### **Invited Editorial**

# Acute Coronary Syndrome in Older Adults: an Update from the 2022 Scientific Statement by the American Heart Association

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#### Abstract

On December 2022, the American Heart Association (AHA) released a new scientific statement on management of acute coronary syndrome (ACS) in older adults. (1) Here we summarize and comment on some of the key points from the paper.

**Key words:** Acute coronary syndrome, heart disease, aged, frailty, multimorbidity, polypharmacology, AHA Scientific Statements

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### Acute coronary syndrome (ACS) pathophysiology in elderly

Elderly patients frequently present with a number of age-related changes that increase their risk of ACS (Fig. 1) (1).

Fibrotic degeneration increases arterial stiffness, determining increased impedance to left ventricular (LV) ejection, dysregulation of blood pressure, and a higher myocardial O2 demand. To compensate for increased impedance, hypertrophy develops in cardiac myocytes, resulting in altered LV contraction and increased myocardial stiffness. Potential consequences are higher resistance to coronary perfusion, predisposition to atrial fibrillation and heart failure with preserved ejection fraction. Decreased responsiveness to **B**-adrenergic stimulation determines downregulation of inotropic, lusitropic, and chronotropic responses. Endothelial dysfunction impairs the self-regulation capacity of coronary arteries, preventing them from increasing blood flow in response to increased demand. A shift towards a pro-thrombotic phenotype increases the risk of both venous and arterial thromboembolism, and chronic inflammation (inflammaging) increases atherogenesis. Furthermore, aging also affects the kidney.

The authors recommend a careful assessment of renal function and proper kidney-saving measures during diagnostic and therapeutic procedures. Due to decreased muscle mass, the estimated glomerular filtration rate calculated using serum creatinine may be overestimated. (1)

#### ACS and geriatric syndromes

The authors highlight that people with a higher cardiovascular risk frequently present with multiple geriatric syndromes (1). Geriatric syndromes are multifactorial clinical conditions that do not fall under the "disease" category, but are responsible for complex clinical presentation of diseases, physical and cognitive decline, and poor outcomes (2).

Frailty represents the cornerstone of geriatric medicine. It is a measurable state of vulnerability to developing increased dependency and/or mortality when exposed to a stressor.

Measuring frailty can provide prognostic and therapeutic information that eludes many diseasecentered measurement tools. Indeed, some authors have emphasized the significance of frailty in predicting major bleeding (3). Boreskie et al. (4) highlight the main issues arising in various clinical settings and list possible frailty assessment methods which may be more appropriate in each context. Clinical Frailty Scale (CFS), for example, is a quick assessment tool that can accurately predict mortality, clinical course, and adverse events. It can be combined with instruments that take into account more variables, such as the Frailty Index or Fried's Criteria, to provide a more precise evaluation (4).

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Impaired endotheliummediated vasodilation

Figure 1. Age-related changes predisposing to acute coronary syndrome (Created with BioRender.com by authors based on recommendations from reference 1)

Frail patients are more vulnerable to delirium. Delirium leads to longer hospital stays, rehospitalization. functional decline. falls. institutionalization, and death. Disorientation, sensory impairment, pain, bed rest, sedation, and medications should all be avoided as delirium-precipitating factors. Multimorbidity ( $\geq 2$  chronic conditions) is a potential confounder for clinical ACS presentation and a potential predictor of adverse outcomes. Furthermore, polypharmacy (the use of multiple medications, ≥ 5), leads to pharmacological interactions and may compromise the implementation of an optimal treatment (1).

Cognitive decline may present either as mild cognitive impairment (MCI) or dementia. Reduced cognitive function occurs in MCI without loss of function. In dementia, cognitive dysfunction interferes with daily activities and leads to loss of independence. The mere presence of cognitive impairment, according to the AHA, is not an exclusion criterion for denying diagnostic and therapeutic interventions. Nonetheless, it should be taken into account in clinical evaluations and when determining the appropriateness of invasive procedures (1).

#### Management of ACS in elderly

The AHA statement addressed the dependability of cardiac biomarkers. The standard of care for detecting myocardial injury is high-sensitivity cardiac troponin I (hs-cTn). However, certain conditions, such as myocardial fibrosis or chronic kidney disease, can result in higher baseline values and a lower positive predictive value (1).

Compared with the first scientific statement on Acute Coronary Care in the Elderly published in 2007, (5, 6) the latest document reported that more randomized controlled trials (RCTs) have involved older adults (1). Both the After Eighty (2016) (7) and the SENIOR-NSTEMI (2020) (8) studies included patients over the age of 80, and both found that invasive treatments outperformed conservative treatments for non-STelevation (NSTE)-ACS and non-STelevation myocardial infarction (NSTEMI). The Italian Elderly ACS (2012, patients aged  $\geq$  75 with NSTE-ACS) (9), the MOSCA trial (2016, patients aged  $\geq$  70 with NSTEMI) (10), and a RCT by Hirlekar et al. (2020, patients aged ≥80 years old with NSTE-ACS) (11) found no long-term differences in invasive vs conservative treatments.

RINCAL (2021) (12) concluded that an invasive approach was not superior to optimized medical therapy alone in treating patients aged  $\geq$ 80 with NSTEMI. Unpublished data from the recently concluded MOSCA-Frail trial (2019) (13) revealed no benefit of invasive strategy on primary or co-primary end-points in older adults with NSTEMI (1).

Interestingly, AHA Scientific Statement points out that among those trials, only the MOSCA-Frail and Hirlekar et al. (11, 13) conducted frailty assessment. MOSCA-Frail enrolled patients with a CFS score of 4 or higher (13). Hirlekar et al. (11) used the Canadian Study of Health and Aging Clinical Frailty Scale, reporting a low prevalence of frailty in their sample and not stratifying results based on frailty status. The lack of a widely used assessment of frailty represents a significant limitation for trials on the therapeutic management of ACS in the elderly.

Cardiovascular diseases are often associated with progressive disability. AHA identifies incorrect management and suboptimal transition of care as potential causes of loss of independence (1).

Management of ACS in elderly patients should be tailored to the patients' preferences, quality of life, and life expectancy. This includes deciding whether to use invasive or noninvasive treatment for isolated coronary artery disease (CAD) or a combination of CAD and other conditions (e.g., aortic stenosis) (14), as well as medical treatment after the acute phase. In this regard, Sabouret et al. (15) recently questioned the long-term use of antiplatelet therapy. In fact, in older patients, the benefit of preventing ischemic events does not always outweigh the risk of major bleeding. For this reason, the authors recommend keeping a critical eye on medication reviews and tailoring interventions to the individual patient.

An important section focuses on patients approaching the end-of-life. For them, AHA recommends focusing on outcomes such as avoiding re-hospitalizations and relieving pain and discomfort. A multidisciplinary discussion may aid in determining a treatment's lack of medical efficacy (futility). Before invasive procedures, do-not-resuscitate orders should be carefully discussed with the patient, family, or power of attorney (1).

A proper discharge from the hospital and continuity of care are essential for improving outcomes and reducing disability. A RCT conducted by Sanchis et al. (16) discovered that intensive cardiac rehabilitation was beneficial in older survivors of an acute myocardial infarction. Again, as Bencivenga et al. (17) point out, assessing frailty is critical for determining prognosis and treatment goals in the elderly after the acute phase. At discharge, the AHA Statement suggests considering a medication review and deprescribing, lifestyle modifications and cardiac rehabilitation, comorbidity management, psychosocial support, socioeconomic factors, and education of both patients and caregivers. All of these domains are part of the comprehensive geriatric assessment. Furthermore, at follow-up, the AHA recommends focusing on symptom burden, functional status, and quality of life.

## The two sides of ACS management in geriatric patients

A recent paper by Roth et al. (18) highlighted that cardiovascular risk has grown globally from 1990 to 2019. According to the authors, one of the main demerits in this regard is not having effectively translated prevention knowledge into practice.

The situation may be even worse after COVID-19 pandemic. In recent years, elderly population saw a dramatic deterioration in quality-of-life and well-being (19). The Pandemic showed also that longevity does not always come with "healthy aging" and "healthy frailty" (20). For this reason, one could provocatively say that proper management of ACS in the elderly begins in childhood (21). The Longevity Check-up 7+ initiative conducted by our group (2015 - ongoing) showed that in community-dwelling population the presence of poorly controlled risk factors is often accompanied by low awareness (22). One point that needs to be strongly emphasized is that all forms of prevention may help reducing the burden of cardiovascular diseases. An example is influenza vaccination in the elderly. Albeit not directly acting on cardiovascular risk, it can be effective in reducing influenza-related cardiovascular complications (23).

Although not further explored by the AHA Scientific Statement, frailty is related to sarcopenia. Sarcopenia is a decrease in muscle quality and quantity and represents a powerful predictor of adverse outcomes, including for ACS. (24). an intervention based on physical exercise and proper nutrition could bring about a more robust generation of older adults (25).

Therefore, the final paragraph of this editorial would like to serve as a little addition to the AHA Scientific Statement. The geriatric approach today cannot but be two-sided. Respect for individual expectations, human dignity, and death assume an ever more holy significance as one approaches the end of life. However, in order to achieve more sustainable health care, ensure a higher quality of life, and truly make a difference, a careful assessment of the patient in order to set commensurate goals becomes a critical aspect at all stages of life. Peer-review: Internal Conflict of interest: None to declare Authorship: All authors participated in manuscript design and drafting. All authors read and approved the final version. Acknowledgement and funding: None to declare Authors' disclosure: The authors have not declared a specific grant for this work from any funding agency in the public, commercial or not-for-profit sectors.

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