Chronic Coronary Disease in Older Adults

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KEYWORDS

• Aging • Older adults • Geriatrics • Coronary artery disease • Revascularization

KEY POINTS

- The number of older adults living with chronic coronary disease is on the rise.
- Geriatric syndromes make diagnosing, treating, and managing complications of chronic coronary disease more complex.
- Medical and interventional therapies for chronic coronary disease have similar benefits for both younger and older adults; however, older adults experience more side effects, trade-offs, and complications.
- Medical decision-making should consider patient symptoms, preferences, and goals of care.
- A comprehensive geriatric heart team approach should be implemented when deciding upon treatment option.

INTRODUCTION

Chronic coronary disease (CCD) is a major cause of morbidity and mortality in older adults.[1,2] Despite this, older adults are underrepresented in the current literature supporting treatments in patients living with CCD. This poses a challenge for clinicians attempting to appropriately weigh the risks and benefits of therapeutic options during shared decision-making with patients. This review focuses on CCD in older adults and outlines the current literature, discusses current medical and invasive treatment options, recommends a patient-centered approach to complex decision-making, and suggests areas for future research.

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What Is an Older Adult?

The traditional definition of older adults in the United States is age ≥65 years. As the population of the United States and the world ages, adults are remaining active and healthier for longer. To reflect this change, current cardiovascular literature now classifies the older adult as age ≥75 years.[3] This population, however, is heterogeneous in its cognitive and functional status, level of social and financial support, and medical complexity. Therefore, the management of medical conditions in older adults requires a comprehensive and individualistic approach.

Defining Chronic Coronary Disease

CCD, also referred to as stable ischemic heart disease and stable angina, encompasses a variety of cardiac conditions. These can include individuals with obstructive or nonobstructive coronary artery disease (CAD), the presence or absence of prior myocardial infarction, symptoms of chronic angina or anginal equivalents, and coronary artery disease diagnosed with noninvasive testing.[3] The pathophysiology of CAD involves plaque formation and vascular remodeling that is mediated by modifiable and non-modifiable risk factors, including chronologic age.[4] Older adults often have a higher burden of these risk factors and chronic medical conditions that can mimic or mask the symptoms of CCD. On presentation, older adults are more likely to have silent ischemia and experience non-chest pain symptoms compared with younger adults.[3] Anginal equivalents or accompanying symptoms can include fatigue, dyspnea, and epigastric pain, which can be difficult to distinguish from conditions such as anemia, gastroesophageal reflux disease, chronic pulmonary disease, or deconditioning.[5] These complex phenotypic profiles of CCD in older adults can make it difficult to diagnose and identify the need for advancing therapies. This further highlights the importance of taking a thorough clinical history when identifying and managing older patients with suspected CCD.

Prevalence of Chronic Coronary Disease in Older Adults

Roughly 30% of adults aged ≥75 years are living with CCD, with similar prevalence observed in men and women.[1,2] The overall prevalence is expected to rise due to multiple factors, including (1) the aging of the population at large (2) the incidence of new CCD is highest in older adults, (3) mortality after acute coronary syndrome (ACS) has improved with modern therapies, and (4) increased performance of existing noninvasive and invasive testing tools to detect more clinically silent disease.[1,2] It is important to note that while the disease burden is greatest in older adults, disease complexity is also increased due to underlying physiologic and anatomic differences. For example, older adults frequently present with more diffuse, calcified, and anatomically complex CAD, increased vessel tortuosity, microvascular disease, and endothelial dysfunction.[1] Additional data suggest that the onset of CCD is a better prognostic marker of future disability than myocardial infarction.[6] Therefore, with an aging population, CCD represents an expanding burden on patients, caregivers, and the health care system at large.

Geriatric Syndromes

Geriatric syndromes are a collection of clinical conditions that occur frequently with aging and influence cardiovascular outcomes.[7,8] Common geriatric syndromes include falls, delirium, frailty, polypharmacy, and functional or cognitive decline. Geriatric syndromes contribute to the complex clinical phenotype of patients with CCD and therefore must influence management strategies and response to treatment. It is important

for clinicians to complete a cardiovascular risk assessment alongside a focused geriatric assessment including evaluation of multimorbidity, cognition, frailty, and social support. A recent Expert Panel recommended a minimum geriatric risk assessment that includes functional assessment, activities of daily living (ADLs), instrumental activities of daily living (IADLs), and goals of care, with further targeted comprehensive geriatric assessment of multimorbidity, polypharmacy, cognitive impairment, frailty, and falls (Fig. 1).[9,10]

Diagnosing Chronic Coronary Disease in Older Adults

All patients with CCD are at increased risk for future major adverse cardiovascular events (MACE) and require regular follow-up. Further diagnostic workup is indicated in patients with CCD when there is clinical uncertainty, or a change in symptoms or functional capacity while on guideline-directed medical therapy (GDMT).[3] There are multiple factors that impact the utility of functional and anatomic assessment of CAD in older adults. Barriers to completing exercise stress testing in older adults, even with modified exercise protocols, include decreased muscle mass, reduced

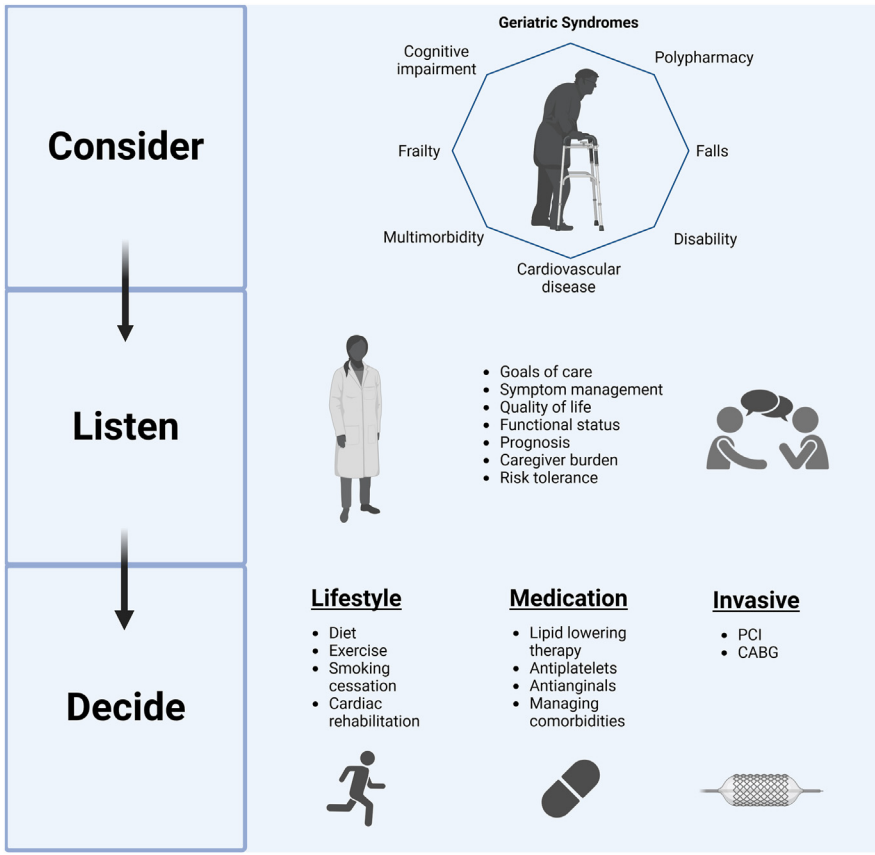

Fig. 1. CCD in Older Adults: "Consider, Listen, Decide" is a framework for approaching shared decision-making in the geriatric population. It highlights the need to consider different geriatric syndromes, listen to patients' goals of care, and decide which treatment options are best. CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention.

maximal heart rate, musculoskeletal pain, unsteadiness, and baseline electrocardiogram (ECG) abnormalities.[11] Pharmacologic stress tests with accompanying ECG, myocardial perfusion imaging, or echocardiography are feasible alternatives to exercise. Coronary computed tomography angiography (CCTA) presents some challenges in older adults given its increased likelihood of uninterpretable scans, either due to highly calcified plaques or motion artifact.[12] Recent guidelines suggest that CCTA is favored for patient age <65 years, but data are scarce and further dedicated studies are needed to assess generalizability across different ages.[13,14] Diagnostic coronary angiography should be considered within the context of candidacy for percutaneous coronary intervention (PCI) or surgical revascularization and broader goals of care.[3]

Therapeutic Options

The overarching goal of treatment is to prevent disease progression, control symptoms, and maintain patients' level of functioning, independence, and cognition. It is imperative that clinicians understand the risks and benefits of medical therapies and revascularization strategies as they specifically apply to older adults in order to provide the optimal guidance to patients. GDMT is indicated for all patients who have been diagnosed with CAD, regardless of chronologic age. Maximal GDMT for CCD includes preventive measures, optimizing comorbidities, medications aimed at preventing future cardiovascular events, and symptom-directed therapies. Current American and European guidelines recommend an initial medical therapy approach with revascularization reserved for patients with intolerable symptoms despite medical therapy.[3,15]

Lifestyle Modification

Lifestyle modification is essential to managing CCD. Encouraging healthy diet, exercise, and smoking cessation are indicated in all patients. Cardiac rehabilitation can help older adults initiate exercise regimens, improve quality of life, and decrease the risk of hospitalization and cardiovascular mortality.[16] Optimizing comorbidities such as glycemic control, weight, blood pressure, and stress are also key. Importantly, lifestyle modifications have more favorable risk-benefit profiles than medications.

Medical Therapies

Aging causes significant changes to the pharmacokinetics and pharmacodynamics of medical therapies used in CCD.[17] Older adults are more likely to have impaired kidney function, hepatic blood flow, and reduced lean muscle mass which affect the metabolism of certain medications.[17] It is important to recognize that all medical therapies that have been proven to be effective in younger adults can still be used in older adults with additional considerations.

Secondary Prevention

First-line secondary prevention treatment for CAD includes statin and antiplatelet therapy. American Heart Association (AHA) guidelines recommend either moderate-intensity or high-intensity statin for older adults, whereas European guidelines recommend high-intensity statin treatment regardless of age.[3,15] Goals of lipid-lowering therapy are a low-density lipoprotein (LDL) reduction of $\geq$ 50% and LDL $\leq$ 70 while on high-intensity statin.[3] Recommendations also include additional lipid-lowering therapies, including ezetimibe and proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors if cholesterol goals are not achieved with maximally tolerated statin.[3] Older adults have been underrepresented in trials for novel lipid-lowering therapies, though available data suggest that the benefits of lipid-lowering therapy for preventing

secondary atherosclerotic cardiovascular disease events remain consistent across the age spectrum.[18] Additional research supports the use of high-intensity statin over moderate-intensity statin in older adults because of improved survival, however, this is not reflected in current guidelines.[19,20] Furthermore, older adults are less frequently given statins, especially high-intensity statins, for secondary prevention despite having a higher burden of disease and similar tolerability compared to younger adults.[21,22]

Dual antiplatelet therapy (DAPT) with low-dose aspirin and P2Y12 inhibitors have been the cornerstone of medical therapy among those with recent PCI or ACS. DAPT, notably, is not recommended in CCD without recent stent placement or ACS due to higher bleeding risk and absence of reduction in MACE.[3] Clopidogrel and ticagrelor are the preferred P2Y12 inhibitors to use in older adults as prasugrel is associated with increased bleeding risk in those age $\geq$75 years.[23,24] Current guidelines recommend 6 months of DAPT following PCI and potentially shorter durations of DAPT in those with high risk of bleeding.[3] Overall, DAPT is safe to use in older adults but bleeding risk does increase as patients age.[25] Further evidence is required to establish the optimal duration of DAPT in older adults following PCI in the current era of newer generation drug-eluting stents.[26,27] Aspirin monotherapy has historically been preferred as a single antiplatelet agent once transitioned off DAPT; however, recent data suggest that P2Y12 inhibitor monotherapy may reduce the risk of MACE with similar bleeding risk compared to aspirin alone.[28,29] In patients requiring oral anticoagulation following PCI, a short course (less than 30 days duration) of "triple therapy" with a direct oral anticoagulant (DOAC) and DAPT, followed by treatment with a DOAC plus single antiplatelet therapy with clopidogrel is the standard of care based on multiple randomized controlled trials.[3,30] DOAC monotherapy is another potential option for patients with chronic coronary disease (ie, >12 months from PCI) with low ischemic risk and who otherwise require oral anticoagulation.[13,31]

Antianginals

Recommended antianginal therapy includes either a beta-blocker (BB), calcium channel blocker (CCB), or long-acting nitrate for relief of angina and anginal-equivalents.[3] BB and CCB are the current first-line therapies based on US and European guidelines.[3,15] BB work by decreasing myocardial oxygen demand through reduction in heart rate and blood pressure, with the added benefit of disrupting maladaptive ventricular remodeling.[3,32] CCB increase coronary and peripheral vasodilation while also altering myocardial oxygen demand.[33] Use of BB in older adults may be limited by hypotension, bradycardia, dizziness, fatigue, sleep disturbances, sexual dysfunction, and possible cognitive and functional decline.[34] Limitations of CCB vary among dihydropyridine and non-dihydropyridine classes, though they are associated with peripheral edema and constipation. BB should not be initiated in CCD for patients without angina, anginal equivalents, or prior MI or heart failure with reduced ejection fraction.[3] The trials investigating BB and CCB are limited in their inclusion of older adults.[35,36]

Nitrates are just as effective at treating angina as CCB and BB; however, long-acting nitrates are considered second-line antianginals.[37,38] Both short-acting and long-acting nitrates improve exercise tolerance.[39] Common issues faced when using nitrates included headache and tachyphylaxis and they should be avoided in patients with severe aortic stenosis and those taking phosphodiesterase inhibitors.[40]

Refractory angina can be treated with combination therapy of BB, CCB, and nitrates, or with the addition of ranolazine. Ranolazine is an inhibitor of late inward sodium current.[41] Concerns specific to older adults include nausea, constipation, and prolongation of the QTC interval.[15,42]

Additional considerations for further reduction in MACE include sodium-glucose cotransporter-2 (SGLT2) inhibitors, glucagon-like peptide-1 (GLP1) agonists, and angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARB) in patients with comorbidities such as diabetes, obesity, chronic kidney disease, and systolic dysfunction.[3]

Managing Side Effects

To mitigate the risks of bothersome side effects and polypharmacy, the authors recommend that clinicians routinely screen for adverse events related to cardiovascular medications. If present, consider reducing the dose, switching drug classes, or discontinuing, before re-evaluating at subsequent visits.[43] Other helpful strategies include deliberate dosing schedules and collaboration with primary care providers, pharmacists, nurses, and home health care workers to ensure the maintenance of appropriate medication lists.

Revascularization Strategies

Revascularization in CCD represents a complex clinical scenario with limited data to guide management in older adults. Like medical therapy, the goals of revascularization are to improve symptom burden, prevent secondary events, and improve mortality. Current AHA guidelines recommend revascularization to improve symptoms in patients with CCD and lifestyle-limiting angina despite optimal medical therapy.[3] Mortality benefits have only been demonstrated following coronary artery bypass grafting (CABG) with medical therapy compared with medical therapy alone for either severe left main disease or multivessel disease with left ventricular (LV) systolic dysfunction (ejection fraction $\leq$35%) or diabetes.[3] A similar survival benefit is also demonstrated with either CABG or PCI for non-complex left main disease with normal LV systolic function.[3,44] When patients are poor surgical candidates, PCI can be used in place of CABG to improve symptoms and reduce MACE.[3] Unfortunately, older adults with complex multimorbid disease and those with geriatric syndromes were underrepresented in these studies.[45–48] Furthermore, current guidelines recommend a heart team approach, including interventionalists, general cardiologists, and surgeons, when there is complex triple vessel disease or when the optimal treatment plan is unclear.[3]

While many of the recommendations in the current guidelines are extrapolated from studies evaluating younger adults, the most compelling data evaluating invasive therapy compared to medical therapy in older adults demonstrate that (1) revascularization can improve angina and quality of life and (2) there is no significant difference in mortality with revascularization versus medical therapy, except in those with severe left main disease, multivessel disease with LV systolic dysfunction, and multivessel disease with diabetes (**Table 1**).[49–53] These factors must be considered within the context of older adults being at increased risk of in-hospital mortality, periprocedural mortality, and readmission following PCI.[54] With increasing age, patients also have worse outcomes after CABG compared with younger patients.[55] This is at least partially driven by the higher prevalence of frailty in older adults, which is associated with adverse outcomes and mortality following CABG surgery.[56,57] While clinicians may integrate assumptions about known natural life expectancy into therapeutic strategies, survival to older age is a strong predictor of longer life expectancy and many older adults have more than a decade of quality life-years remaining.[58] Furthermore, significant heterogeneity exists in biological aging across patients of similar chronologic ages, which has clear implications for therapeutic decisions.[59] Quantitative pre-procedural risk calculators that incorporate cardiovascular, physiologic, anatomic, and hemodynamic

Table 1
Characteristics and results of randomized trials of revascularization strategies in patients with chronic coronary disease with secondary analyses related to older adults

Trial (Author, Year Published)	Study Population (Sample Size)	Randomized Intervention	Average Age (Years)	Primary Endpoint	Implications for Older Adults
TIME (TIME Investigators, 2001)[49]	Patients ≥75 y with chronic angina classified as CCSC >2 despite ≥2 antianginals (n = 305)	Revascularization vs medical therapy	Mean age = 80	QoL (SF36[a]) at 6 mo: Revascularization = 11.4 vs medical therapy = 3.8; $P = .008$ MACE at 6 mo: Revascularization 19% vs medical 49% ($P < .0001$).	Older adults with angina despite medical management have improved QoL with revascularization vs medical therapy alone.
COURAGE (Sedlis et al,[60] 2017)	Patients with chronic stable angina or silent ischemia and angiographic CAD > 70% stenosis (n = 2287)	PCI and medical therapy vs medical therapy alone	Mean age (extended follow up) = 64	Death at 11.9 y: PCI = 25% vs medical therapy = 24%; adjusted HR = 1.03, 95% CI 0.83–1.21, $P = .76$	In sub-group analysis of age ≥ 65 y, similar clinical events with PCI and medical therapy vs medical therapy alone were observed[52]
BARI-2D (Ikeno et al,[46] 2017)	Patients with type II diabetes and evidence of ischemia (n = 2368)	Prompt revascularization (included CABG and PCI strata) vs medical therapy	Mean age = 62	Death, MI, or stroke at 5 y: low syntax ≤22; CABG 26.1% vs medical therapy 29.9%; $P = .41$; PCI 17.8% vs medical therapy 19.2%; $P = .84$; moderate to high syntax ≥23; CABG 15.3% vs medical 30.3%; $P = .02$; PCI 35.6% vs medical 26.5%; $P = .12$	Age ≥70 y (n = 514) with no difference in death, MACE, angina, or health status outcomes for revascularization vs medical therapy[53]

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Table 1
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Trial (Author, Year Published)	Study Population (Sample Size)	Randomized Intervention	Average Age (Years)	Primary Endpoint	Implications for Older Adults
ISCHEMIA (Maron et al,[61] 2020)	Patients with stable CAD and moderate or severe ischemia (n = 5179)	Invasive vs conservative strategy	Mean age = 64	MACE at median 3.2 y: invasive vs conservative HR 0.93 (95% CI, 0.8–1.08); P = .34. Estimated cumulative event rate 6 mo: invasive = 5.3% vs conservative = 3.4% (95% CI, 0.8–3.0). Estimated cumulative event rate 5 y: invasive 16.4% vs conservative 18.2% (95% CI, −4.7–1.0)	Age ≥75 y (n = 665) had decreased frequency of angina but less improvement in angina-related health status with invasive management compared with younger adults[50]

Abbreviations: BARI-2D, The bypass angioplasty revascularization investigation 2 diabetes trial; CABG, coronary artery bypass grafting; CAD, coronary artery disease; CCSC, canadian cardiac society class; CI, confidence interval; COURAGE, the clinical outcomes utilizing revascularization and aggressive drug evaluation trial; HF, heart failure; HR, hazard ratio; ISCHEMIA, international study of comparative health effectiveness with medical and invasive approaches; MACE, major adverse cardiovascular events; MI, myocardial infarction; PCI, percutaneous coronary intervention; QoL, quality of life; TIME, Trial of Invasive versus Medical Therapy in Elderly Patients With Chronic Symptomatic Coronary-Artery Disease; UA, unstable angina.

[a] SF36 indicates Short Form 36 Health Survey. SF36 score 0 to 100 with higher scores indicating more favorable status.

risk are improved upon with the addition of a geriatric assessment.[10] These tools can help clinicians provide nuanced risk stratification in this medically complex cohort.

DISCUSSION

In the absence of compelling evidence to recommend medical therapy versus invasive revascularization, it is imperative that clinicians elicit patient preferences regarding treatment of CCD. The authors recommend utilizing the "Consider, Listen, Decide" framework (see **Fig. 1**) that was proposed as a standardized method for approaching treatment decisions in older adults with CCD.[5,43] In this framework, clinicians must first consider a patient's symptoms, comorbidities, and medications to create an impression of the broader clinical context of that individual patient. This can aid in identifying the symptoms that are leading to the greatest functional limitation and allow the clinician to appraise whether therapeutic options are likely to improve those symptoms or, conversely, worsen accompanying symptoms such as fatigue and lightheadedness. Next, clinicians listen to the patient's goals of care, priorities, and preferences. Eliciting a top health goal(s) facilitates the patient-clinician partnership and assists the multidisciplinary heart team in guiding the most appropriate treatment course, weighing the risks and benefits of lifestyle modification, medical therapies, and invasive options to arrive at a person-centered decision.

FUTURE DIRECTIONS

Older adults with CCD are a vulnerable and heterogeneous population with distinct priorities and preferences. To better serve them, there is a significant need for clinical trials enrolling older adults age $\geq$ 75 years with CCD to evaluate the most beneficial medical and revascularization strategies. One ongoing study, LIVEBETTER (A Trial Comparing the Effectiveness and Tolerability of Medications in Older Adults With Stable Angina and Multiple Chronic Conditions, NCT05786417), aims to determine the optimal antianginal approach in older adults with CCD and multiple chronic conditions while also focusing on patient-centered outcomes such as quality of life, symptom control, and mobility. Further evidence, testing of shared decision-making tools, improved risk models, and exploration of patient-centered outcomes that matter most to patients are essential to inform medical decisions and promote the care of older adults.

SUMMARY

The prevalence of CCD is increasing as our population ages and older adults are more likely to experience CCD than younger adults. However, older adults are underrepresented in current CCD literature, and they often present with complex geriatric phenotypes which increase the complexity of shared decisions. A holistic shared decision-making approach considering the broader patient context can assist patients in the delicate balance between treatment benefits, harms, and tradeoffs. Dedicated studies in representative geriatric populations are urgently needed to better inform clinicians and patients in these complex decisions.

CLINICS CARE POINTS

- Incorporating geriatric syndromes is necessary to guide optimal treatment decisions for CCD in older adults.

- Older adults should be optimized on GDMT, albeit with close attention to the potential burden of adverse effects, drug-drug interactions, and polypharmacy.
- Older adults generally derive similar benefits from most medical and invasive treatments compared to younger adults.
- Older adults have increased risk of morbidity and mortality when undergoing invasive treatments for CCD compared with younger adults.
- A geriatric heart team approach is critical to person-centered revascularization decisions in older adults with CCD.

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