## Journal of

#### Cardiology and Therapy

Online Submissions: http://www.ghrnet.org/index./jct/doi:10.17554/j.issn.2309-6861.2015.02.92

Journal of Cardiol Ther 2015 October 2(5): 418-421 ISSN 2309-6861(print), ISSN 2312-122X(online)

REVIEW

# 2015 Guidelines on Treatment of Hypertension in Patients With Coronary Artery Disease

#### Wilbert S. Aronow

Wilbert S. Aronow, Cardiology Division, Department of Medicine, Westchester Medical Center, New York Medical College, Valhalla, New York, the United States

Correspondence to: Wilbert S. Aronow, MD, FACC, FAHA, Cardiology Division, Department of Medicine, Westchester Medical Center, New York Medical College, Valhalla, New York, the United

States.

Email: wsaronow@aol.com

Telephone: +1-914-493-5311 Fax: +1-914-235-6274 Received: July 6, 2015 Revised: July 26, 2015

Accepted: July 30, 2015

Published online: October 10, 2015

## **ABSTRACT**

Patients with coronary artery disease should have intensive treatment of modifiable coronary risk factors. Dietary sodium should be decreased. Hypertension should be treated with beta blockers and angiotensin-converting enzyme inhibitors or angiotensin receptor blockers. Long-acting nitrates are effective antianginal and antiischemic medications. Calcium channel blockers may be added if angina pectoris persists despite beta blockers and long-acting nitrates. The American Heart Association/American Society of Cardiology 2015 guidelines recommend a target blood pressure below 140/90 mm Hg in patients with coronary artery disease and with an acute coronary syndrome if they are aged 80 years and younger but below 150 mm Hg if they are ≥80 years of age. Octogenarians should be checked for orthostatic changes with standing, and a a systolic blood pressure below 130 mm Hg and a diastolic blood pressure below 65 mm Hg must be avoided. Caution is advised in lowering the diastolic blood pressure below 60 mm Hg in diabetics or in patients older than 60 years of age. In addition to the beta blockers carvedilol, metoprolol CR/XL, and bisoprolol, patients with hypertension and heart failure should be treated with diuretics and angiotensinconverting enzyme inhibitors or angiotensin receptor blockers, and patients with persistent severe symptoms with aldosterone antagonists if not contraindicated.

© 2015 ACT. All rights reserved.

**Key words:** Coronary artery disease; Hypertension; Beta blockers; Angiotensin-converting enzyme inhibitors; Angiotensin receptor blocker; Aldosterone antagonists; Calcium channel blockers; Nitrates

Aronow WS. 2015 Guidelines on Treatment of Hypertension in Patients With Coronary Artery Disease. *Journal of Cardiology and Therapy* 2015; 2(5): 418-421 Available from: URL: http://www.ghrnet.org/index.php/jct/article/view/1400

## INTRODUCTION

Hypertension is a major risk factor for coronary artery disease<sup>[1-7]</sup>. Hypertension is present in approximately 69% of patients with a first myocardial infarction<sup>[8]</sup>. Hypertension is also a major risk factor for angina pectoris and for sudden cardiac death<sup>[1-7]</sup>.

The blood pressure should be reduced to less than 140/90 mm Hg in patients younger than age 80 years and to less than 150/90 mm Hg in patients aged 80 years and older if tolerated<sup>[1-7]</sup>. This editorial will discuss the 2015 American Heart Association/American College of Cardiology/American Society of Hypertension guidelines on treatment of hypertension in patients with coronary artery disease<sup>[7]</sup>.

In 4,162 patients with an acute myocardial infarction with or without ST-segment elevation or high-risk unstable angina pectoris, the lowest cardiovascular events rates occurred with a systolic blood pressure between 130 to 140 mm Hg and a diastolic blood pressure between 80 to 90 mm Hg with a nadir of 136/85 mm<sup>[9]</sup>.

In 8,354 patients aged 60 years and older with coronary artery disease in the International VErapamil SR Trandolapril (INVEST)

study, a baseline systolic blood pressure of 150 mm Hg and higher, and 22,308 patient years of follow-up, the primary outcome of all-cause mortality, nonfatal myocardial infarction, or nonfatal stroke occurred in 9.36% of adults with a systolic blood pressure below 140 mm Hg, in 12.71% of adults with a systolic blood pressure of 140-149 mm Hg, and in 21.3% of adults with a systolic blood pressure of 150 mm Hg and higher  $(P<0.0001)^{[10]}$ . Using propensity score analyses, compared with a systolic blood pressure below 140 mm Hg, a systolic blood pressure of 140 to 149 mm Hg increased cardiovascular mortality by 34% (P=0.04), total stroke by 89% (P=0.002), and nonfatal stroke by 70%  $(P=0.03)^{[10]}$ . Compared with a systolic blood pressure below 140 mm Hg, a systolic blood pressure of 150 mm Hg and higher increased the primary outcome by 82% (P<0.0001), all-cause mortality by 60% (P<0.0001), cardiovascular mortality by 218% (P<0.0001), and total stroke by 283%  $(P<0.0001)^{[10]}$ .

A meta-analysis of 147 randomized trials of 464,000 persons with hypertension reported an extra protective effect of beta blockers given after myocardial infarction<sup>[11]</sup>. If beta blockers are used to treat persons with hypertension, atenolol should not be used<sup>[12-14]</sup>.

## **BLOOD PRESSURE GOAL**

The American Heart Association/American Society of Cardiology/American Society of Hypertension 2015 guidelines recommend that the target blood pressure should be below 140/90 mm Hg in patients with coronary artery disease and with an acute coronary syndrome if they are aged 80 years and younger and the systolic blood pressure below 150 mm Hg if they are older than 80 years of age<sup>[7]</sup>. Consideration can be given to lower the blood pressure to below 130/80 mm Hg with a class IIb C indication<sup>[7]</sup>. Octogenarians should be checked for orthostatic changes with standing, and a a systolic blood pressure below 130 mm Hg and a diastolic blood pressure below 65 mm Hg should be avoided<sup>[7]</sup>. Caution is advised in reducing a diastolic blood pressure below 60 mm Hg in patients with diabetes mellitus or in persons older than 60 years of age<sup>[7]</sup>.

## ANTIHYPERTENSIVE THERAPY

#### **Coronary Artery Disease**

Coronary risk factors should be treated including cessation of smoking and treatment of hypertension, dyslipidemia, diabetes mellitus, obesity, and physical inactivity<sup>[7]</sup>. Dietary sodium should be reduced

Beta blockers are the initial antihypertensive drugs to use in patients with coronary artery disease who have angina pectoris, who have had a myocardial infarction, and in those who have left ventricular systolic dysfunction unless contraindicated<sup>[7]</sup>. Persons with prior myocardial infarction and hypertension should be treated with beta blockers and angiotensin-converting enzyme inhibitors<sup>[1-4,6,7,11,14-26]</sup>. Atenolol should not be administered<sup>[12-14]</sup>. If a third drug is needed, aldosterone antagonists may be administered<sup>[27]</sup>. Patients treated with aldosterone antagonists should not have significant renal dysfunction or hyperkalemia.

In addition to the beta blockers carvedilol, metoprolol CR/XL, and bisoprolol<sup>[7,28-32]</sup>, patients with hypertension, coronary artery disease, and congestive heart failure should be treated with diuretics and angiotensin-converting enzyme inhibitors or angiotensin receptor blockers<sup>[7,28,33-40]</sup>, and patients with persistent severe symptoms with aldosterone antagonists<sup>[7,27,28,41]</sup>. Hydralazine plus isosorbide dinitrate should be added to African-American patients with New York Heart Association class III or IV heart failure with a reduced left ventricular ejection fraction already receiving diuretics, beta blockers, and an

angiotensin-converting enzyme inhibitor or angiotensin receptor blocker<sup>[7,28,42]</sup>. Drugs to avoid in patients with hypertension and heart failure with a reduced left ventricular ejection fraction include verapamil, diltiazem, doxazosin, clonidine, moxonidine, hydralazine without a nitrate, and nonsteroidal anti-inflammatory drugs<sup>[7]</sup>.

In patients with hypertension, coronary artery disease, and heart failure with a preserved left ventricular ejection fraction, class I theraputic indications include control of systolic and diastolic hypertension, control of the ventricular rate in patients with atrial fibrillation, and treatment of pulmonary congestion and peripheral edema with diuretics<sup>[7,28]</sup>. Class IIb therapeutic indications include use of beta blockers, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, or calcium channel blockers<sup>[7,28]</sup>.

#### **Stable Angina Pectoris**

Patients with hypertension and chronic stable angina pectoris should be treated with beta blockers plus nitrates as antianginal agents<sup>[7]</sup>. Hypertension in these patients should be treated with beta blockers plus an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker with addition of a thiazide or thiazide-like diuretic if needed. If either the angina pectoris or the hypertension remains uncontrolled, a long-acting dihydropyridine calcium channel blocker can be added to the therapeutic regimen. Nondihydropyridine calcium channel blockers such as verapamil and diltiazem cannot be used if there is left ventricular systolic dysfunction. Combining a beta blocker with either verapamil or diltiazem must be used cautiously because of the increased risk of bradyarrhythmias and heart failure developing<sup>[7]</sup>.

#### **Acute Coronary Syndromes**

In patients with an acute coronary syndrome, initial management of hypertension should include a short-acting beta1 selective beta blocker without intrinsic sympathomimetic activity such as metoprolol tartrate or bisoprolol<sup>[7]</sup>. Treatment with beta blockers should be started initially within 24 hours of symptoms. In patients with severe hypertension or ongoing ischemia, intravenous esmolol may be used<sup>[7]</sup>. In hemodynamically unstable patients or those with decompensated heart failure, administration of beta blockers should be delayed until the patient is stabilized<sup>[7]</sup>.

In patients with acute coronary syndromes with hypertension, nitrates can be used to reduce blood pressure or to reduce ongoing myocardial ischemia or pulmonary congestion<sup>[7]</sup>. However, nitrates should not be administered to patients with suspected right ventricular infarction or in those with hemodynamic instability. Intravenous or sublingual nitroglycerin is preferred initially<sup>[7]</sup>.

An angiotensin-converting ernzyme inhibitor or angiotensin receptor blocker should be given to patients with an acute coronary syndrome, especially in patients with an anterior myocardial infarction if hypertension persists, if there is an decreased left ventricular ejection fraction, or if diabetes mellitus is present<sup>[7]</sup>. If hypertension persists after use of a beta blocker plus an angiotensinconverting enzyme inhibitor or angiotensin receptor blocker, a longacting dihydropyridine calcium channel blocker may be added to the therapeutic regimen<sup>[7]</sup>. Aldosterone antagonists are indicated in patients receiving beta blockers plus angiotensin-converting enzyme inhibitors or angiotensin receptor blockers after myocardial infarction who have left ventricular systolic dysfunction and either heart failure or diabetes mellitus<sup>[7]</sup>. However, aldosterone antagonists should not be administered if the serum potassium is ≥5.0 mEq/L or if the serum creatinine is  $\geq 2.5 \text{ mg/dL}$  in men or  $\geq 2.0 \text{ mg/dL}$  in women<sup>[7]</sup>. Loop diuretics are preferred to thiazide and thiazide-type diuretics in

patients with heart failure or in patients with chronic kidney disease and an estimated glomerular filtration rate less than 30 mL/minute<sup>[7]</sup>.

#### CONFLICT OF INTERESTS

There are no conflicts of interest with regard to the present study.

#### REFERENCES

- Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, et al. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. The JNC 7 Report. JAMA 2003; 289:2560-2572.
- 2 Rosendorff C, Black HR, Cannon CP, Gersh BJ, Gore J, et al. Treatment of hypertension in the prevention and management of ischemic heart disease. A scientific statement from the American Heart Association Council for High Blood Pressure Research and the Councils on Clinical Cardiology and Epidemiology and Prevention. Circulation 2007; 115: 2761-2788
- 3 Aronow WS, Fleg JL, Pepine CJ, Artinian NT, Bakris G, et al. ACCF/AHA 2011 expert consensus document on hypertension in the elderly: a report of the American College of Cardiology Foundation Task Force on Clinical Expert Consensus Documents. J Am Coll Cardiol 2011; 57: 2037-2114
- 4 Mancia G, Fagard R, Narkiewicz K, Redon J, Zanchetti A, et al. 2013 ESH/ESC guidelines for the management of arterial hypertension: the Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). Eur Heart J 2013; 34: 2159-2219.
- Banach M, Bromfield S, Howard G, Howard VJ, Zanchetti A, Aronow WS, et al. Association of systolic blood pressure levels with cardiovascular events and all-cause mortality among older adults taking antihypertensive medication. Int J Cardiol 2014; 176: 219-22
- 6 Weber MA, Schiffrin EL White WB, Mann S, Lindholm LH, et al. Clinical practice guidelines for the management of hypertension in the community. A statement by the American Society of Hypertension and the International Society of Hypertension. 2014; 16: 14-26.
- 7 Rosendorff C, Lackland DT, Allison M, Aronow WS, Black HR, et al. AHA/ACC/ASH scientific statement. Treatment of hypertension in patients with coronary artery disease: a scientific statement from the American Heart Association, American College of Cardiology, and American Society of Hypertension. J Am Coll Cardiol 2015; 65:1998-2038.
- 8 Lloyd-Jones D, Adams R, Carnethon M, De Simone G, Ferguson TB, et al. Heart disease and stroke statistics-2009 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Circulation 2009; 119: e21-e181.
- 9 Bangalore S, Qin J, Sloan S, Murphy SA, Cannon CP, et al. What is the optimal blood pressure in patients after acute coronary syndromes? Relationship of blood pressure and cardiovascular events in the Pravastatin or Atorvastatin Evaluation and Infection Therapy-Thrombolysis in Myocardial Infarction (PROVE IT-TIMI) 22 trial. Circulation 2010; 122: 2142-2151.
- Bangalore S, Gong Y, Cooper-DeHoff RM, Pepine CJ, Messerli FH. 2014 Eighth Joint National Committee Panel recommendation for blood pressure targets revisited: results from the INVEST study. J Am Coll Cardiol 2014; 64: 784-793.
- 11 Law MR, Morris JK, Wald NJ. Use of BP lowering drugs in the prevention of cardiovascular disease: meta-analysis of 147 randomised trials in the context of expectations from prospective epidemiological studies. BMJ 2009; 338:b1665.doi.10.1136/bmj. b1665
- 12 Aronow WS. Might losartan reduce sudden cardiac death in diabetic patients with hypertension? Lancet 2003; 362: 591-592.

- 13 Carlberg B, Samuelson O, Lindholm LH. Atenolol in hypertension: is it a wise choice? Lancet 2004; 364: 1684-1689.
- 14 Aronow WS. Current role of beta blockers in the treatment of hypertension. Expert Opin Pharmacotherap 2001; 11:2599-2607.
- 15 Hansteen V. Beta blockade after myocardial infarction: The Norwegian Propranolol Study in high-risk patients. Circulation 1983; 67(suppl I):I-57-I-60.
- Hjalmarson A, Elmfeldt D, Herlitz J, Holmberg S, Malek I, et al. Effect on mortality of metoprolol in acute myocardial infarction. Lancet 1981; 2:823-827.
- 17 Gundersen T, Abrahamsen AM, Kjekshus J, Ronnevik PK. Timolol-related reduction in mortality and reinfarction in patients ages 65-75 years surviving acute myocardial infarction. Circulation 1982; 66:1179-1184.
- Pedersen TR for the Norwegian Multicentre Study Group. Sixyear follow-up of the Norwegian Multicentre Study on Timolol after acute myocardial infarction. N Engl J Med 1985; 313:1055-1058
- 19 Beta-Blocker Heart Attack Trial Research Group. A randomized trial of propranolol in patients with acute myocardial infarction. JAMA 1982; 247:1707-1714.
- 20 The CAPRICORN Investigators. Effect of carvedilol on outcome after myocardial infarction in patients with left-ventricular dysfunction: the CAPRICORN randomised trial. Lancet 2001; 357: 1385-1390.
- 21 Park KC, Forman DE, Wei JY. Utility of beta-blockade treatment for older postinfarction patients. J Am Geriatr Soc 1995; 43:751-755.
- 22 Chadda K, Goldstein S, Byington R, Curb JD. Effect of propranolol after acute myocardial infarction in patients with congestive heart failure. Circulation 1986; 73:503-510.
- 23 The Beta-Blocker Pooling Project Research Group. The Beta-Blocker Pooling Project (BBPP): subgroup findings from randomised trials in post-infarction patients. Eur Heart J 1988; 9:8-16.
- 24 HOPE (Heart Outcomes Prevention Evaluation) Study Investigators. Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. N Engl J Med 2000; 342:145-153.
- 25 Aronow WS, Ahn C, Kronzon I. Effect of beta blockers alone, of angiotensin-converting enzyme inhibitors alone, and of beta blockers plus angiotensin-converting enzyme inhibitors on new coronary events and on congestive heart failure in older persons with healed myocardial infarcts and asymptomatic left ventricular systolic dysfunction. Am J Cardiol 2001; 88:1298-1300.
- 26 Aronow WS, Ahn C. Incidence of new coronary events in older persons with prior myocardial infarction and systemic hypertension treated with beta blockers, angiotensin-converting enzyme inhibitors, diuretics, calcium antagonists, and alpha blockers. Am J Cardiol 2002; 89:1207-1209
- 27 Pitt B, White H, Nicolau J, Martinez F, Gheorghiade M, et al. Eplerenone reduces mortality 30 days after randomization following acute myocardial infarction in patients with left ventricular systolic dysfunction and heart failure. J Am Coll Cardiol 2005; 46:425-431.
- Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE Jr, et al. 2013 ACCF/AHA guidelines for the management of heart failure: executive summary. A report of the American College of Cardiology Foundation /American Heart Association Task Force on Practice Guidelines. Developed in collaboration with the American College of Chest Physicians, Heart Rhythm Society, and International Society for Heart and Lung Transplantation. Endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation. J Am Coll Cardiol 2013; 62:1495-1539.
- 29 Packer M, Bristow MR, Cohn JN, Colucci WS, Fowler MB, et al. The effect of carvedilol on morbidity and mortality in patients with chronic heart failure. N Engl J Med 1996; 334:1349-1355.
- 30 CIBIS-II Investigators and Committees. The Cardiac Insufficiency

- Bisoprolol Study II (CIBIS-II): a randomised trial. Lancet 1999; 353:9-13.
- 31 MERIT-HF Study Group. Effect of metoprolol CR/XL in chronic heart failure: Metoprolol CR/XL Randomised Intervention Trial in Congestive Heart Failure (MERIT-HF). Lancet 1999; 353:2001-2007
- 32 Packer M, Coats AJS, Fowler MB, Katus HA, Krum H, et al. Effect of carvedilol on survival in chronic heart failure. N Engl J Med 2001; 344:651-658.
- 33 Garg R, Yusuf S, for the Collaborative Group on ACE Inhibitor Trials. Overview of randomized trials of angiotensin-converting enzyme inhibitors on mortality and morbidity in patients with heart failure. JAMA 1995; 273:1450-1456.
- 34 Pfeffer MA, Braunwald E, Moye LA,Basta L, Brown EJ Jr, et al. Effect of captopril on mortality and morbidity in patients with left ventricular dysfunction after myocardial infarction. Results of the Survival and Ventricular Enlargement Trial. N Engl J Med 1992; 27:669-677.
- 35 The Acute Infarction Ramipril Efficacy (AIRE) Study Investigators. Effect of ramipril on mortality and morbidity of survivors of acute myocardial infarction with clinical evidence of heart failure. Lancet 1993; 342:821-828.
- 36 Ambrosioni E, Borghi C, Magnani B, for the Survival of Myocardial Infarction Long-Term Evaluation (SMILE) Study Investigators. The effect of the angiotensin-converting-enzyme inhibitor zofenopril on mortality and morbidity after anterior myocardial infarction. N Engl J Med 1995; 332:80-85.
- 37 Kober L, Torp-Pedersen C, Carlsen JE, Bagger H, eliasen P, et al. A clinical trial of the angiotensin-converting-enzyme inhibitor

- trandolapril in patients with left ventricular dysfunction after myocardial infarction. N Engl J Med 1995; 333:1670-1676.
- 38 The European trial on reduction of cardiac events with perindopril in stable coronary artery disease investigators. Efficacy of perindopril in reduction of cardiovascular events among patients with stable coronary artery disease: randomised, double-blind, placebocontrolled, multicentre trial (the EUROPA study). Lancet 2003; 362: 782-788.
- 39 Pfeffer MA, McMurray JJV, Velazquez EJ, Rouleau JL, Kober L, et al. Valsartan, captopril, or both in myocardial infarction complicated by heart failure, left ventricular dysfunction, or both. N Engl J Med 2003; 349:1893-1906.
- 40 Granger CB, McMurray JJV, Yusuf S, Held P, Michelson EL, et al. Effects of candesartan in patients with chronic heart failure and reduced left-ventricular systolic function intolerant to angiotensinconverting-enzyme inhibitors: the CHARM-Alternative trial. Lancet 2003; 362:772-776.
- 41 Pitt B, Zannad F, Remme WJ, Cody R, Castaigne A, et al. The effect of spironolactone on morbidity and mortality in patients with severe heart failure. N Engl J Med 1999; 341:709-717.
- 42 Taylor AL, Ziesche S, Yancy C, Carson P, D'Agostino R Jr, et al. Combination of isosorbide dinitrate and hydralazine in blacks with heart failure. N Engl J Med 2004; 351:2049-2057

**Peer reviewers:** Chi-Wen Cheng, Division of Cardiology, Department of Internal Medicine, Chang Gung Memorial Hospital, Keelung, Taiwan; Alexander E Berezin, Internal Medicine Department, State medical University, 26, Mayakovsky av., Zaporozhye, Ukraine.