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A HOPE FOR PEACE?

Update on the role of ACE inhibition in CAD patients

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- Role of angiotensin II in destabilization of atherosclerotic plaque.
- Activation of the renin-angiotensin-aldosterone system (RAAS) and its effect on fibrinolytic balance.
- Results of recent trials of angiotensin-converting enzyme inhibitors (ACEIs) in patients with stable coronary artery disease (CAD) and preserved left ventricular (LV) function.

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A HOPE FOR PEACE?

CORONARY ARTERY DISEASE (CAD) CONTINUES to be a major problem. In 2001, 1,680,000 survivors of acute coronary syndromes were discharged from the hospital.[1] With advances in interventional techniques, further thrombotic events in these patients are driven largely by disruption of plaques at sites other than the original culprit lesion.[2] Thus, while in-hospital management strategies focus on passivation of the culprit lesion, long-term management is designed to prevent disease progression at nonculprit lesions.

Implicit in long-term management is the role of angiotensin-converting enzyme inhibitors (ACEIs). Guidelines on the role of these agents (Table 1)[3,4] were driven largely by the results of two major trials—The Heart Outcomes Prevention Evaluation (HOPE)[5] and the EUropean trial on Reduction Of cardiac events with Perindopril in patients with stable coronary Artery disease (EUROPA).[6] These trials expand the benefit of ACEIs to CAD patients with preserved left ventricular (LV) function. A third trial of ACEIs in CAD patients, Prevention of Events with Angiotensin Converting Enzyme inhibition (PEACE),[7] has now been completed. The insight this trial provides on prevention of cardiovascular (CV) events with ACEIs is the subject of this monograph.

Table 1. ACC/AHA Recommendations on the Role of ACEIs in Post-MI Patients at Discharge[3,4]

UA/NSTEMI 1999*	STEMI 2004†
Class I	Class I
ACEIs for patients with CHF, LV dysfunction (EF <0.40), hypertension or diabetes. (Level of evidence: A)	An ACEI should be prescribed at discharge for all patients without contraindications after STEMI. (Level of evidence: A)

*Based on HOPE. †Based on HOPE and EUROPA.
NSTEMI = non–ST-elevation myocardial infarction;
STEMI = ST-elevation myocardial infarction; UA = unstable angina

UPDATE ON RAAS ACTIVATION AND ATHEROTHROMBOSIS

Modulation of plaque stability: Angiotensin II (Ang II) may modulate plaque stability through a number of mechanisms mediated through its AT_1 receptor.[8-11] Through its vasoconstrictive action, Ang II induces mechanical stress on the plaque's fibrous cap. By stimulating NAD(P)H oxidase to generate superoxide and other reactive oxygen species, Ang II also induces vascular oxidative stress. Adverse consequences of this

oxidative stress include:

- Impaired endothelium-dependent vasodilation (a result of nitric oxide [NO] scavenging by reactive oxygen species)
- Endothelial cell apoptosis
- Increase in oxidized lipoprotein content of plaque
- Increased monocyte recruitment by induction of mediators such as vascular cell adhesion molecule-1 (VCAM-1), intracellular adhesion molecule, and monocyte chemoattractant protein-1 (MCP-1)
- Increased vascular smooth muscle cell proliferation and migration
- Activation of inflammatory pathways such as nuclear factor-κB (NF-κB) and the Janus kinase/signal transducers and activators of transcription (JAK/STAT) cascade. The inflammatory cytokine interleukin-6 (IL-6) stimulates matrix metalloproteinases, a family of enzymes important in matrix regulation and which has been implicated in weakening of the fibrous cap.

Development of a prothrombotic environment: Oxidative scavenging of NO diminishes the ability of the endothelium to inhibit platelet adherence and aggregation.[11] Ang II also increases expression of plasminogen activator inhibitor-1 (PAI-1), which opposes the fibrinolytic activity of tissue plasminogen activator (tPA).[11] Decreased NO bioavailability may also contribute to altered fibrinolytic balance, since NO has been shown to suppress Ang II-stimulated PAI-1 release in vascular smooth muscle cells.[12]

UPDATE ON ANTIATHEROSCLEROTIC EFFECTS OF RAAS MANIPULATION

At least two enzymes, ACE (angiotensin-converting enzyme) and chymase, convert Ang I to Ang II. However, recent studies suggest that ACE is the predominant pathway,[13] a conclusion that is supported by observation of ACE, Ang II, and IL-6 in the shoulder region of atherosclerotic plaque, the main site of cap rupture.[14] ACE also converts bradykinin to inactive metabolites. Bradykinin exerts a number of vasoprotective effects through release of NO and tPA.[15]

The Study to Evaluate Carotid Ultrasound changes in patients treated with Ramipril and vitamin E (SECURE), a substudy of HOPE, demonstrated that patients treated with full-dose ramipril (10 mg) had significantly lower atherosclerosis progression rates than placebo patients.[16] A 2.5-mg dose had a smaller effect that did not reach statistical significance. The PERindopril–Thrombosis,

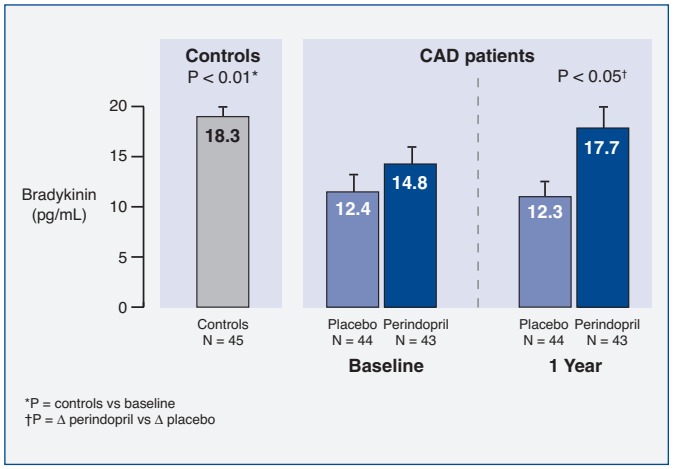

Figure 1. Increase in bradykinin levels with ACE inhibition. Bradykinin was measured by radioimmunoassay of serum from healthy volunteers or EUROPA patients at baseline and 1 year.[17]

INflammation, Endothelial dysfunction and Neurohormonal activation Trial (PERTINENT) was a substudy of EUROPA.[17] In this substudy, human umbilical-vein endothelial cells were incubated with serum from either healthy volunteers or EUROPA patients. Versus placebo, treatment with 8 mg perindopril was associated with increased expression and activity of endothelial NO synthase and decreased apoptosis. Increased serum bradykinin levels were also demonstrated (Figure 1). Thus, SECURE and PERTINENT show that the antiatherosclerotic effects of ramipril and perindopril are mediated through reduction in Ang II levels and increase in bradykinin levels in the vascular wall.

PEACE IN THE CONTEXT OF OTHER MAJOR ACEI TRIALS (HOPE, EUROPA, QUIET)

PEACE randomized 8290 patients with proven CAD and LV ejection fraction (LVEF) >40% to either trandolapril 4 mg or placebo.[7] Patients were followed for 4.8 years. The original primary outcome was CV death or nonfatal myocardial infarction (MI). To demonstrate a significant reduction in this outcome required 14,100 patients. However, recruitment was slow and after enrolling 1584 subjects, the investigators chose to expand the primary outcome to include coronary revascularization, thereby permitting a marked reduction in sample size.

HOPE randomized 9297 patients to either ramipril 10 mg or placebo for 4.5 years.[5] Inclusion criteria were LVEF ≥40%, CV disease, peripheral arterial disease, stroke, or diabetes plus at least one other CV risk factor. The primary outcome was combined CV death, MI, and stroke.

EUROPA randomized 12,218 patients with proven CAD and no clinical heart failure to perindopril 8 mg daily or placebo. Patients were followed for 4.2 years.[6] The primary outcome was combined CV death, MI, and cardiac arrest with successful resuscitation.

The Quinapril Ischemic Event Trial (QUIET) randomized 1750 patients with CAD and LVEF ≥40% to quinapril 20 mg or placebo.[18] Patients were followed for a mean of 27 months. The primary outcome was cardiac death, resuscitated cardiac arrest, nonfatal MI, coronary revascularization, or hospitalization for angina.

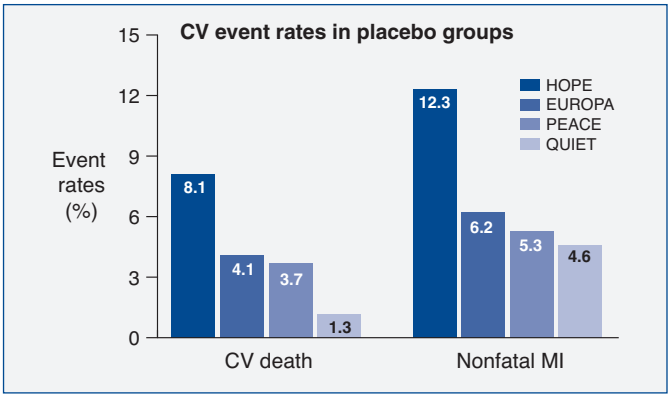

Figure 2. Differing levels of baseline risk. All four trials were conducted in at-risk patients, with some variation between the trials. As indicated by event rates in the placebo groups, HOPE participants were at higher global risk than EUROPA, PEACE, and QUIET participants.[5-7,18]

Differences in baseline risk of patients: Baseline blood pressure (BP) was lowest in QUIET compared with PEACE, HOPE, and EUROPA (123/74, 133/78, 139/79, and 137/82 mm Hg, respectively). PEACE, EUROPA, and QUIET enrolled significantly fewer patients with diabetes than HOPE (17%, 12%, 16%, and 39%, respectively).[5-7,18] Thus, baseline risk, indicated by CV event rates in placebo groups, was highest in HOPE participants, while PEACE, EUROPA, and QUIET participants had roughly similar risk levels (although QUIET patients had a very low risk for CV death) (Figure 2). However, the absolute risk in all four trials was high.

Treatment effects: In PEACE, at 3 years only 51% of the active-treatment group were taking the ACEI at the target dose of 4 mg, compared with 70.9% and 79% in HOPE and EUROPA, respectively.[5-7] BP reduction for active treatment versus placebo was 3/1 (PEACE), 3/2 (HOPE), and 5/2 mm Hg (EUROPA). HOPE and EUROPA demonstrated comparable reductions in the primary outcomes and in components of the primary outcome (Figure 3). The exceptions were stroke and cardiac arrest in EUROPA, the event rates of which were too low to permit any conclusions. The same trends were shown in the diabetic cohorts of HOPE and EUROPA as in the overall study populations (Table 2).[19,20]

Table 2. Benefit Demonstrated in Patients With and Without Diabetes

	Perindopril 8 mg		Ramipril 10 mg	
	EUROPA[6]	**PERSUADE**[20]	**HOPE**[5]	**MICRO-HOPE**[19]
Patients with:	CAD	Diabetes + CAD	High risk of CV events	Diabetes + ≥1 risk factor
RRR (%)				
Primary*	20	19	22	25
MI	24	23	20	22
CV death	14	NR	26	37

*EUROPA (combined CV death, MI, and cardiac arrest with successful resuscitation); HOPE (combined CV death, MI, and stroke). NR = not reported; RRR = relative risk reduction

PEACE did not demonstrate a significant effect on primary or secondary outcomes (Table 3).[7] However, the confidence intervals for the hazard ratios overlapped with those of HOPE and EUROPA, and pooled analysis of the data from these three trials demonstrated significant relative risk reductions in all-cause death, MI, stroke, and coronary revascularization.[21]

QUIET also did not demonstrate a significant treatment effect, although incidence rates of all-cause death and MI were directionally similar to those in the other trials. When the QUIET data were pooled with those of HOPE, EUROPA, and PEACE, the risk reductions in all-cause death, MI, stroke, and revascularization remained significant (Figure 4).

Questions raised by the apparent neutral effect in PEACE

Were PEACE subjects more aggressively treated at baseline? No. The percentages of ACEI patients receiving lipid-lowering therapy at baseline were 58% (EUROPA) and 70% (PEACE). Further, at 3 years 69% of EUROPA subjects were receiving lipid-lowering therapy. Thus, utilization of lipid-lowering therapy did not differ

Table 3. Treatment Effect of Trandolapril 4 mg in PEACE[7]

Outcome	Event rates (%)		Hazard ratio (95% CI)
	Trandolapril	Placebo	
Primary*	21.9	22.5	0.96 (0.88–1.06)
CV death	3.5	3.7	0.95 (0.76–1.19)
Nonfatal MI	5.3	5.3	1.00 (0.83–1.20)
CABG	6.5	7.1	0.91 (0.77–1.07)
PCI	12.4	12.0	1.03 (0.91–1.16)
All-cause death	7.2	8.1	0.89 (0.67–1.03)
Non-CV death	3.7	4.4	0.83 (0.67–1.03)

*CV death, nonfatal MI, and coronary revascularization

markedly in EUROPA and PEACE, trials that enrolled patients with comparable risk profiles. Use of other CV medications also did not differ markedly between the two trials. On the other hand, a lower proportion of patients in PEACE were taking the full dose of study medication than in EUROPA.

Was the dose sufficient? The overall poor adherence, with only 51% taking trandolopril 4 mg at 3 years, suggests that the ACEI arm was undertreated. In addition, the Trandolapril Cardiac Evaluation (TRACE) trial was used to select the 4-mg dose used in PEACE.[22] TRACE was conducted in 1749 post-MI patients with LVEF ≤35%. Risk of all-cause death was reduced significantly by 25% (P = 0.001). Risk of MI was not significantly reduced (14% relative risk reduction, P = 0.29). In addition, when subjects were stratified according to LVEF, the risk reduction remained significant in those with LVEF 25% to 30%, but not in those with LVEF >30%. This finding suggests an attenuation in clinical benefit with the 4-mg dose at lesser degrees of LV dysfunction.

Data from HOPE showing dose-dependent effects of ramipril on atherosclerosis progression and on LV structure and function[16,23] also suggest that a higher trandolapril dose might have provided additional direct vascular and protective myocardial effects.

Did revascularization confound the results? The relative subjectivity involved in the decision to proceed to revascularization may have led to significant background noise that had the potential to mask treatment effects. An insufficient dose of quinapril and inclusion of outcomes such as revascularization and hospitalization for angina were discussed as possible limitations of QUIET.[18] In addition, all patients in QUIET and 72% of patients in PEACE had undergone successful coronary angioplasty with or without stents.[7,18]

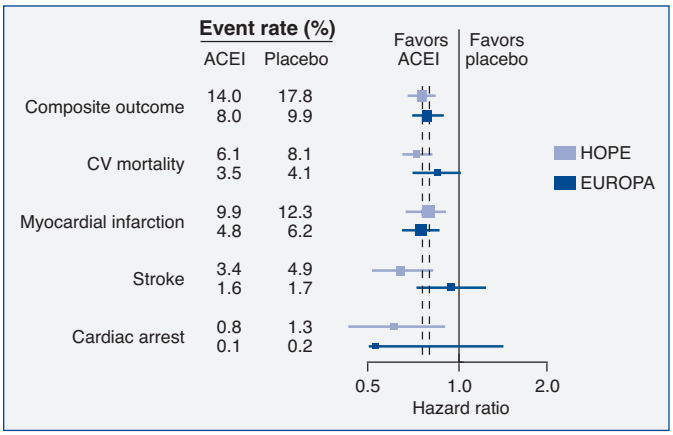

Figure 3. Consistency of benefit in HOPE and EUROPA.[5,6]

Are all ACEIs alike? A German observational study reported lower in-hospital mortality with ramipril compared with other ACEIs in patients admitted with ST-elevation MI.[24] Finally, a study of hospital discharge records in Canada found that ramipril and perindopril were associated with lower 1-year mortality than captopril, fosinopril, and quinapril, but were not significantly different from lisinopril.[25]

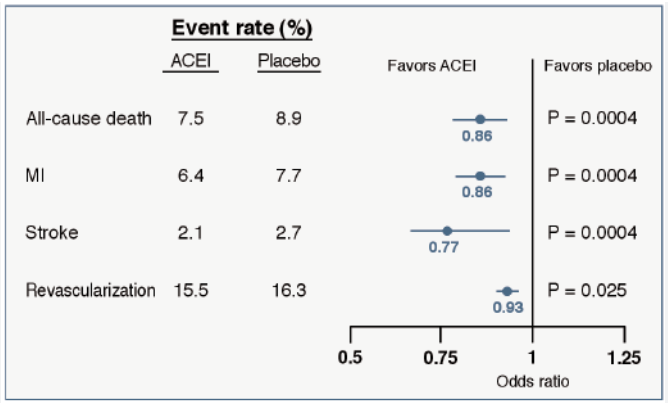

Figure 4. HOPE, EUROPA, PEACE, QUIET. Pooled results demonstrate overall benefit of ACEIs in CAD patients.

The dosage of either trandolapril or quinapril needed to provide vascular protection cannot be concluded from the PEACE or QUIET results.

Conclusions and clinical implications

Clinical data support the use of ACEIs along with aggressive lipid-lowering and antiplatelet therapy in a broad range of post-MI patients following hospital discharge. The absolute benefit achieved depends on baseline risk. Further, not all ACEIs can be assumed to have comparable effects on survival.

HOPE demonstrated benefit with ramipril in a broad range of patients with vascular disease and preserved LV function who are at high risk of CV events. EUROPA extended this finding to include perindopril and a population of CAD patients at lower relative risk. PEACE and QUIET, smaller trials than HOPE or EUROPA, were not powered to provide evidence of risk reduction in hard outcomes such as CV death or MI. Pooled analysis of the four trials provides clear evidence of benefit with ACE inhibition. However, the dosage of either trandolapril or quinapril needed to provide vascular protection cannot be concluded from the PEACE or QUIET results. Selection of an ACEI and the dose should be based on clinical judgment in conjunction with data from clinical outcomes trials.

References

1. American Heart Association. *Heart Disease and Stroke Statistics–2004 Update.* Dallas, Tex: American Heart Association; 2003.
2. Cutlip DE, Chhabra AG, Baim DS, Chauhan MS, Marulkar S, Massaro J, et al. Beyond restenosis: Five-year clinical outcomes from second-generation coronary stent trials. *Circulation.* 2004;110:1226-1230.
3. Braunwald E, Antman EM, Beasley JW, Califf RM, Cheitlin MD, Hochman JS, et al. ACC/AHA 2002 guideline update for the management of patients with unstable angina and non-ST-segment elevation myocardial infarction: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on the Management of Patients With Unstable Angina.). 2002. Available at: http://www.acc.org/clinical/guidelines/unstable/unstable.pdf.
4. Antman EM, Anbe DT, Armstrong PW, Bates ER, Green LA, Hand M, et al. ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction–executive summary: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to revise the 1999 guidelines for the management of patients with acute myocardial infarction). *J Am Coll Cardiol.* 2004;44:671-719.
5. The 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.
6. Fox KM. 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, placebo-controlled, multicentre trial (the EUROPA study). *Lancet.* 2003;362:782-788.
7. PEACE Trial Investigators. Angiotensin-converting-enzyme inhibition in stable coronary artery disease. *N Engl J Med.* 2004;351:2058-2068.
8. Schieffer B. Interaction of interleukin-6 and angiotensin II in atherosclerosis: Culprit for inflammation? *Eur Heart J.* 2003;5(suppl A):A25-A30.
9. Taniyama Y, Griendling KK. Reactive oxygen species in the vasculature: Molecular and cellular mechanisms. *Hypertension.* 2003;42:1075-1081.
10. Brasier AR, Recinos A III, Eledrisi MS. Vascular inflammation and the renin-angiotensin system. *Arterioscler Thromb Vasc Biol.* 2002;22:1257-1266.
11. Jacoby DS, Rader DJ. Renin-angiotensin system and atherothrombotic disease: From genes to treatment. *Arch Intern Med.* 2003;163:1155-1164.
12. Bouchie JL, Hansen H, Feener EP. Natriuretic factors and nitric oxide suppress plasminogen activator inhibitor-1 expression in vascular smooth muscle cells: Role of cGMP in the regulation of the plasminogen system. *Arterioscler Thromb Vasc Biol.* 1998;18:1771-1779.
13. Campbell DJ, Alexiou T, Xiao HD, Fuchs S, McKinley MJ, Corvol P, Bernstein KE. Effect of reduced angiotensin-converting enzyme gene expression and angiotensin-converting enzyme inhibition on angiotensin and bradykinin peptide levels in mice. *Hypertension.* 2004;43:854-859.
14. Schieffer B, Schieffer E, Hilfiker-Kleiner D, Hilfiker A, Kovanen PT, Kaartinen M, et al. Expression of angiotensin II and interleukin 6 in human coronary atherosclerotic plaques: Potential implications for inflammation and plaque instability. *Circulation.* 2003;101:1372-1378.
15. Linz W, Wohlfart P, Schölkens BA, Malinski T, Wiemer G. Interactions among ACE, kinins and NO. *Cardiovasc Res.* 1999;43:549-561.
16. Lonn E, Yusuf S, Dzavik V, Doris C, Yi Q, Smith S, Moore-Cox A, Bosch J, Riley W, Teo KK, for the SECURE Investigators. Effects of ramipril and vitamin E on atherosclerosis: The study to evaluate carotid ultrasound changes in patients treated with ramipril and vitamin E (SECURE). *Circulation.* 2001;103:919-925.
17. Ferrari R. PERTINENT—PERindopril – Thrombosis, Inflammation, Endothelial dysfunction and neurohormonal activation Trial, a subanalysis of EUROPA. Presented at European Society of Cardiology Congress 2004; August 31, 2004; Munich, Germany. Available at: www.europa-trial.org.
18. Pitt B, O'Neill B, Feldman R, Ferrari R, Schwartz L, Mudra H, et al, for the QUIET Study Group. The Quinapril Ischemic Event Trial (QUIET): Evaluation of chronic ACE inhibitor therapy in patients with ischemic heart disease and preserved left ventricular function. *Am J Cardiol.* 2001;87:1058-1063.
19. Heart Outcomes Prevention Evaluation (HOPE) Study Investigators. Effects of ramipril and microvascular outcomes in people with diabetes mellitus: Results of the HOPE study and MICRO-HOPE substudy. *Lancet.* 2000;355:253-259.
20. Fox KM. Cardiovascular morbidity and mortality in patients with diabetes in the EUROPA study: Results from the PERSUADE substudy. Presented at: 53rd Annual Scientific Session 2004; American College of Cardiology; March 7-10, 2004; New Orleans, La. Available at: www.europa-trial.org.
21. Yusuf S. The HOPE trial. Presented at: ACE inhibition in patients with stable coronary artery disease: Results of the trio of trials. Held in conjunction with AHA Scientific Sessions. November 9, 2004; New Orleans, La.
22. Køber L, Torp-Pedersen C, Carlsen JE, Bagger H, Eliasen P, Lyngborg K, et al, for the Trandolapril Cardiac Evaluation (TRACE) Study Group. 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.
23. Lonn E, Shaikholeslami R, Yi Q, Bosch J, Sullivan B, Tanser P, et al. Effects of ramipril on left ventricular mass and function in cardiovascular patients with controlled blood pressure and with preserved left ventricular ejection fraction: A substudy of the Heart Outcomes Prevention Evaluation (HOPE) trial. *J Am Coll Cardiol.* 2004;43(12):2200-2206.
24. Wienbergen H, Schiele R, Gitt AK, Juenger C, Heer T, Meisenzahl C, et al, for the MITRA PLUS Study Group. Impact of ramipril versus other angiotensin-converting enzyme inhibitors on outcome of unselected patients with ST-elevation acute myocardial infarction. *Am J Cardiol.* 2002;90:1045-1049.
25. Pilote L, Abrahamowicz M, Rodrigues E, Eisenberg MJ, Rahme E. Mortality rates in elderly patients who take different angiotensin-converting enzyme inhibitors after acute myocardial infarction: A class effect? *Ann Intern Med.* 2004;141:102-112.

Self-Assessment Questions

Please check the appropriate answer for each question on the Answer Key.
Instructions for obtaining CME credit are provided on the back of the Answer Key.

1. Increased serum bradykinin levels with ACE inhibitor treatment was directly demonstrated by a substudy of which trial?
   a. HOPE b. EUROPA c. PEACE

2. Increased expression and activity of endothelial NO synthase with ACEI treatment was demonstrated by a substudy of which trial?
   a. HOPE b. EUROPA c. PEACE

3. Which trials achieved a difference of at least 3 mm Hg in systolic BP between the placebo and ACE inhibitor groups?
   a. HOPE, EUROPA b. HOPE, PEACE c. EUROPA, PEACE d. All three

4. The PEACE results suggest that ACEI doses for vascular protection can be extrapolated from data obtained in heart failure patients.
   a. True b. False

5. The PEACE results may not support a class effect for ACEIs in CAD patients.
   a. True b. False

A HOPE FOR PEACE?

Update on the role of ACE inhibition in CAD patients

Answer Key

Please check the correct box for each question. There is only 1 correct response for each question.

1. [A] [B] [C]
2. [A] [B] [C]
3. [A] [B] [C] [D]
4. [A] [B]
5. [A] [B]

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