

Tight Versus Standard Blood Pressure Control in Patients With Hypertension With and Without Cardiovascular Disease

Gianpaolo Reboldi, Fabio Angeli, Giovanni de Simone, Jan A. Staessen, Paolo Verdecchia;
on behalf of the Cardio-Sis Investigators

Abstract—An excessive blood pressure (BP) reduction might be dangerous in high-risk patients with cardiovascular disease. In the Studio Italiano Sugli Effetti CARDIOvascolari del Controllo della Pressione Arteriosa SISTolica (Cardio-Sis), 1111 nondiabetic patients with systolic BP ≥ 150 mmHg were randomly assigned to a systolic BP target <140 mmHg (standard control) or <130 mmHg (tight control). We stratified patients by absence ($n=895$) or presence ($n=216$) of established cardiovascular disease at entry. Antihypertensive treatment was open-label and tailored to each patient's needs. After 2-year follow-up, the primary end point of the study, electrocardiographic left ventricular hypertrophy, occurred less frequently in the tight than in the standard control group in the patients without (10.8% versus 15.2%) and with (14.1% versus 23.5%) established cardiovascular disease (P for interaction=0.82). The main secondary end point, a composite of cardiovascular events and all-cause death, occurred less frequently in the tight than in the standard control group both in patients without (1.47 versus 3.68 patient-years; $P=0.016$) and with (7.87 versus 11.22 patient-years; $P=0.049$) previous cardiovascular disease. In a multivariable Cox model, allocation to tight BP control reduced the risk of cardiovascular events to a similar extent in patients with or without overt cardiovascular disease at randomization (P for interaction=0.43). In conclusion, an intensive treatment aimed to lower systolic BP <130 mmHg reduced left ventricular hypertrophy and improved clinical outcomes to a similar extent in patients with hypertension and without established cardiovascular disease. (*Hypertension*. 2014;63:475-482.)

Key Words: hypertension ■ hypertrophy, left ventricular ■ myocardial infarction ■ prognosis
■ randomized controlled trial ■ stroke

Despite the epidemiological evidence of a linear relation between the risk of cardiovascular disease and blood pressure (BP),¹ and the evidence from intervention trials that the reduction in systolic BP accounts for most of treatment benefit,^{2,3} the application of the view that lower BP is better has been disputed in high-risk individuals.^{4,5} After the observations by Anderson,⁶ Stewart⁷ and Cruickshank,⁸ several studies suggested that in the presence of established coronary artery disease (CAD), excessively low levels of achieved BP might be harmful.^{9,10} According to a meta-analysis, achieved systolic and diastolic BP did not show any J-shaped association with the risk of stroke, whereas diastolic BP showed a J-shaped association with the risk of cardiac events.¹¹ Unfortunately, only a limited number of randomized studies provided a direct head-to-head comparison between different BP targets,¹²⁻¹⁷ and it is not clear whether the results of these studies are applicable to subjects with and without previous cardiovascular disease or CAD.

In view of this uncertainty, the present post hoc analysis of the Studio Italiano Sugli Effetti CARDIOvascolari del

Controllo della Pressione Arteriosa SISTolica (Cardio-Sis)¹⁸ was aimed to test the hypothesis that a tight (<130 mmHg) compared with a standard control (<140 mmHg) of systolic BP might result in a different benefit depending on the absence or presence of overt cardiovascular disease at randomization. We could not address CAD because of the small size of the subset with CAD at baseline.

Methods

The Cardio-Sis study (ClinicalTrials.gov identifier: NCT00421863)¹⁹ is a multicenter trial endorsed by the Italian Association of Hospital Cardiologists (ANMCO) to assess the prognostic value of tight (<130 mmHg) compared with standard control (<140 mmHg) of systolic BP in nondiabetic patients with hypertension. Details of the study have been published.^{18,19} We enrolled treated patients aged ≥ 55 years with systolic BP ≥ 150 mmHg. Eligible patients were required to have ≥ 1 additional risk factor: family history of premature cardiovascular disease in a first degree relative (<65 years in women and <55 years in men), previous transient ischemic attack (TIA) or stroke, or established coronary or peripheral arterial disease. We excluded patients with diabetes mellitus (fasting glucose of ≥ 7.0 mmol/L (126 mg/dL)

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From the Dipartimento di Medicina Interna (G.R.) and Struttura Complessa di Fisiopatologia Cardiovascolare (F.A.), Università di Perugia, Italy; The Hypertension Center, Department of Translational Medical Sciences, Federico II University Hospital, Naples, Italy (G.d.S.); Studies Coordinating Centre, Research Unit Hypertension and Cardiovascular Epidemiology, KU Leuven, Department of Cardiovascular Science, University of Leuven, Belgium, and Department of Epidemiology, Maastricht University, Maastricht, The Netherlands (J.A.S.); and the Department of Medicine, Hospital of Assisi, Italy (P.V.).

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Correspondence to Paolo Verdecchia, Hospital of Assisi, Department of Medicine, Via Valentin Müller, 1. 06081 – Assisi, Italy. E-mail verdec@tin.it

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or history of diabetes mellitus) because a systolic BP target <130 mm Hg was deemed ethical in all these patients at the time when the study was planned.

We excluded patients with any disease reducing life expectancy, renal dysfunction (serum creatinine of ≥ 176.8 mmol/L), clinical relevant hepatic or hematologic disorders, valvular heart disease, congestive heart failure, conditions impairing the ECG diagnosis of left ventricular (LV) hypertrophy (complete right or left bundle block, Wolff–Parkinson–White syndrome, previous Q-wave myocardial infarction, and paced heart rhythm), atrial fibrillation, and substance abuse.

Eligible patients entered a run-in period to ascertain that systolic BP under current antihypertensive drug treatment was ≥ 150 mm Hg at 2 visits, 7 to 14 days apart. Using a computerized random function and stratification by center, patients were randomly allocated in a one-to-one ratio to tight (<130 mm Hg) or standard control (<140 mm Hg) of systolic BP.

The primary study outcome was the prevalence of electrocardiographic LV hypertrophy at the final 2-year visit. Diagnosis of LV hypertrophy^{20,21} required ≥ 1 of 3 criteria: (1) modified Cornell voltage ($SV_3+RaVL > 2.0$ mV in women and > 2.4 mV in men); (2) LV strain (inverted asymmetrical T wave with flat or down-sloping ST-segment and ≥ 0.05 mV depression 80 ms after the J point); (3) or a Romhilt-Estes score ≥ 5 .²² The main prespecified secondary outcome was a composite of all-cause mortality, nonfatal myocardial infarction, nonfatal stroke, TIA, congestive heart failure New York Heart Association stages III or IV requiring hospitalization, angina pectoris with objective evidence of myocardial ischemia, new-onset atrial fibrillation, coronary revascularization, aortic dissection, occlusive peripheral arterial disease, and renal failure requiring dialysis.^{18,19}

After randomization, patients were followed up at 4-month intervals for 2 years. BP was measured at each visit, and an ECG and blood tests were obtained at the second run-in visit and at 1 and 2 years.

Antihypertensive treatment was open-label and tailored to each patient's needs. Antihypertensive drug treatment included various combinations of previous drugs (background therapy) plus drugs made available for the purpose of the study.^{18,19}

Cardio-Sis was performed at 44 centers (see Appendix). An independent end point Committee, unaware of randomization, adjudicated all incident clinical events according to published diagnostic criteria on the basis of the records provided by the clinical investigators (see Appendix). Blinded experts, unaware of the randomization group, read all electrocardiograms in a central facility.

Subgroups of Vascular Risk

For the purpose of the present study, patients randomized to the standard or tight systolic BP control were subdivided according to the

absence or presence of established clinical cardiovascular disease at entry. Thus, we defined 4 subsets of patients:

1. Patients without established cardiovascular disease at entry randomized to standard BP control;
2. Patients without established cardiovascular disease at entry randomized to tight BP control;
3. Patients with established cardiovascular disease at entry randomized to standard BP control;
4. Patients with established cardiovascular disease at entry randomized to tight BP control.

Established cardiovascular disease at entry included stroke, TIA, and coronary and peripheral arterial disease. Established CAD was defined by previous evidence of myocardial infarction or myocardial ischemia (defined by ECG, stress-echocardiography or scintigraphy, or an angiographic stenosis $\geq 50\%$ in ≥ 2 major epicardial vessels, or previous aortocoronary bypass or percutaneous coronary angioplasty). History of peripheral occlusive arterial disease was defined by claudicatio intermittens associated with angiographic or echographic evidence of a stenosis of $\geq 60\%$. Stroke was an acute focal neurological deficit thought to be of vascular origin with signs or symptoms lasting for ≥ 24 hours. TIA was defined as a brief episode of neurological dysfunction (<24 hours) resulting from focal temporary cerebral ischemia not associated with cerebral infarction.

Statistical Analysis

Statistical analysis was performed using the SAS package, version 9.3 (SAS Institute, Cary, NC). Analysis was by intention-to-treat on all available data. We compared means and proportions by the standard normal Z test and χ^2 analysis, respectively. For the primary binary outcome, we used general estimating equations as implemented in the PROC GENMOD procedure of the SAS package, with patients modeled as a random effect, including treatment arm and established cardiovascular disease as main factors, their interaction term, and with age and LV hypertrophy at baseline as covariables. We analyzed changes in continuous outcomes by mixed linear models (PROC MIXED of the SAS package) including baseline values as a covariable. We also assessed the incidence of events, using Kaplan–Meier survival function estimates, the log-rank test, and Cox regression analysis. Multivariable models included age, treatment arm, and history of cardiovascular disease as main factors along with their interaction term. Adjustment for systolic BP was accomplished by entering BP values throughout the study as a time-varying covariate, whereas age entered the model as a time-fixed covariate. In these analyses, we considered only the first event for

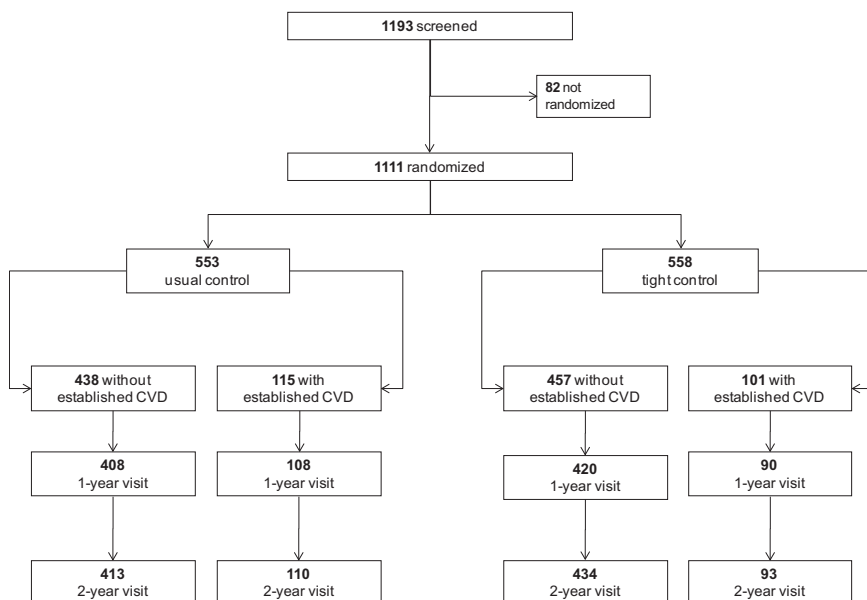


Figure 1. Flowchart of the study. CVD indicates cardiovascular disease.

Table 1. Main Characteristics of Patients With and Without Established Cardiovascular Disease at Entry

Characteristics	Without Established Cardiovascular Disease (n=895)		P Value	With Established Cardiovascular Disease (n=216)		P Value
	Standard BP control (n=438)	Tight BP control (n=457)		Standard BP control (n=115)	Tight BP control (n=101)	
Age, y	66 (7.3)	66 (6.8)	0.46	69.8 (7.1)	71.7 (7.6)	0.07
Women, %	62.3	60.1	0.42	42.6	53.4	0.11
Current smokers, %	23.7	23.4	0.91	6.9	6.9	0.99
LVH at ECG, %	20.0	19.6	0.86	23.5	29.3	0.33
BMI, Kg/m ²	27.9 (4.1)	28.0 (4.1)	0.58	27.4 (3.4)	27.2 (5.0)	0.78
Waist circumference, cm	98.3 (12)	98.8 (12)	0.56	99.1 (11)	97.5 (12)	0.31
Systolic BP, mm Hg	158.4 (8)	157.8 (8)	0.31	159.4 (10)	158.2 (9)	0.37
Diastolic BP, mm Hg	87.9 (7)	87.6 (8)	0.46	85.5 (9)	84.3 (9)	0.34
Heart rate, beats/min	69.4 (10)	70.2 (10)	0.19	66.7 (10)	68.6 (9)	0.14

BMI indicates body mass index; BP, blood pressure; ECG, electrocardiography; and LVH, left ventricular hypertrophy.

each outcome. In 2-side tests, *P* values <0.05 were considered statistically significant.

Results

Figure 1 shows the flow chart of the study. Of 1193 patients screened, 1111 were randomized to standard (n=553) or tight (n=558) control of systolic BP. The proportion of patients with and without established cardiovascular disease at entry was similar in the 2 groups (*P*=0.26). Patients with established CAD at baseline were 69 (13%) in the usual BP control group and 59 (11%) in the tight BP control group. Table 1 shows the main clinical characteristics of the 4 groups. Among the patients with and without established cardiovascular disease at entry, none of the main clinical characteristics showed statistically significant differences between the randomized groups (*P*≥0.05).

BP Reduction

Tables 2 and 3 show the BP time course during the study. Systolic BP decreased to a greater extent in the patients randomized to tight BP control than in the other group (*F*=22.9; *P*<0.0001). In each randomized group, BP levels did not differ significantly (*F*=3.01; *P*=0.08) between patients with and without established cardiovascular disease at entry (*F* for interaction=0.29; *P*=0.59). Diastolic BP decreased to a greater extent in the group randomized to tight BP control than in the other group (*F*=6.72; *P*=0.0096), and in the patients with than in those without established cardiovascular disease at entry (*F*=27.0; *P*<0.0001). The interaction term was not significant (*F*=0.02; *P*=0.87). The proportion of patients with systolic BP <130 mmHg at the final visit was 52.9% and 53.8%, respectively, in the subsets with and without previous cardiovascular disease assigned to the tight control group ($\chi^2=0.02$; *P*=0.89), and 35.1% and 33.0%, respectively, in the subsets with and without previous cardiovascular disease assigned to the standard control group ($\chi^2=0.17$; *P*=0.687).

Prevalence of LV Hypertrophy

The primary end point of the study, LV hypertrophy at 2 years after randomization, was less frequent in the tight

than in the standard control group.¹⁸ Specifically, as shown in Figure 2, the age-adjusted prevalence of LV hypertrophy at 2 years was lower in the tight control group than in the standard control group in both subgroups without (5.6% versus 9.6%) and with (4.2% versus 13.8%) established cardiovascular disease at entry. The interaction term between BP control group (standard versus tight) and the established cardiovascular disease group (yes versus no) was not significant (*P*=0.821).

Clinical Outcomes

The follow-up duration was 2.0 years. Only 1 control patient was lost to follow-up. During follow-up, 79 patients developed a composite secondary outcome (17 patients with unstable angina or coronary revascularization, 9 patients with myocardial infarction, 13 patients with stroke or TIA, 25 patients with new-onset atrial fibrillation, 8 patients with heart failure requiring hospitalization, and 7 patients with death from any cause). Specifically, it occurred in 43 patients (4.8%) in the group without previous cardiovascular disease and in 36 patients (16.7%) in the group with previous cardiovascular disease (log-rank: $\chi^2=40.05$, *P*<0.0001). The composite secondary outcome occurred less frequently in the tight than in the standard control group in patients without (rates: 1.5 versus 3.7 patient-years) and with (rates: 7.9 versus 11.2 patient-years) established cardiovascular disease at entry (log-rank: $\chi^2=48.42$; *P*<0.0001). Figure 3 shows the cumulative hazard (left) and the rate per 100 patients per year (right) of the main secondary outcome. The unadjusted hazard ratios for the composite secondary outcome in the total population

Table 2. Systolic Blood Pressure During the Study, mm Hg

Time	Standard Control		Tight Control	
	No CV Disease at Baseline	CV Disease at Baseline	No CV Disease at Baseline	CV Disease at Baseline
Baseline	158 (8)	159 (10)	158 (8)	158 (9)
1 y	137 (13)	139 (14)	133 (13)	134 (14)
2 y	135 (12)	137 (14)	132 (13)	132 (12)

CV indicates cardiovascular.

Table 3. Diastolic Blood Pressure During the Study, mm Hg

Time	Standard Control		Tight Control	
	No CV Disease at Baseline	CV Disease at Baseline	No CV Disease at Baseline	CV Disease at Baseline
Baseline	88 (8)	86 (9)	86 (8)	84 (9)
1 y	80 (7)	78 (7)	79 (8)	77 (9)
2 y	79 (7)	77 (9)	78 (8)	76 (9)

CV indicates cardiovascular.

and in the patients with and without established cardiovascular disease at baseline are shown in Figure 4. In a multivariable analysis, after adjustment for time-varying systolic BP ($P<0.01$) and age ($P<0.01$), the risk of composite cardiovascular end point was higher in the group with than in that without cardiovascular disease at baseline (hazard ratio 2.61; 95% confidence intervals: 1.64–4.15; $P<0.01$) and lower in patients assigned to the tight than in those assigned to the standard BP control (hazard ratio 0.51; 95% confidence intervals: 0.33–0.85; $P=0.014$). The P value for interaction between the risk group (absence versus presence of established cardiovascular disease at entry) and the strategy group (standard versus tight BP control) was not significant in models without (Figure 4; $P=0.27$) and with (Figure 5; $P=0.43$) adjustment for covariables. In the multivariable analysis, for each 5-mmHg lower systolic BP, entered as a time-varying covariable, there was a 12% lower risk of events ($P=0.0035$) and, for each 10-year older age, there was 95% higher risk of events ($P=0.0001$). Figure 5 shows the relation, adjusted for the other covariables, between achieved systolic BP and risk of new cardiovascular events in the 4 groups.

Discussion

In this post hoc analysis of the Cardio-Sis study, an intensive strategy aimed to achieve a systolic BP <130 mmHg was superior to a strategy of standard BP control (systolic BP <140 mmHg) regardless of the absence or presence of established cardiovascular disease at baseline. The primary end point of the study, electrocardiographic LV hypertrophy 2

years after randomization, was less frequent in the tight than in the standard control group in patients with and without established cardiovascular disease at entry. The secondary end point of the study, a composite of cardiovascular events, was also less frequent in the tight than in the standard control group in the 2 subsets with and without established cardiovascular disease at entry, but the number of events was small. Finally, the advantage of a tight over a standard BP control was found at any level of achieved systolic BP, without any paradoxical rise in the risk of events at low levels of achieved BP during follow-up.

BP Goals

The benefits of BP lowering with respect to stroke, renal, and cardiovascular disease complications led international guidelines to recommend reduction of BP to <140/90 mm Hg for uncomplicated hypertension or <130/80 mm Hg for subjects with concomitant kidney or cardiovascular disease.^{23,24} However, recent post hoc analyses of large outcomes trials suggest that low achieved BP values may be associated with increased cardiovascular morbidity and mortality, especially in patients with preexisting cardiovascular disease. In the International Verapamil-Trandolapril Study, the risk of the primary outcome of the study showed a J-shaped relationship with systolic BP in patients with hypertension with CAD.¹⁰ Similar results have been shown in the Valsartan Antihypertensive Long-Term Use Evaluation²⁵ trial and the Ongoing Telmisartan Alone and in Combination with Ramipril Global End point Trial.⁹ Conversely, some meta-analyses^{26–28} of trial data indicated that the benefit of intense antihypertensive treatment is maintained down BP levels for which a paradoxical increase in the risk might be expected on the basis of post hoc analyses reported above. The recent Secondary Prevention of Small Subcortical Strokes trial randomly assigned 3020 patients with recent lacunar stroke to a systolic BP target of 130 to 149 mm Hg or <130 mm Hg.¹³ Stroke, the primary outcome of the study, was less frequent (by 19%) in the tight control group, but the difference between the 2 groups was not significant.¹³ By contrast, the rate of intracerebral hemorrhage was

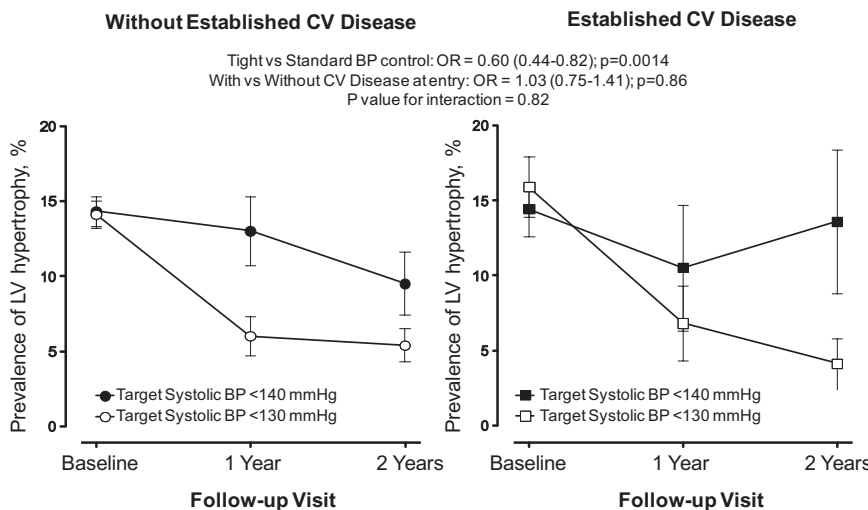


Figure 2. Prevalence of left ventricular hypertrophy at the 2-year visit in patients with and without established cardiovascular disease at baseline randomized to tight or standard blood pressure (BP) control. Estimates are adjusted for age and the rate of left ventricular hypertrophy at baseline. CV indicates cardiovascular; LV, left ventricular; and OR, odds ratio.

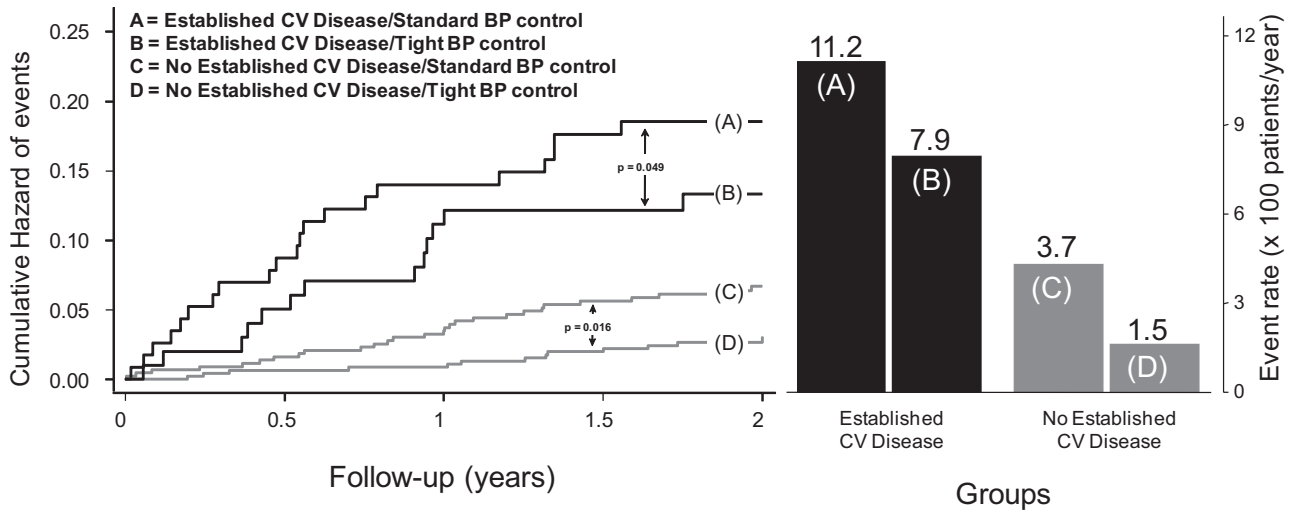


Figure 3. Cumulative hazard and rate of the main secondary outcome of cardiovascular events and total mortality in patients with and without established cardiovascular disease at baseline. BP indicates blood pressure; and CV, cardiovascular.

significantly lower in the tight control group.¹³ These data suggest that lowering systolic BP <130 mmHg is likely to reduce the risk of recurrent stroke in patients with recent lacunar stroke, although the evidence is not conclusive. Two randomized trials from Japan compared a tight systolic BP target (<140 mmHg) with a less tight target of 140 to 149 mmHg¹⁷ or 140 to 159 mmHg²⁹ in elderly patients hypertension. Both studies failed to detect a statistically significant difference between the randomized groups in the risk of a composite pool of cardiovascular events.^{17,29} Differences from Cardio-Sis include the higher age of patients in the Japanese trials (74²⁹ and 76¹⁷ years) than in Cardio-Sis (67 years)¹⁸ and the broader composite outcome in Cardio-Sis, that included coronary revascularization and new-onset atrial fibrillation.¹⁸

A recent meta-analysis²⁶ of trials, including 221 024 patients, that compared different BP-lowering agents with placebo or active treatments in patients with hypertension or composite features of high cardiovascular risk, demonstrated that for each 5-mmHg reduction in systolic BP, there was 13% less risk of a composite cardiovascular end point (95% confidence intervals: 8–19; $P=0.001$) including myocardial infarction, stroke, cardiovascular death, and

congestive heart failure. Such associations were linear without any evidence of J curve.

The recent guidelines for the management of arterial hypertension released by European Society of Hypertension and European Society of Cardiology simplified treatment decisions for physicians with the recommendation that all patients (with exceptions for diabetes mellitus and the elderly) be treated to <140 mmHg systolic BP.⁴ Such recommendation may be viewed as an attempt to translate into clinical practice the results of 3 recent clinical trials,^{14,23,24} which have directly compared different BP targets to test the hypothesis that attained BPs below the standard goal of <140/90 mmHg improve outcomes. Two^{14,29} of these 3 trials^{14,18,29} failed to prove a larger relative advantage of more intensive BP lowering on the primary outcome. However, they recruited special populations (diabetic¹⁴ and elderly²⁹ patients) for whom the new European guidelines do make exceptions in the recommendations of BP goal.⁴

The Present Study

The Cardio-Sis trial¹⁸ evaluated 2 different BP goals in high-risk patients with uncontrolled hypertension (systolic BP ≥150 mmHg) and ≥1 additional cardiovascular risk factor,

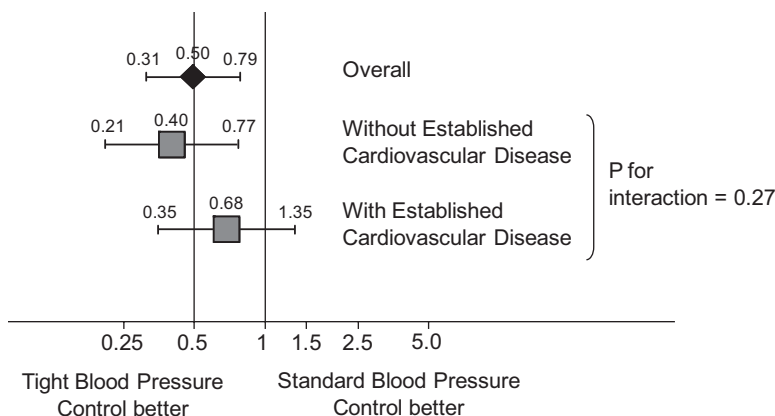


Figure 4. Unadjusted hazard ratios for the main secondary outcome in the total population and in the patients with and without established cardiovascular disease at baseline.

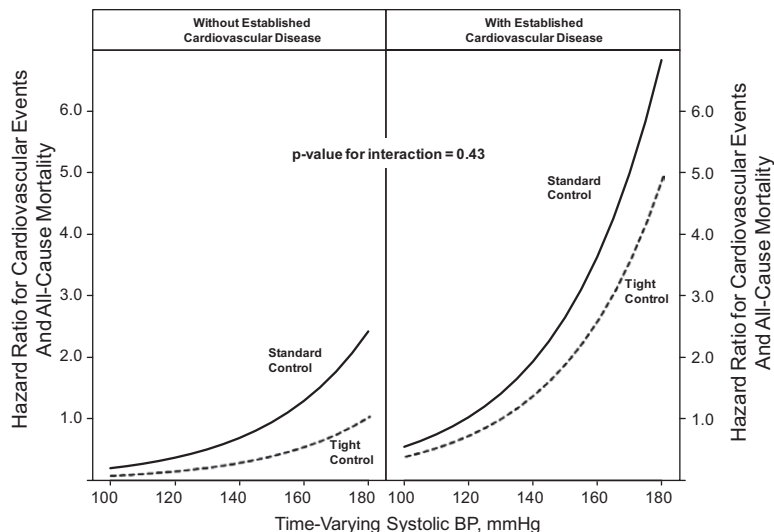


Figure 5. Multivariable relation between achieved systolic blood pressure and risk of composite secondary outcome in the 4 groups. The interaction between blood pressure (BP)-lowering strategy (standard vs tight BP control) and previous cardiovascular disease (yes vs no) is not significant.

but without diabetes mellitus. The trial demonstrated that new development or lack of regression of electrocardiographic LV hypertrophy, and the occurrence of a composite pool of cardiovascular events and death, occurred less frequently in the tight than in the standard BP control group.¹⁸ The present post hoc analysis extends these results by showing that the benefit of an intensified strategy targeted to achieve a more tight BP control equally applies to patients with and without established cardiovascular disease at entry, without any paradoxical rise in the risk of new events at low levels of achieved systolic BP. Even in the ACCORD (Action to Control Cardiovascular Risk in Diabetes) study, performed in patients with diabetes mellitus, there was no significant interaction ($P=0.78$) between the BP-lowering strategy and previous cardiovascular disease.¹⁴ Our results support the hypothesis, derived from previous studies,^{7,30} that the poorer outcome in patients with low values of achieved BP is explained more likely by poor health conditions and frailty associated with concomitant disorders rather than an adverse specific effect of BP reduction caused by treatment.

Limitations of the Study

Duration of follow-up was only 2 years, and the number of outcome events was small. The number of patients and events and the achieved systolic BP difference of 3.8 mm Hg between the 2 groups reduced the power of the study to detect a significant difference between the groups for each of the components of the composite outcome (mortality, myocardial infarction, and stroke). It also reduced the power of the study to test the possibility of a paradoxical rise in the risk of events (J curve) at low levels of achieved BP, as suggested by previous studies.^{31,32} New-onset atrial fibrillation and coronary revascularization were the components of the composite secondary outcome that differed significantly between the groups.¹⁸

Perspectives

This study suggests that an intensive antihypertensive strategy aimed at lowering systolic BP <130 mmHg reduces left

ventricular hypertrophy and improves clinical outcomes to a similar extent in patients with hypertension with and without established cardiovascular disease at baseline. These findings suggest that the fear that a systolic BP target <130 mmHg is dangerous in patients with hypertension with established cardiovascular disease at baseline should be reconsidered. This hypothesis-generating study clearly strengthens the research priority of randomized clinical trials, some of which are ongoing,³³ between different BP targets in patients exposed to a modern management of high BP and other cardiovascular risk factors.

Appendix

Sources of Funding

Cardio-Sis was an investigator-initiated study supported by the *Associazione Nazionale Medici Ospedalieri* (ANMCO) through grants from Boehringer-Ingelheim, Sanofi-Aventis, and Pfizer to ANMCO. The funding sources had no role in the design or the conduct of the trial, data collection, database management, statistical analysis, interpretation of the results, or writing of the report.

Author Roles and Responsibilities

Authors had full access to the database, guarantee the integrity of the statistical analysis, and carry the final responsibility for the decision to submit the results of the trial for publication.

Endpoint Committee

Carlo Porcellati and Giovanni Fornari.

ECG Reading Centre

Associazione Umbra Cuore e Ipertensione.

Participating Centers and Clinical Investigators

Aosta (M.G. Sclavo); Benevento (M. Scherillo, D. Raucchi); Brescia (P. Faggiano); Cagliari Brotzu (M. Porcu, L. Pistis); Caltanissetta (F. Vancheri, M. Curcio); Casarano (M. Ieva, A. Muscella); Castiglione del Lago (M. Guerrieri, C. Dembech); Catania Garibaldi-Nesima (M.M. Gulizia, G.M. Francese); Catanzaro (F. Perticone, G. Iemma); Chiari (G. Zanolini); Chieti (S.D. Pierdomenico, A. Mezzetti); Città della Pieve (G. Benemio, R. Gattobigio, N. Sacchi); Città di Castello Cardiologia (M. Cocchieri, L. Prosciutti); Città di Castello Medicina (O. Garognoli); Cremona (S. Pirelli, C. Emanuelli, G.

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Disclosures

None.

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Novelty and Significance

What Is New?

- An excessive blood pressure (BP) reduction might be dangerous in high-risk patients with overt cardiovascular disease.
- In this post hoc analysis of the Studio Italiano Sugli Eff etti CARDIOvascolari del Controllo della Pressione Arteriosa SISTolica (Cardio-Sis), we investigated whether an intensive strategy aimed to achieve a tight systolic BP control (<130 mm Hg) is superior to a strategy of standard BP control (systolic BP<140 mm Hg) regardless of the absence or presence of overt cardiovascular disease at baseline.

What Is Relevant?

- Electrocardiographic left ventricular hypertrophy 2 years after randomization, the primary outcome of the study, occurred less frequently in the tight than in the standard control group in the patients without and with cardiovascular disease at randomization (*P* for interaction=0.82).

- A composite of cardiovascular events and all-cause death (main secondary outcome) occurred less frequently in the tight than in the standard control group in patients without and with previous cardiovascular disease (*P* for interaction=0.27).

Summary

This study shows that an intensive antihypertensive treatment aimed to lower systolic BP<130 mmHg reduces left ventricular hypertrophy and improves clinical outcomes to a similar extent in patients with hypertension with and without overt cardiovascular disease at baseline. These results should remove the fear that a systolic BP target<130 mmHg may be potentially dangerous in patients with hypertension with established coronary or cerebrovascular disease at baseline.

Tight Versus Standard Blood Pressure Control in Patients With Hypertension With and Without Cardiovascular Disease

Gianpaolo Reboldi, Fabio Angeli, Giovanni de Simone, Jan A. Staessen and Paolo Verdecchia
on behalf of the Cardio-Sis Investigators

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