Antihypertensive Therapy Does Not Decrease the Risk of SCD in Patients With Hypertension

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Reducing blood pressure with antihypertensive therapy is associated with significant reductions in the risk for stroke and myocardial infarction (MI), but its impact on sudden cardiac death (SCD) remains unknown. In fact, recent studies suggest that treatment of hypertension may not lead to reductions in SCD. Pierre-Henri Gacon, MD, University Hospital of Dijon, Dijon, France, presented 2 analyses reviewing some of the risk factors associated with SCD in patients with hypertension.

Prof. Gacon first discussed the results of 5 randomized controlled trials that included > 16,000 patients with hypertension. The trials all assessed the effect of antihypertensive treatment on the occurrence of cardiovascular end points, including SCD. His analysis evaluated several covariates as risk factors for SCD using logistic regression, adjusting for trial and treatment group. The risk model was based on two-thirds of the patients and converted to a risk score that was validated on the remaining one-third of the patients. SCD was defined as an unexplained death occurring within 24 hours after symptom onset for 4 studies (the Multiple Risk Factor Intervention Trial [MRFIT], Coope et al., the Systolic Hypertension in Europe trial, and the European Working Party on High Blood Pressure in the Elderly trial) and within 1 hour after symptom onset for 1 study (the Swedish Trial in Old Patients With Hypertension). The 5 studies are outlined in Table 1.

According to Prof. Gacon's analyses, the risks for SCD in the other studies are outlined in Table 2.

On the basis of a multivariate analysis of the reviewed randomized trials, the risk for SCD was significantly associated with age, male gender, smoking, systolic blood pressure, and total cholesterol level (Table 3).

Prof. Gacon also analyzed 17 additional trials that included ~ 45,000 patients, comparing antihypertensive therapy with placebo, no treatment, or less intensive treatment on the risk for SCD. The mean duration of follow-up was 1.5 to 8.4 years. Major coronary events in the control group included nonfatal MI (46%), fatal MI (24%), and SCD (30%). Significantly lower rates in the treatment versus control group were found for fatal MI (relative risk [RR], .67; 95% CI, .54 to .82; $p < .001$) and nonfatal MI (RR, .80; 95% CI, .70 to .92; $p = .002$) but not for SCD (RR, 1.02; 95% CI, .86 to 1.21; $p = .80$) (Figure 1).

Prof. Gacon also discussed the MRFIT post hoc study comparing special intervention (SI) with usual care. In the post hoc analysis, the men in the SI group received

Table 1. Trials Included in Review of Sudden Cardiac Death in Hypertensive Patients

Study/Design	Population/Intervention	Key End Point(s)	Outcomes/Results
MRFIT [*JAMA* 1982]; randomized primary prevention trial	12,866 high-risk men aged 35–57 years; randomly assigned to SI vs UC; average follow-up, 7 y	Mortality from CHD	CHD mortality, 17.9/1000 with SI vs 19.3/1000 with UC, nonsignificant difference of 7.1% (90% CI, –15% to 25%)
Coope J, Warrender TS. *Br Med J (Clin Res Ed)* 1986; randomized treatment trial	884 men aged 60–79 years; randomly assigned to antihypertensive drugs or placebo; average follow-up, 4.4 years	Difference in CV outcomes between treatment groups	30% reduction in stroke mortality with treatment ($p < .025$); 42% reduction in stroke incidence with treatment ($p < .03$); no significance between group reductions in incidence of MI and total mortality
Syst-Eur 1 [Stassen JA et al. *Am J Cardiol* 1998]; randomized treatment trial	4695 patients aged > 60 years with isolated systolic hypertension; randomly assigned to antihypertensive drugs or placebo; average follow-up, 6.3 years	Difference in CV outcomes between treatment groups	Compared with placebo, active treatment reduced mortality, 24% ($p = .05$); fatal and nonfatal CV end points, 32% ($p < .001$); strokes, 44% ($p = .004$); nonfatal strokes, 48% ($p = .005$); and all cardiac end points, 26% ($p = .05$)
EWPHE [Amery A et al. *Clin Exp Hypertens A* 1982; Amery A et al. *Lancet* 1985]; randomized treatment trial	840 patients with hypertension aged > 60 years with isolated systemic hypertension; randomly assigned to antihypertensive drugs or placebo; average follow-up, 4.3 years	Difference in CV outcomes between treatment groups	ITT analysis: no significant difference in TMR between treatment groups; compared with placebo, active treatment reduced CV mortality (–27%, $p = .037$) due to reductions in cardiac mortality (–38%, $p = .036$) and cerebrovascular mortality (–32%, $p = .16$)
STOP-Hypertension [Dahlof B et al. *Lancet* 1991]; prospective randomized treatment trial	1627 patients with hypertension aged 70–84 years; randomly assigned to antihypertensive drugs or placebo; average follow-up, 25 months	Difference in CV outcomes between treatment groups	Compared with placebo, active treatment significantly reduced MACEs ($p = .0031$) and stroke morbidity and mortality (53 vs 29, $p = .008$)

CHD=coronary heart disease; CV=cardiovascular; EWPHE=European Working Party on High Blood Pressure in the Elderly; ITT=intention-to-treat; MACE=major adverse cardiac event; MI=myocardial infarction; MRFIT=Multiple Risk Factor Intervention Trial; SI=special intervention; STOP-Hypertension=Swedish Trial in Old Patients With Hypertension; Syst-Eur 1=Systolic Hypertension in Europe; TMR=total mortality rate; UC=usual care.

Table 2. Risk for Sudden Cardiac Death in Additional Study Analyses

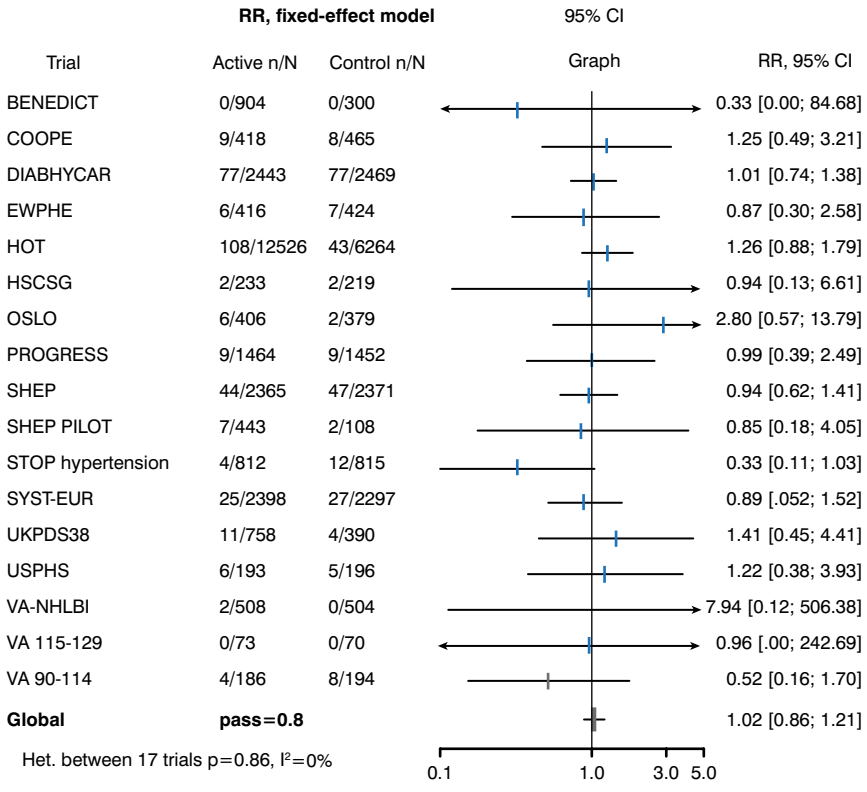
Study	RR (95% CI)
Coope et al.	1.25 (.49 to 3.21), p < .06
Syst-Eur 1	.89 (.52 to 1.52), p < .005
EWPHE	.87 (.30 to 2.58), p < .04
STOP-Hypertension	.33 (.11 to 1.03), p < .03

EWPHE=European Working Party on High Blood Pressure in the Elderly; RR=relative risk; STOP-Hypertension=Swedish Trial in Old Patients With Hypertension; Syst-Eur 1=Systolic Hypertension in Europe.

Table 3. Risk Factors Associated With Sudden Cardiac Death in Multivariate Analysis

Covariates	Odds Ratio (95% CI)	p Value
Age (10 years)	1.95 (1.87–2.03)	.001
Male gender	4.16 (1.45–11.89)	.007
Smoking	1.91 (1.21–3.00)	.005
Systolic blood pressure (mm Hg)	1.14 (1.13–1.16)	.035
Total cholesterol level	1.36 (1.11–1.67)	.002

Figure 1. Sudden Cardiac Death Analysis



Het.=global sudden death relative risk.

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stepped-care treatment for hypertension and cigarette smoking and dietary advice for lowering blood cholesterol levels. SCD occurred in 73 men in the special intervention group and 81 men in the usual care group (HR, .90; 95% CI, .66 to 1.24; p=.52) [Stamler J et al. *J Am Heart Assoc* 2012]. The results of the 20-year analysis demonstrated that men in the SI group had significant reductions in coronary heart disease (CHD) and cardiovascular disease (CVD) outcomes. These findings support recommendations for improved dietary and other lifestyle practices to prevent and control established major CHD and CVD risk factors.

Prof. Gacon concluded that although blood pressure–lowering drugs have been shown to reduce the risk for stroke and MI, they have not been shown to decrease the risk for SCD in patients with hypertension.