Available online at www.sciencedirect.com

ScienceDirect

www.onlinepcd.com

Secondary Prevention of Cardiovascular Disease in Older Adults

*Michael W. Rich**

Washington University School of Medicine, St. Louis, Missouri

ARTICLE INFO

Keywords:
Cardiac rehabilitation
Diabetes mellitus
Hypertension
Prevention
Smoking

ABSTRACT

Atherosclerotic cardiovascular disease is extremely common in older adults and the potential benefits of secondary prevention are perhaps greater in this population than in younger patients. While there is good evidence that secondary prevention efforts are justified in patients up to 80 years of age, limited data are available on secondary prevention in octogenarians and there is no evidence to guide treatment in patients ≥90 years of age. Further, the value of secondary prevention may be confounded by prevalent comorbidities, polypharmacy, and limited life expectancy. It is therefore essential that all management decisions be made in relation to individual preferences and goals of care, with understanding by patients that benefits as well as risks may increase with age. Furthermore, research is needed to refine markers to better delineate which older adults are most likely to benefit from preventive therapies.

The incidence and prevalence of atherosclerotic cardiovascular disease (ASCVD), including coronary artery disease (CAD), peripheral arterial disease (PAD), and ischemic stroke, increase progressively with age, and it is estimated that over 80% of men and women 75 years of age or older have clinically manifest CVD.[1] This population is at heightened risk for recurrent CVD events, including death, as well as impaired quality of life, and there is thus substantial opportunity for older patients with CVD to benefit from interventions aimed at secondary prevention (SP). Conversely, older adults may be at increased risk for adverse outcomes associated with all diagnostic and therapeutic interventions, in part due to age-associated non-cardiac vulnerabilities, such as cognitive impairment and frailty. Therefore, the applicability of SP measures based on evidence derived largely from younger and healthier populations to older adults is uncertain and requires careful scrutiny. Accordingly, all recommendations must be individualized, taking into consideration not only the patient's cardiac condition, but also prevalent comorbidities, functional limitations, goals of care, and personal preferences.

In 2013, the American Heart Association published a comprehensive Scientific Statement on Secondary Prevention of ASCVD in Older Adults.[2] The current article provides an overview of the role of SP in older adults and highlights challenges and controversies to implementing preventive measures in elderly patients. As noted above, general concerns relate to availability and quality of data as well as the relevance of preventive goals to older adults who often have comorbid conditions that may be of equal or greater concern than their cardiac issues.

Statement of Conflict of Interest: see page 174.

* Address reprint requests to Michael W. Rich, MD, Professor of Medicine, Washington University School of Medicine, 660 S. Euclid Avenue, Campus Box 8086, St. Louis, MO 63110.
E-mail address: mrich@wustl.edu.

http://dx.doi.org/10.1016/j.pcad.2014.03.006
0033-0620/

Abbreviations and Acronyms

ACE = angiotensin converting enzyme

ACS = acute coronary syndrome

ADL = activities daily living

ARB = angiotensin receptor blocker

ASCVD = atherosclerotic cardiovascular disease

BP = blood pressure

CAD = coronary artery disease

CR = cardiac rehabilitation

CVD = cardiovascular disease

DM = diabetes mellitus

HF = heart failure

HTN = hypertension

MI = myocardial infarction

PAD = peripheral arterial disease

SP = secondary prevention

General measures

Among patients at high risk for ASCVD events, including those with prior myocardial infarction (MI), PAD, or stroke, aspirin reduces the risk of recurrent events by about 25%,[3] and aspirin 75–162 mg daily is recommended for SP in all patients with ASCVD in the absence of contraindications.[2] Clopidogrel 75 mg daily is recommended in patients intolerant to aspirin.[2] Moreover, in the Clopidogrel in Unstable angina to prevent Recurrent Events (CURE) trial, the addition of clopidogrel to aspirin provided a further 20% reduction in CVD death, MI, or stroke among patients with non-ST-elevation acute coronary syndromes (ACS), and the absolute benefit was similar in patients younger or older than age 65.[4] Data are limited on the effectiveness of aspirin and other anti-platelet agents among patients over 80 years of age, whereas the risk of major and minor bleeding is higher among older patients prescribed dual anti-platelet therapy compared to aspirin alone. In addition, in patients ≥75 years of age with ACS treated with aspirin, the addition of prasugrel has been associated with increased risk of bleeding compared to clopidogrel.[2] Similarly, bleeding risks are increased when anti-platelet therapy is used in combination with systemic anticoagulants.

Although data in patients 75 years of age or older are limited, long-term beta-blocker therapy is recommended following an ACS.[2] Older patients may be at higher risk for adverse events with beta-blockers, including bradyarrhythmias and fatigue, and dosing should be adjusted accordingly. Several large trials have demonstrated the efficacy of angiotensin-converting enzyme (ACE) inhibitors for SP in patients with or at high risk for ASCVD, even in the absence of left ventricular systolic dysfunction or heart failure (HF).[5] These studies enrolled patients up to 80 years of age with up to 5 years follow-up. Therefore, ACE inhibitors are recommended for SP in older adults with established vascular disease.[2] Angiotensin-receptor blockers (ARBs) are a suitable alternative in patients intolerant to ACE inhibitors due to cough or allergic reactions.[2] ACE inhibitors and ARBs should be used with caution in older adults with significant renal impairment (est. glomerular filtration rate <45 cc/min), and renal function and serum potassium levels should be monitored during initiation and titration. Combination therapy with an ACE inhibitor and ARB is not recommended due to increased risk for adverse events without proven benefits.

Hypertension (HTN)

The prevalence of HTN increases with age, exceeding 70% among persons over age 75, and HTN is both the most common and strongest modifiable risk factor for CAD, PAD, and stroke in older adults.[1,2,6] In addition, numerous randomized trials have demonstrated that treatment of HTN is associated with reductions in stroke, incident HF, and CAD events in elderly patients.[6] In the Hypertension in the Very Elderly Trial (HYVET), 3845 patients ≥80 years of age with systolic blood pressures (BP) ≥160 mmHg were randomized to indapamide supplemented by perindopril as needed to achieve a target BP <150 mmHg or to matching placebo. Over a median follow-up of 1.8 years, active treatment was associated with a 30% reduction in fatal or nonfatal strokes ($p = 0.06$), 64% reduction in HF ($p < 0.001$), 34% reduction in all-cause CVD events ($p < 0.001$), and 21% reduction in all-cause mortality ($p = 0.02$).[7]

From the perspective of SP, an important limitation of HYVET is that only 11.8% of patients had pre-existing ASCVD, and subgroup analysis in this cohort has not been reported. In the Avoiding Cardiovascular Events through Combination Therapy in Patients Living with Systolic Hypertension (ACCOMPLISH) trial, 11,506 patients with HTN were randomized to receive benazepril in combination with either amlodipine or hydrochlorothiazide (HCTZ).[8] The trial was stopped after a mean follow-up of 36 months due to a 20% reduction in CVD events in the benazepril-amlodipine arm compared to amlodipine-HCTZ (9.6% vs. 11.8%, $p < 0.001$). Approximately 41% of patients enrolled in ACCOMPLISH were age 70 or older, 23.5% had prior MI, 13% had prior stroke, and 36% had a prior revascularization procedure. Outcomes were similar in pre-specified subgroups defined by age, gender, and presence of diabetes mellitus (DM), but subgroup analysis by pre-existing CVD was not reported. Nonetheless, based on these findings and the proven benefits of renin-angiotensin system inhibitors for SP in older adults discussed above, it seems reasonable to prescribe an ACE-inhibitor or ARB as first line therapy for hypertension in older patients with established ASCVD.

Despite limited data to support treatment of HTN for SP in older patients with CAD, there is robust evidence that anti-HTN therapy is effective for reducing recurrent stroke in patients with an incident cerebrovascular accident.[9,10] In the Perindopril Protection Against Recurrent Stroke Study (PROGRESS), a flexible regimen of perindopril with or without indapamide reduced the risk of recurrent stroke by 28% ($p < 0.0001$) and major ASCVD events by 26% among 6105 patients with a mean age of 64 years, 16% of whom had concomitant CAD.[9] A subsequent meta-analysis of 10 trials involving a total of 38,421 patients with incident stroke confirmed that anti-HTN therapy reduced the risk of recurrent stroke by 30% and all CVD events by 25%.[10]

Taken together, these findings strongly suggest but do not prove that treatment of HTN is likely to be beneficial for SP of CVD in older patients, including octogenarians. Correspondingly, the AHA scientific statement on SP recommends treatment of hypertension in accordance with published guidelines.[2] Similarly, the recently revised guideline for SP of stroke provides a