressure, air pollution, persistent inflammation, vascular remodeling, and disruptions in intercellular signaling – have the potential to affect physiological regulation and deteriorate blood vessels [36,44]. Interestingly, changes in the bone marrow associated with aging enhance the occurrence of clonal hematopoiesis of indeterminate potential (CHIP). This, in turn, can create a bias in the process of myelogenesis and further promote atherosclerosis [41]. Consequently, the elevated risk of ASCVD could be determined by CHIP-related changes, the higher level of IL-6, and an inappropriately regulated mitochondrial cycle, which are related to the aging process [40,41].

Senescence-linked atherosclerosis is a complex and heterogeneous process in which both internal and external factors contribute to the deterioration of the circulatory system, working in conjunction with the immunological system, independent of any lipid disorders [41].

Vascular aging mechanisms and their clinical implications

As individuals age, the arterial walls undergo thickening, which is primarily caused by a decrease in elastin content alongside an accumulation of collagen fibers, which lack elasticity [45]. Consequently, the aorta and other major arteries become stiffer, which is reflected by higher systolic blood pressure (SBP), lower diastolic blood pressure, wider pulse pressure, and higher pulse wave velocity. This heightened vascular resistance contributes to left ventricular hypertrophy, augmented myocardial workload, and a mismatch between the oxygen supply and the demand of the myocardium [6,46]. Additionally, reduced nitric oxide synthase activity impairs the coronary circulation's ability to adapt to the higher oxygen demands of the myocardium. Together, these factors increase the susceptibility of elderly individuals to a higher incidence of type 2 myocardial infarction (MI) and NSTEMI [6]. Although inflammation contributes to the onset and advancement of CAD, the coexistence of age-related conditions, including multimorbidity, cognitive impairment, and frailty, exacerbates the emergence of subclinical CAD. Chest pain is more commonly associated with ACS in younger patients, whereas in older individuals it is often attributable to noncardiac causes [47]. ACS in these individuals often presents with symptoms such as dyspnea, syncope, or abrupt cognitive changes [6,47]. Advancing age is associated with an increased prevalence of abnormalities on resting electrocardiograms (ECGs) – affecting nearly 70% of elderly patients. These disturbances – such as left bundle branch block, arrhythmias (e.g., atrial fibrillation), and paced rhythms – pose challenges to accurately interpreting ECGs in older individuals suspected of ACS, especially when compared to younger populations [48].

Similar mechanisms of vascular aging play a role in the pathogenesis of ischemic stroke. Impaired cerebral microvasculature contributes to altered resistance with a reduced ability to vasodilate. These key changes lead to a predisposition to hypoperfusion and diminished oxygen and nutrient delivery, resulting in the progression of cerebral microvascular disease. Compared to older vasculature, that of younger individuals shows a heightened ability to withstand ischemic damage, which is evidenced by the prompt initiation of angiogenic pathways and robust vasodilatory mechanisms [49,50]. In addition, elderly patients exhibit a greater prevalence of comorbidities, including atrial fibrillation, hypertension, and a history of coronary heart disease. Older age is correlated with more pronounced neurological deficits upon stroke onset; however, there is also a higher incidence of cardioembolic stroke, attributed to the higher occurrence of atrial fibrillation, which carries a mortality risk exceeding that of atherosclerotic infarctions. Conversely, smoking has been identified as a significant factor linked to an earlier onset of acute ischemic stroke [51].

Risk factors

The main CVD risk factors in older adults were found to be consistent across both sexes. The primary health risks for both include elevated SBP, dietary risks, high levels of LDL cholesterol (LDL-C), and higher fasting plasma glucose levels (Table I) [16].

Table I. Primary CVD risk factors for the elderly in 2019

1. High systolic blood pressure
2. Dietary risk
3. High fasting plasma glucose
4. High LDL cholesterol

Among the elderly, hypertension is a dominant driver of cardiovascular disease, cerebrovascular disease, and increased mortality [52]. It is estimated that more than 60% of individuals over the age of 60 are affected by hypertension; this prevalence is expected to rise as the population continues to age [53,54]. Inadequate control of blood pressure can lead to various complications affecting the vascular, cardiovascular, neurological, and renal systems, which represents a significant challenge to global public health. Consequently, antihypertensive treatment offers considerable advantages for older adults [52,55].

Malnutrition is a common issue among the elderly that represents a considerable strain on healthcare and welfare services. This demographic is especially susceptible to malnutrition due to factors such as the physiological deterioration associated with aging, restricted access to nutritious food, and the presence of comorbidities [56]. While the causes of malnutrition are intricate and multifaceted, extensive research has recognized it as a significant risk factor for arteriosclerosis, in addition to the well-documented traditional risk factors for CVD [57,58]. Poor nutrition is linked to negative health consequences across many types of cardiovascular disease [59]. Malnourished elderly individuals are more prone to death if they undergo percutaneous coronary intervention and are more susceptible to long-term complications after MI [60]. Furthermore, in patients diagnosed with heart failure, a diet deficient in essential nutrients may

exacerbate deterioration, as reflected by elevated levels of brain natriuretic peptides [59,61]. Moreover, together with protein deficiency and a decline in bone mineral mass, accelerated muscle atrophy contributes to an increased likelihood of premature bone loss and fractures. This compromised physical state can further impair immune function by enhancing susceptibility to infection and prolonging the duration of an illness. Additionally, it decreases functional reserve and increases reliance on others [62]. According to the ESPEN guidelines [63], older adults should aim to consume around 30 kcal per kilogram of their body weight daily. Protein consumption should be a minimum of 1 g per kilogram daily. Diets should include fiber-rich foods and sufficient hydration; healthy women are advised to drink around 1.6 liters of fluids daily – and men at least 2.0 liters. Dietary limitations are typically discouraged, micronutrients should be consistently supplied, and physical activity is promoted to preserve or enhance muscle mass and function.

In light of the above-discussed factors, regular evaluation of nutritional status is crucial for identifying malnutrition in elderly patients and facilitating timely preventive interventions. The Malnutrition Universal Screening Tool and the Mini Nutritional Assessment are widely employed to evaluate nutritional status. The former evaluates risk based on BMI, recent weight loss, and acute illness, whereas the latter incorporates anthropometric measurements, overall health, dietary habits, cognitive conditions (e.g., dementia or depression), and mobility restrictions [64]. Consequently, this approach enables healthcare providers to tailor diagnostic and therapeutic strategies to an individual patient's needs [65].

Elevated LDL-C level in middle-aged individuals is a significant risk factor for future cardiovascular events [1,66]. However, previous studies indicate that there is no correlation between elevated levels of LDL-C and an increased risk of ASCVD in patients aged ≥70 [67]. Consequently, the efficacy of LDL-C--lowering treatment in older adults remains a subject of ongoing debate [68,69]. According to Mortensen and Nordestgaard [67], among the 91,131 individuals enrolled in the CGPS study, the highest incidence of MI and ASCVD was observed in those aged 70 to 100 years, which was associated with an increase of 1.0 mmol/L in LDL-C levels (hazard ratio [HR] = 1.34 for MI and HR = 1.16 for ASCVD). Preventive strategies for older adults without ASCVD are an important issue, as they may reduce morbidity and mortality in this globally growing population; however, shared decision-making is essential and the advantages, potential side effects, anticipated lifespan, and any age-related disorders must be taken into consideration [68,69,70].

Fasting plasma glucose serves as a significant risk factor for overall glycemic control and is associated with an elevated risk of ASCVD and heart failure [71,72]. Interestingly, different cut-off values for diagnosing pre-diabetes are established by various health organizations: 5.6–6.9 mmol/L according to the American Diabetes Association and the European Society of Cardiology (ESC), and levels from 6.1 to 6.9 mmol/L according to the WHO [73]. According to the findings of Dong et al. [74], the burden of CVD attributable to impaired fasting glucose (IFG) is significantly greater in the elderly population compared to their younger counterparts. Furthermore, males exhibit a higher prevalence of CVD associated with IFG than females across all age groups. In 2019, the primary contributors to the global CVD burden linked to IFG were ischemic heart disease, stroke, and peripheral arterial disease. Furthermore, Gao et al. [75] conducted a cohort study which revealed that IFG elevates the risk of both all-cause mortality and mortality due to cancer. In this regard, it is important to explore the development of more focused and tailored strategies for mitigating various negative health outcomes associated with IFG.

It is noteworthy that there is a significant correlation between advancing age and the prevalence of diabetes mellitus (DM) [76]. Elderly individuals who are 65 years of age or older represent almost 50% of all DM diagnoses worldwide [77]. Type 2 DM is the predominant form of diabetes in older adults, accounting for over 90% of cases. Over time, the aging process leads to a progressive decline in β-cell function, which exacerbates insulin secretion deficiencies and contributes to insulin resistance through multiple mechanisms [68]. In advanced stages, this progression gives rise to both microvascular and macrovascular complications, thereby elevating the risk of ASCVD, with a particular emphasis on CAD, stroke, and PAD [78]. DM can negatively impact overall well-being and may lead to reduced self-determination among older adults. Diabetic seniors face an elevated risk of developing various age-related conditions: they are 1.5 to 2 times more likely to develop Alzheimer's disease and vascular dementia [79]. Reports indicate that 50% to 90% have at least one additional chronic disease, with 40% having four or more comorbidities [80]. Polypharmacy increases the risk of drug interactions and adverse effects [80]. Additionally, they are 1.5 times more likely to experience sarcopenia than non-diabetics [81]. Furthermore, frailty affects around 25% of diabetics over 65 years of age [82]. As a consequence of the higher risk of developing cardiovascular and non-cardiovascular disorders associated with diabetes, it is essential for elderly diabetics to receive holistic, specialized care management. Clinical decisions should take into

account the advantages and disadvantages of treatment goals to avoid detrimental effects and maintain a comfortable life. An appropriate level of effort and dietary status should be chosen to address sarcopenia, physical inactivity, and frailty in these diverse groups [76,77,78,79,80,81,82].

Considering the significant association between frailty and CVD, it is essential that the diagnostic and therapeutic approach for older adults commence with a comprehensive evaluation of frailty [83]. Although numerous definitions exist, two key approaches to understanding frailty stand out: frailty as a biological syndrome linked to aging, as defined by Fried et al. [84], and frailty as a condition characterized by a build-up of health shortcomings, as proposed by Rockwood and Mitnitski [85]. Research by Shamsalinia et al. [86] identifies several factors that can potentially elevate the risk of CVD in frail individuals, including advanced age (>84 years), female sex, obesity, elevated uric acid levels (>7 mg/dL), hyperglycemia (fasting glucose ≥126 mg/dL), and diabetes. Apart from the existence of traditional cardiovascular risk factors, frailty elevates the likelihood of cardiovascular incidents and is frequently observed among elderly individuals with aortic stenosis and heart failure [87]. Regardless of age, coexisting conditions, and impairment, frailty contributes to the worst outcomes in patients with CVD, including increased mortality, hospitalization, and major adverse cardiovascular events [88,89]. Moreover, frailty is associated with changes in muscle force and physical performance. Frailty is commonly linked to low body mass index (BMI), yet paradoxically, individuals with higher BMI are also at a higher risk of frailty. This phenomenon is partly attributed to the growing incidence of sarcopenic obesity, a condition in which muscle mass is substituted with adipose tissue [83,90]. Sarcopenia is precipitated by a disruption in anabolic-catabolic equilibrium. Contributory factors include chronic diseases, sedentary lifestyle, and inadequate nutrition. Ultimately, sarcopenia leads to enhanced susceptibility to CVD and increased likelihood of death, loss of balance, and diminished general well-being [91]. These conditions co-occur with higher frequency among the elderly and are modifiable. Therefore, implementing several early interventions may help in preventing these conditions along with their negative impacts on older adults, which include well-balanced exercise routines and dietary practices [92].

Roughly two in three older adults experience multimorbidity, while the overwhelming proportion of patients with chronic CVD have comorbidities [93]. Among individuals with multimorbidity, CVD is the leading comorbidity and CAD stands out as a particularly common chronic disorder [94]. Multimorbidity is associated with an enhanced likelihood of mortality and necessitates greater consumption of medical services such as hospitalization, outpatient care, and consultations with specialists. It also has a deleterious effect on physical function and overall wellbeing. The complexity introduced by multiple comorbidities often leads to disjointed care due to the participation of numerous healthcare professionals, resulting in substantial challenges for both the patients and those providing care for them [93,95]. A substantial hurdle arises when healthcare practices adhere strictly to disease-centric guidelines that fail to effectively address the multifaceted nature of multimorbidity. Moreover, clinical trials typically have a limited number of participants with multiple chronic conditions due to restrictive eligibility requirements. Consequently, these studies yield data that may not adequately reflect real-world scenarios involving patients with complex health profiles. The inconsistency among these guidelines poses a considerable obstacle in devising an effective care plan for patients with multimorbidity. Furthermore, managing one disease can inadvertently exacerbate coexisting health issues. It is crucial not to overlook potential drug interactions and associated complications that may arise during treatment [93,94,95,96,97].

Polypharmacy, typically characterized by the simultaneous use of five or more medications, is especially common among older adults who frequently experience multiple chronic health issues. Although the use of several medications can be essential for addressing intricate healthcare needs, it also constitutes an independent risk factor for significant cardiovascular events, as well as mortality – both cardiovascular disease-specific and overall – in individuals aged 65 and older [96,97,98].

Given the prevalence of these factors in older adults, integrating recommendations from multiple disease-specific guidelines can reduce therapeutic conflicts. Key strategies include developing unified protocols, delivering individualized care, enhancing communication and coordination, applying deprescribing and medication reviews, and utilizing epidemiological and real-world data. This holistic approach promotes comprehensive patient management [99,100].

Diagnosis and risk assessment

Methods for assessing ASCVD risk in older adults

The global phenomenon of population aging represents one of the most significant demographic shifts of our era [13]. Concurrently, because the incidence of cardiovascular events rises steadily with advancing age, evaluating cardiovascular risk in older adults becomes an increasingly critical responsibility [101]. The application of diverse cardiovascular risk

calculators in clinical settings has been instrumental in managing patients at risk for cardiovascular issues. Nevertheless, it is important to recognize that most of these calculators were based on studies primarily involving middle-aged populations [95]. This focus has resulted in a significant gap in the literature regarding the specific factors and algorithms that should be adapted to accurately evaluate cardiovascular risk in older adults [102,103]. When assessing cardiovascular risk in older adults, several commonly used tools are available:

1. SCORE2-OP – an algorithm developed by the ESC, it assesses the 10-year cardiovascular event risk in older adults (70–89 years old) across four different geographic regions. The key factors considered in this model are age, sex, smoking status, non-HDL cholesterol levels, and SBP [1]. The model, developed mainly from European cohorts such as the CONOR study, may have limited generalizability to populations with varying demographic and epidemiological characteristics. Furthermore, evidence suggests that it may underestimate or overestimate risk in individuals over 80, largely due to diminished risk discrimination in this age group. Moreover, important factors such as multimorbidity, functional status, and geriatric indicators are not incorporated, which may potentially affect the accuracy of predictions [104,105].
2. QRISK3 – this model, applicable to those between 25 and 84 years old, includes parameters such as age, sex, ethnicity, smoking status, diabetes status, cardiovascular events, chronic kidney disease, atrial fibrillation, blood pressure, migraine, rheumatoid arthritis, systemic lupus erythematosus, severe mental illness, atypical antipsychotic medications, steroid tablets, erectile dysfunction, lipid status, SBP, and BMI [106]. The QRISK3 model is not specifically calibrated for the very elderly, especially those over 80, which may overestimate the risk. This is because aging increases the likelihood of non-cardiovascular mortality, a factor not fully accounted for in the model. Although QRISK3 includes multiple comorbidities, its precision is limited by the challenges in accurately capturing competing risks of death in this age group [107].
3. CVDPoRT – a model which can be used for patients ranging from 20 to 105 years, it evaluates a comprehensive set of sociodemographic factors, such as academic achievement, culture, resident status, neighborhood poverty, and measures of community integration. Importantly, it does not incorporate conventional biomarkers such as lipid levels or direct blood pressure measurements [108]. Developed and validated with large Canadian population health surveys, this predictive algorithm focuses on sociodemographic and behavioral factors. Nevertheless, it insufficiently addresses competing mortality risks and excludes specific geriatric risk indicators, potentially resulting in overestimated risk among older adults, especially those over 80 years old [108].
4. Pooled cohort equations – these encompass a range of factors, including age, total and HDL cholesterol levels, SBP readings, diabetes status, and smoking habits, to evaluate risk in individuals aged 40 to 79 years [109].
5. Revised WHO CVD risk estimation charts – intended for patients aged 40 to 74 years, these encompass a laboratory-based model that considers factors such as age, smoking habits, SBP, diabetes history, and total cholesterol levels and a non-laboratory-based model that uses age, smoking status, SBP, and BMI [110].

In 2021, the ESC introduced the SCORE2-OP model as a novel tool to evaluate the 10-year risk of cardiovascular outcomes resulting in death or survival among seniors (individuals aged 70 years or older) who appear healthy [1]. A novel algorithm, modified to account for comorbidities unrelated to CVD, provides an assessment of cardiovascular risk across four distinct geographic areas. These regions are stratified according to their risk levels: low, moderate, high, or very high [104]. When utilizing these risk calculators, it is important to recognize that some rely on traditional risk factors, which tend to have a diminishing effect on CVD risk as individuals age [1]. Additionally, they do not incorporate data from radiological assessments and circulating biomarkers [111], which may also cause considerable misjudgments of the 10-year cardiovascular risk, with potential discrepancies ranging from 3% to as much as 1430% [112]. Given that no ideal risk assessment calculator exists, easy-to-use predictive tools combined with a comprehensive approach to treatment and prognosis are likely to be most effective in routine medical care [101,103].

Primary prevention

Finally, primary prevention of ASCVD in older adults is crucial because individuals who reach the age of 65 without any signs of ASCVD still face a lifetime risk of over 50% for developing cardiovascular issues [113]. Furthermore, ASCVD accounts for 39% of all fatalities in the population aged 75 to 84 [114]. Based on the 2021 ESC Guidelines for preventing cardiovascular disease in clinical settings [1], statin therapy for primary prevention is supported by class IIb and level B evidence for older individuals (70 and older) who are regarded as at least high risk for CVD. Although the cut-off for LDL-C levels of <2.6 mmol/L (<100 mg/dL) seems rational, there are no strict goals for primary prevention in older

individuals [1]. Nevertheless, additional evidence indicates that statin therapy for primary prevention is clinically significant for older adults without a diagnosis of ASCVD. The PROSPER study marked the first major investigation into the effects of statin therapy in older adults aged 70 to 82. This trial included 5,804 participants and found that pravastatin significantly reduced the rates of CAD deaths, non--fatal MI, and strokes [115]. Following the PROSPER study, several other trials – such as ASCOT-LLA, CARDS, JUPITER, and HOPE-3 – further confirmed the advantages of statins for primary prevention in older adults, especially those between 70 and 75 years of age. These studies revealed notable reductions in cardiovascular event risks for older patients receiving statin treatment. For example, atorvastatin led to a 37% decrease in non-fatal MI and fatal CAD among participants aged 65 and older in the ASCOT-LLA trial [116]. Similarly, the JUPITER trial found that rosuvastatin treatment resulted in a 39% reduction in first cardiovascular events among individuals aged 70 and over [117]. It is crucial to note that as individuals age, the relationship between the duration of life free from CVD and overall life expectancy begins to diverge due to the increasing risk of death unrelated to CVD, often referred to as "competing risk." This significant factor may contribute to the potential benefits of treatment being overestimated [1]. Despite the reduced relative impact of statins, the notably elevated absolute risk of CVD in older adults indicates that the overall advantages of statin therapy may remain considerable [118]. In two randomized trials, JUPITER and HOPE-3, participants aged 70 and older made up 32% and 24% of the study cohort, respectively. Nonetheless, in the first trial, older adults were responsible for 55% of the recorded cardiovascular events, while in the second trial, they accounted for 43% [119]. However, the recommendation from the 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease [120] and the US Preventive Services Task Force [121] is more liberal, as both recommend statin management for up to 75 years of age (class I for a 10-year risk of ≥7.5% and grade B for a risk of ≥10%, respectively). Based on the guidelines mentioned earlier, there is a discrepancy in the recommendations for statin treatment, which highlights the uncertainty surrounding the benefits of such treatment for older individuals, especially those aged 75 and above [122]. Two major ongoing randomized trials aim to clarify the effectiveness of atorvastatin at a dosage of 40 mg daily compared to a placebo in elderly populations:

- The PREVENTABLE trial, currently underway in the United States, seeks to recruit 20,000 individuals at least 75 years old [123]
- The STAREE trial in Australia is a randomized, double-blind, placebo-controlled study designed to evaluate overall survival and disability-free survival among 18,000 participants aged 70 and over [124].

Conclusions

The older adult population is highly heterogeneous, presenting unique challenges in the context of cardiovascular health. ASCVD represents a significant concern among elderly individuals, particularly given the aging global population and its implications for future healthcare needs. While CAD remains the most prevalent form of ASCVD in this demographic, the distribution of other types varies significantly. In high--income countries, there has been a decline in the burden of ASCVD; however, low-income areas continue to experience substantial challenges due to factors such as culture, habits, education system, and ecological conditions. Additionally, geriatric issues – including multimorbidity, polypharmacy, frailty, sarcopenia, and cognitive impairments – complicate both diagnosis and treatment strategies for older adults. These critical conditions necessitate a tailored approach that integrates geriatric principles into cardiovascular care. To better understand and address the patterns of CVD burden in this population, it is essential to increase the inclusion of older adults in randomized clinical trials. Furthermore, developing specific guidelines and recommendations for this group, alongside adopting a holistic approach to care, is imperative to optimizing outcomes.

Authors' contribution

Study design – W. Żurański, M. Gąsior, B. Hudzik
Manuscript preparation – W. Żurański, M. Gąsior, B. Hudzik
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