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Acute coronary syndrome in the older adults

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1 Introduction

Coronary heart disease remains the leading cause of death in the developed world. Advanced age is the single strongest risk factor for coronary artery disease (CAD) and independent predictor for poor outcomes following an acute coronary syndrome (ACS). ACS refers to a spectrum of conditions compatible with acute myocardial ischemia and/or infarction due to various degrees of reduction in coronary blood flow as a result of plaque rupture/erosion and thrombosis formation or supply and demand mismatch. Unstable angina and non-ST segment elevation myocardial infarction are often continuous and clinically indistinguishable, collectively referred as non-ST elevation ACS (NSTE-ACS). An abrupt total occlusion of a coronary artery causing transmural myocardial ischemia/necrosis and displaying ST segment elevation or new left bundle branch block on a12-lead ECG leads to the diagnosis of ST segment elevation myocardial infarction (STEMI). NSTE-ACS and STEMI require acute cardiac care. Professional societies have established guidelines for high quality contemporary care for ACS patients, i.e., American Heart Association/American College of Cardiology guidelines for STEMI and NSTE-ACS, European Society of Cardiology guidelines for STEMI and NSTE-ACS, and the United Kingdom National Institute for Health and Care Excellence guidelines for STEMI and NSTE-ACS.[1−6] Implementation of evidence-based therapies has significantly decreased mortality and morbidities of ACS.[3,7,8] However, these advancements in ACS management have not equally improved outcomes for older adults. Vulnerable older patients continue to be at high risk of poor outcomes, are less likely to receive evidence based care, and have high mortality rates regardless of treatments given.[9,10] These disparities and challenges in caring for ACS in older adults are well recognized.[11−13] This review summarizes the increasing burden and persistent unfavorable outcome of ACS in older adults, and discusses the clinical presentation, diagnosis and strategies for medical and invasive therapy.

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2 ACS in older adults

2.1 Epidemiology

The exact prevalence and incidence rate of ACS among older adults (≥ 75 years of age) is not known. About 60% of hospital admissions for ACS are for patients older than 65 years of age, and approximately 85% of ACS related deaths occur in this age group. Large registries show 32% to 43% of NSTE-ACS,[11,14] and about 24%–28% of STEMI admissions were for patients aged ≥ 75 years.[12] Elderly ACS patients were under-represented in clinical trials in which subjects older than 75 years of age account for less than 10%, and older than 85 years account for less than 2% of all NSTE-ACS subjects.[15] In both STEMI and NSTE-ACS, advanced age independently associates with increased mortality. Mortality is at least three fold higher in patients older than 85 years compared with the younger than 65 years of age group. The median survival time after a first myocardial infarction (MI) is 3.2 years for men and women age ≥ 75 while it is 9.3 years for men and 8.8 years for women aged between 65 and 74 years; 17.0 for men and 13.3 for women at age 55 to 64 years, respectively.[8] Each 10-year increase in age resulted in a 75% increase in hospital mortality in ACS patients. Both the Global Registry of Acute Coronary Events (GRACE) and UK Myocardial Ischemia National Audit Project database revealed ACS of older adults are more likely to present as NSTE-ACS instead of STEMI, and

are more likely to be women, white, and have lower body mass indices, higher prevalence of such comorbidities as hypertension, heart failure (HF), atrial fibrillation, transient Ischemic attack/stroke, anemia and renal deficiency.[16,17]

As a result of improved prevention and treatment, there is a constant trend of steady decline of death rate due to cardiovascular disease in the USA and other countries. Paradoxically, the burden of ACS in older adults is expected to rise due to (1) expansion of the population age ≥ 65 as society ages; (2) increased life expectancy; and (3) increased population of older adults with history of CAD due to improved therapies. This also means that ACS is an increasingly common presentation in the last stages of life.

2.2 Pathophysiology

Atherosclerotic CAD is a result of multi-decade processes that intertwine with general aging mechanisms.[18] The process of atherogenesis includes endothelial injury; lipid particle deposition (fatty streak formation); and local cellular and inflammatory response (early atheroma formation) further followed by progression of atheroma with the formation and expansion of necrotic core, fibrous cap, matrix accumulation and various degree of plaque instability, intertwined with various degrees of thrombosis formation. The "open-artery theory" suggests thrombosis at the site of rupture, erosion or fissuring of the atherosclerotic plaque leading to STEMI or NSTE-ACS, depending on the degree and duration of obstruction.[19] The hallmark of ACS is the sudden imbalance between myocardial oxygen consumption and demand. This can be due to acute thrombosis and plaque rupture, or to increased supply and demand from comorbid disease presentations (e.g., tachycardia, hypotension or anemia). In older adults, there are more extensive calcifications of coronary atherosclerosis with more multi-vessel and left main disease.[20] These adverse changes increase the risk for myocardial injury without new thrombosis.

3 Clinical presentation and diagnosis

3.1 Symptoms

Elderly ACS patients are less likely to present with typical ischemic chest pain (pressure-like quality, substernal location, radiating to jaw, neck, left arm/shoulder and exertional component) compared with younger counterparts. Typical angina symptoms predictive of AMI in younger patients were less helpful in predicting AMI in the elderly population.[21] Autonomic symptoms such as dyspnea, diaphoresis, nausea and vomiting, pre-syncope or syncope are more common accompaniments to chest discomfort in elderly ACS patients. Symptoms may also be less likely to be induced by physical exertion; instead, they are often precipitated by hemodynamic stressors such as infection or dehydration. These may either be type 1 myocardial infarction if chest symptoms are present, or may also be considered type 2 MI, if the presentation is more consistent with another comorbid condition (e.g., tachycardia, hypoxia from pneumonia, chronic lung disease).[22] Other comorbid conditions, such as altered mental status, bleeding episodes, falls history, impaired activities of daily living, impaired communication skills are also important presenting features in guiding ACS care.[23,24] High index of suspicion for ACS, along with an appreciation of its context, must be maintained in assessing elderly patients to achieve timely diagnosis and appropriate treatment.

3.2 Physical examination

A careful physical examination focused on mental status, vital signs, cardiac murmurs, signs of decomposition of heart failure and peripheral artery disease is critical for accurate diagnosis. The elderly patient's general appearance also may provide information about nutritional status and frailty. An increased number of comorbid conditions may render the older ACS patient less cooperative, and more susceptible for hemodynamic instability.

3.3 Diagnostic testing and differential diagnosis

3.3.1 Early and serial ECG

With a high index of suspicion, early acquisition and interpretation of a12-lead ECG, with subsequent serial tracings (e.g., at 15- to 30-min intervals during the initial hour of evaluation or recurrence of symptoms) are critical for early diagnosis of ACS in the elderly person. Dynamic ST segment and T wave changes provide high sensitivity for detecting ischemia. ECG interpretation may be challenged by pre-existing alterations, pacing rhythm and conduction delays. The results of an ECG are less likely to demonstrate marked ST-segment deviation. Elderly patients present more frequently with NSTE-ACS than STEMI. Due to the increased prevalence of left bundle branch block (LBBB) with age, older adults with LBBB pose unique challenges, as many of these may be previously documented.[11]

3.3.2 Serial cardiac biomarkers

Initial and serial cardiac enzymes, with the most sensitive biomarker cardiac troponin (cTn) levels, are sensitive and specific in diagnosing ACS. Elderly individuals have high levels of baseline cTn level: 20% community dwelling older adults ≥ 70 years old have above 99% cTn level as baseline. Careful clinical assessment is essential to separate ACS from a variety of acute and chronic conditions also leading

to low-level myocardial necrosis (type 2 MI).[25] A bigger proportion of the elderly population with ACS has high levels of B-type natriuretic peptide (BNP). Elevated BNP in ACS predicts worse outcome.[26,27] Therefore, measurement of BNP may provide prognostic information about HF with ACS in elders and their risk of mortality.

3.3.3 Differential diagnosis and diagnostic testing

Early assessment of cardiac structure and function by echocardiography adds diagnostic and prognostic value, and guides therapy. A non-ischemic cardiovascular cause of chest pain (e.g., aortic dissection, expanding aortic aneurysm, pericarditis, pulmonary embolism, severe valvular disease, acute decompensation of HF) requires an appropriate imaging study to thoroughly evaluate as a possible differential diagnosis. Tachy-arrythmias such as atrial fibrillation are common in the older adults who present with ACS symptoms requiring ECGs and telemetry. Non-cardiac causes of chest pain and abnormal cardiac biomarkers also include anemia, renal insufficiency, dehydration, metabolic and electrolytes derangements, and infections. To achieve an accurate and timely diagnosis requires a focused history and physical examination, laboratory tests, and the appropriate imaging studies.

Table 1. Clinical information critical to diagnosis and management of ACS in the older adults.

Clinical symptoms for ACS diagnosis
Typical symptoms (less predictive for ACS in elderly)
Atypical symptoms (more common in elderly)
Non-CV acute disease presentation (tachycardia, hypoxia, anemia, hypotension)
Autonomic symptoms (more common in elderly)
Altered mental status (more common in elderly)
Exertion-induced symptoms (less common in elderly)
Hemodynamic stressor-induced symptoms (more common in elderly)
History relevant to ACS management
Prior MI and intervention history
Baseline functional and mental status
Baseline quality of life/preferences
Expected life expectancy/advanced directive
Comorbid conditions (indication for multiple anticoagulants)
Frailty/fall risk
Bleeding risk
Nutritional status
Medical compliance/financial concerns
Social/family support
Physical signs relevant to ACS management
Mental status
Hemodynamic stability
Murmurs
Signs of decompensated heart failure
Peripheral vascular conditions
Significant degenerative conditions (scoliosis suggestive for aortic tortuosity, etc)
Laboratory tests
Renal function (creatinine clearance calculation)
Baseline hemoglobin
Cardiac biomarkers
Baseline endocrine insufficiency
Electrolytes derangement

ACS: acute coronary syndrome. MI:

4 Risk stratification

In general, the greater ischemic risk patients with ACS warrant more aggressive strategies, in particular, antithrombotic, anticoagulation and revascularization strategies, to reduce the risk of major negative clinical outcome (death, recurrent ischemia/MI) and often gain the greater benefit from these treatments. Prognostic factors predicting higher ischemic risk in ACS validated score systems, such as TIMI risk score, GRACE score, and TIMI risk index also predict higher bleeding risk when receiving aggressive therapies (Table 2). Age is one of the most important predictors of risk in NSTE-ACS. Patients aged ≥ 75 years have at least double the mortality rate of those ≤ 75 years. As predicted, all older adults experiencing ACS (NSTE-ACS and STEMI) with elevated cTn with or without ECG changes are high risk and who could potentially benefit from aggressive therapy, also have an increased risk of bleeding.[28,29] Frailty denoting increased vulnerability and decreased physiological reserve in the elderly population, is a strong and independent predictor of increased mortality, longer hospital stay, and increased risk of bleeding and morbidity in elderly

Table 2. Risk factors included in major risk scoring systems to predict ischemic and bleeding outcomes in ACS.

Clinical factors	Predicting CV risk	Predicting bleeding risk	Predicting long-term survival
Advanced age	↑↑	↑↑	↓
Diabetes mellitus	↑	↑	?
Male gender	↑	↓	?
Renal insufficiency	↑	↑↑	↓↓
Anemia	↑	↑↑	?
Prior CAD, PAD, CVA	↑	↑	
Killip class (HF symptoms)/ Hemodynamics	↑	?	↓↓
ST deviation	↑	?	?
Elevated cardiac biomarkers	↑	?	↓
Frailty/Functional decline	↑	?	↓↓

Up-ward arrows: increasing risk; down-ward arrows: decreasing risk; question marks: undetermined. ACS: acute coronary syndrome; CAD: coronary artery disease; CV: cardiovascular: CVA: cerebrovascular accident; HF: heart failure; PAD: peripheral arterial disease.

ACS patients.[30,31] Baseline functional decline in elders is also predictive of poor outcome for these patients.[32] Recent study found that a positive status suggested by Gold Standards Framework (GSF) score which incorporated end-stage illness criteria and GRACE score cardiovascular criteria, independently predicts non-cardiovascular events in ACS patients, while GRACE score predicts cardiovascular events in this population.[33]

5 Treatment

The approach to management of elderly patients with ACS should be individualized and balanced based on ischemic risks, complication risks, estimated life expectancy, co-morbidities, quality of life, patient wishes, and the estimated risks and benefits of revascularization.[11,12]

5.1 Pharmacotherapy

The standard of care for patients with ACS in general applies to older adults, with the common goals to achieve immediate relief of ischemia, prevent further myocardial damage, and avoid complications and death. However, medication side effects are generally more common in elderly ACS patients; therefore, special attention is required to monitor and reduce side effects, particularly in the setting of polypharmacy. Adjunctive antiplatelet and/or anticoagulant therapies are indicated (Table 3). Bivalirudin may provide benefit in reducing bleeding in comparing to unfractionated heparin (UFH) plus glycoprotein (GP) IIb/IIIa inhibitor to support revascularization. The combination of GP IIb/IIIa inhibitors and full dose fibrinolytic medications is associated with high rates of bleeding and intracranial hemorrhage (ICH) in older people. Oxygen support for hypoxemic patients, anti-angina, antiplatelet, and anticoagulant therapies are also generally indicated with special caution for elderly patients with ACS (Table 3).

5.2 Revascularization therapy

In general, high risk elderly ACS patients benefit from invasive revascularization therapy, not only in terms of survival but also improving quality of life and functional capacity. Practice guidelines in revascularization therapy for STEMI and NSTE-ACS are generally applicable to older adults (Table 4). Angiography and percutaneous coronary intervention (PCI) are generally safe with high successful rates. However, increased risks of stroke and bleeding associated with revascularization require careful consideration and balance of benefits and risks.[34–36] In addition, older patients with thrombosis and plaque rupture in coronary arteries are more likely to benefit from initial invasive care.

Table 3. Pharmacotherapy for ACS in older adults.

Agents	Special comment in older adult
Oral antiplatelet agents	
Aspirin	Beneficial: indicated, well tolerated
P2Y12 receptor inhibitors	
Clodiogrel	Beneficial: indicated, well tolerated
Prasugrel	Relatively contra-indicated in age ≥ 75 years of age; body weight < 60 kg; and history of CVA/TIA
Ticagrelor	More potent than clopidogrel, may be better outcome, without increased risk of bleeding; twice daily and cost may be troublesome for older adults
GP IIb/IIIa inhibitor (GPI)	Beneficial in conjunction with PCI and heparin in elderly with increased risk of bleeding requiring transfusion
Anti-coagulants	
UFH	Beneficial: may add GPI with PCI
Enoxaparin	May be used prior to PCI; no bolus with reduced dosage for ≥ 75 years of age; increased bleeding risk
Fondaparinux	Not recommended as sole anticoagulant for PCI due to catheter thrombosis; increased bleeding risk in elderly
Bivalirudin	Mono-agent for PCI has comparable efficacy as UFH+GPI, but reduces bleeding risk than UFH+GPI in elderly ACS
Factor Xa inhibitors	Rivaroxaban and Apixaban (only rivaroxaban approved for secondary prevention)
Fibrinolytics	Only for STEMI when expected to delay > 120 min from FMC to FDA; advanced age increases risk of intracranial hemorrhage; half-dose for ≥ 75 year-old; Fibrin-specific agents have lower risk of bleeding in elderly
Nitroglycerin	Ameliorates symptoms, reduces LV preload, increases coronary flow. Be cautious of hypotension
Beta-blockers	Oral beta-blockers benefit elderly more than younger adults IV beta-blockers are harmful in ACS with HF presentation
ACEi/ARB	Beneficial with reduced EF – caution if CKD for creatinine and potassium level changes
Statins	Greater beneficial in elderly than younger adults, side-effects are more common as well, moderate intensity maybe as good as high intensity statin. Cautions are required – Guidelines now for moderate intensity statin age ≥ years

ACEi: angiotensin converting enzyme inhibitors; ACS: acute coronary syndrome; ARB: angiotensin receptor blockers; CKD: chronic kidney disease; CVA: cerebrovascular accident; EF: ejection fraction; FDA: first device activation; FMC: first medical contact; GPI: glycoprotein IIb/IIIa inhibitors; LV: left ventricle; PCI: percutaneous coronary intervention; STEMI: segment elevation myocardial infarction; TIA: transient ischemic attack; UFH: unfractionated heparin.

Table 4. Statements in major guidelines relevant to management of ACS in the older adults.

ACS	Guideline statements	Class, level of evidence	Guidelines
STEMI	A high index of suspicion for MI must be maintained in women, diabetics, and elderly patients with atypical symptoms	I, B	2011 ESC Guidelines for STEMI
	Special attention must be given to proper dosing of antithrombotics in elderly and renal failure patients	I, B	
NSTE-ACS	Because of the frequent atypical presentation, elderly patients (> 75 years) should be investigated for NSTE-ACS at low level of suspicion	I, C	2011 ESC Guidelines for NSTE-ACS
	Treatment decisions in the elderly (> 75 years) should be made in the context of estimated life expectancy, co-morbidities, quality of life, and patient wishes and preferences	I, C	
	Choice and dosage of antithrombotic drugs should be tailored in elderly patients to prevent the occurrence of adverse effects	I, C	
	Elderly patients should be considered for an early invasive strategy with the option of possible revascularization, after careful weighing up of the risks and benefits	IIa, B	
	Older patients with NSTE-ACS should be treated with GDMT, an early invasive strategy, and revascularization as appropriate	I, A	2014 AHA/ACC guideline for NSTE-ACS
	Pharmacotherapy in older patients with NSTE-ACS should be individualized and dose adjusted by weight and/or CrCl to reduce adverse events caused by age-related changes in pharmacokinetics/dynamics, volume of distribution, comorbidities, drug interactions, and increased drug sensitivity	I, A	
	Management decisions for older patients with NSTE-ACS should be patient centered, and consider patient preferences/goals, comorbidities, functional and cognitive status, and life expectancy	I, B	
	Bivalirudin, rather than a GPIIb/IIIa inhibitor plus UFH, is reasonable in older patients with NSTE-ACS, both initially and at PCI, given similar efficacy but less bleeding risk	IIa, B	
	It is reasonable to choose CABG over PCI in older patients with NSTE-ACS who are appropriate candidates, particularly those with diabetes mellitus or complex 3-vessel CAD (e.g., SYNTAX score > 22), with or without involvement of the proximal LAD artery, to reduce CVD events and readmission and to improve survival	IIa, B	

ACS: acute coronary syndrome; CABG: coronary artery bypass grafting; CrCl: creatinine clearance; CVD: cardiovascular disease; GDMT: guideline-directed medical therapy; GP: glycoprotein; LAD: left anterior descending; NSTE: non-ST elevation; PCI: percutaneous coronary intervention; STEMI: ST elevation myocardial infarction; UFH: unfractionated heparin.

However, data to guide this invasive risk stratification in older adults is limited, so the treatment decision remains in the realm of clinical judgment.

5.2.1 STEMI

Timely reperfusion is the cornerstone in caring patients with STEMI and is applicable to elderly patient population. Even the very elderly STEMI patients have reasonable post-MI outcomes when treated aggressively with reperfusion therapy. In all age groups, primary PCI with stent placement is the preferred strategy over thrombolysis, when primary PCI is feasible and timely. In high risk elderly STEMI patients, primary PCI is generally safe as well. It results in even greater survival benefit for older compared with younger counterparts, reduces re-infarction and target-vessel revascularization, and is associated with less ICH. Emergent primary PCI may also provide survival benefit in elderly STEMI with cardiogenic shock.[37] An integrated regional STEMI transfer program is applicable to elderly patients, and proven to lessen age-related treatment disparities and to improve outcome.[38] In comparison with placebo, fibrinolytic therapy reduces STEMI mortality in elders up to the age of 85 years.[39] Today, in elderly STEMI patients, fibrinolytic therapy should be only used in confirmed STEMI, presenting ≤ 12 h after symptom onset and expected to have system delay ≥ 120 min before first-device activation (FDA) and without contraindications.[34,35,40,41] Elderly STEMI patients receiving fibrinolytic therapy should be immediately transferred to a PCI center with continued assessment of reperfusion, and early angiography and revascularization.[42,43] In older adults, coronary artery bypass grafting (CABG) has a limited role in the acute phase of STEMI with excess mortality risk, unless in the settings of failed PCI, coronary anatomy not amenable to PCI, or requiring surgical repair of mechanic complications [ventricular septal defect (VSD), papillary muscle rupture, free-wall rupture].

5.2.2 NSTE-ACS

Older adults with NSTE-ACS are generally at higher ischemic risk than younger groups. An early invasive strategy compared with an ischemia-guided strategy was found to have more benefit in the elderly than younger patients, unless there were extensive and prohibitive comorbidities

(e.g. hepatic, renal, pulmonary failure, cancer etc.).[34,44,45] The advancement of equipment and technique has made PCI safer for even very elderly patients (≥ 90 years of age) with high success rates and declining major bleeding risk. Although the highest risk reduction in death/MI with an early invasive strategy occurred in those ≥ 75 years of age, this strategy was associated significantly increased bleeding risk. Older patients with NSTE-ACS, and diabetes mellitus have a greater survival advantage with CABG as revascularization modalities. However, operative mortality rates and risk of complications (i.e., stroke) for CAGB in elderly patients were substantial (up to 8% at ≥ 80 years of age). Prolonged hospitalization and post-surgery recovery in older persons were also significant.

5.3 On-going care

The elderly ACS patients require close inpatient monitoring for potential complications from ischemic events, invasive procedures and side effects from medical treatment, in particular for the risk of bleeding with antiplatelet agents and anticoagulants, and also for hypotension, bradycardia, and renal failure. Acute ACS hospitalization of older adults often provides the healthcare system an opportunity to re-assess the patients' social status and supportive networks, re-establish aggressive risk modification strategies (smoking cessation, treating hypertension, hyperlipidemia, diabetes mellitus, and physical inactivity, etc), secondary prevention and provide guideline directed medical therapy.

6 Post-ACS care for the older adults

Older adults are susceptible to experience complications from ACS. In the acute phase, these complications include but are not limited to (1) ischemia related complications (HF due to pump failure; post-MI pericarditis; arrhythmia (both ventricular and atrial arrhythmia, conduction system malfunctions); mechanical complications from ischemia, i.e., papillary muscle rupture, VSD, free wall rupture); (2) procedural complications (access site bleeding/hematoma, retroperitoneal bleeding, stroke, pericardial effusion); (3) bleeding due to anti-platelet therapy and anemia; (4) renal insufficiency; (5) hypotension due to excessive medications; and (6) adverse effects from new medications. Post ACS, elderly patients have a high risk of re-hospitalization and death both from cardiovascular and non-cardiovascular etiologies. There is a 50% increased mortality risk per 10-year increase in age starting from 65 years of age.[46]

6.1 Patient education and social support

Elderly patients suffering from ACS are particularly vulnerable. Due to comorbid conditions, polypharmacy, frailty and often impaired communication skills and cognitive function, a comprehensive discharge planning process involving patient, family and advocates is essential and often challenging. Failure to understand and comply with a plan of care contributes to high rate of ACS re-admission rates and poor outcomes. The post-hospitalization care plan should include (1) detailed medication lists and instructions; (2) clear follow-up arrangement; (3) dietary instructions; (4) physical activity instructions; (5) reaction plan for adverse effects from medications and interventions; and (6) cardiac rehabilitation.

6.2 Secondary prevention and lifestyle modification

Aggressive lifestyle modification (smoking cessation, weight control, dietary intervention, etc) and pharmacological secondary prevention (tighter blood pressure and serum glucose control, statin therapy, etc) are indicated for older adults treated for ACS. Close collaboration among cardiologists, general practitioner, patient's rehabilitation specialists, pharmacists, dieticians, and patients and caregivers are crucial for the ongoing care.

6.3 Cardiac rehabilitation and exercise

Comprehensive cardiac rehabilitation programs provide patient education, identify and monitor risk factors, address lifestyle modification; provide psychosocial support and enhance exercise training for patients with ACS.[47] These programs were robustly tested and proven to be beneficial to all spectrums of age group ACS patients and endorsed by societal guidelines and healthcare administration. Exercise therapy improves functional capacity, cardiorespiratory fitness, and perception of well-being, as well as reduces cardiac event rate. Each step of increase in peak exercise capacity is associated with a reduction in all-cause mortality risk in all age groups, including elderly patients. Elderly ACS patients should be encouraged to participate in cardiac rehabilitation. However, low rate of referral and participation in cardiac rehabilitation by eligible elderly ACS patients were repeatedly reported. Healthcare providers must eliminate barriers to referrals and enrollment, and facilitate participation and monitor progress.

7 Opportunities for future research and clinical pearls

For research, there are urgent needs to: (1) Establish effective approaches to improve public awareness of symptoms and signs of ACS to minimize patient delays in presentation; (2) Advocate the expansion of enrollments of older adults in ACS clinical trials; (3) Develop or optimize risk

stratification algorithm incorporating frailty and functional data for ischemia outcomes and complication risks and their efficacy in guiding clinical decision making; (3) Study individualized, targeted strategies for coronary revascularization that achieve optimized goal of care for elderly ACS patients; (4) Study new safety, efficacy and optimal duration of novel P2Y12 antagonists in older adults; (5) Optimize cardiac rehabilitation programs for elderly ACS patients.

The clinical pearls are: (1) Older adults make up an increasingly large proportion of ACS patients. However, there are significant disparities in collecting clinical evidence and delivery of evidence-based effective therapy to these patients compared with their younger counterparts. (2) Type 2 MI is increasingly common with highly sensitive troponin assays. Judgment regarding coronary risk and revascularization is warranted, and initial strategy should focus on treatment of presenting non-cardiac conditions with monitoring for CAD complications. (3) High risk elderly ACS patients may derive more benefit from aggressive antithrombotic therapy and invasive revascularization, but also carry higher risks of complications, such as bleeding and stroke. (4) Optimized approach requires careful considerations of the individual patient's ischemic risk, comorbidities, risk of complications, frailty, cognitive function, life expectancy and advanced directive (patient's wish). (5) All older adults who survived from ACS should be encouraged and referred for cardiac rehabilitation. Exercise training improves long term survival and well-being of ACS patients.

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