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Hypertension. 1990;16:19-25

doi: 10.1161/01.HYP.16.1.19

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Print ISSN: 0194-911X. Online ISSN: 1524-4563

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Original Contributions

ST Segment Depression Elicited by Dipyridamole Infusion in Asymptomatic Hypertensive Patients

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In asymptomatic patients with essential hypertension, electrocardiographic changes suggestive of myocardial ischemia can be elicited by rapid pressure lowering or by pronounced coronary arteriolar dilation. The aim of this study was to assess whether dipyridamole infusion might induce ischemiclike electrocardiographic changes in asymptomatic essential hypertensive patients and to describe the clinical and echocardiographic correlates possibly associated with this response. We therefore studied a control group of 20 normotensive individuals and a group of 28 asymptomatic patients with mild-to-moderate essential hypertension. All underwent dipyridamole-echocardiography testing (12-lead electrocardiogram and two-dimensional echocardiographic monitoring with dipyridamole infusion, 0.84 mg/kg over 10'). No patient showed transient regional dyssynergy during dipyridamole infusion. None of the normotensive and 10 of 28 of the hypertensive participants had horizontal or downsloping ST segment depression more than 0.1 mV during dipyridamole (0% versus 36%, $p < 0.01$). Hypertensive patients with ("responders") ($n = 10$) and without ("nonresponders") ($n = 18$) ST segment depression showed similar values of percent fractional shortening in baseline conditions (32 ± 5 versus 33 ± 6 , $p = \text{NS}$) and at peak dipyridamole infusion (45 ± 8 versus 43 ± 5 , $p = \text{NS}$). The peak early to peak late velocity ratio values (evaluated from transmitral flow tracings by Doppler technique) were also similar in baseline conditions (0.86 ± 0.14 versus 0.94 ± 0.30 , $p = \text{NS}$) and at peak dipyridamole (0.72 ± 0.15 versus 0.78 ± 0.32 , $p = \text{NS}$). Responders had higher values of left ventricular mass index (149 ± 35 versus 124 ± 28 g/m², $p < 0.05$) and duration of hypertension (11.0 ± 6.3 versus 5.5 ± 4.7 years, $p < 0.05$) than nonresponders. All responders showed angiographically normal coronary arteries. Thus, a significant number of asymptomatic essential hypertensive patients showed dipyridamole-induced ischemiclike ST segment depression, in spite of angiographically normal coronary arteries, in the absence of any detectable regional or global, systolic or diastolic, left ventricular dysfunction. (*Hypertension* 1990;16:19-25)

In asymptomatic patients with essential hypertension, electrocardiographic changes suggestive of myocardial ischemia can be elicited by rapid pressure lowering or by pronounced coronary arteriolar dilation.¹⁻⁴ Whether these ischemiclike electrocardiographic alterations reflect true subendocardial underperfusion or are mere nonspecific "innocent" alterations remains an unsettled although pivotal

question. A rational approach would be to identify this subset of hypertensive patients in a simple, inexpensive, and feasible way to assess the possible pathophysiological and clinical meaning of these abnormalities.

Dipyridamole-echocardiography testing (DET) has recently been proposed for the diagnosis of coronary artery disease,^{5,6} and it is especially useful in hypertensive patients.⁷ Dipyridamole has a mild hypotensive effect and a pronounced coronary arteriolar dilating action.⁸ Therefore, it might well induce ischemiclike electrocardiographic changes in asymptomatic hypertensive patients as it does in other subsets of patients with "microvascular angina" (reduced coronary flow reserve and angiographically normal epicardial coronary arteries)⁹ such as Syndrome X,¹⁰ acute rejection of transplanted heart,¹¹ and hypertensive patients with history of chest pain

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Presented in part at the 60th Scientific Sessions of the American Heart Association, Anaheim, California, November 16-19, 1987.

A.R.L. is recipient of a grant from Squibb for Cardiovascular Research in Hypertension. C.M. is a visiting research fellow from Clinica Medica I, Florence University, Florence, Italy.

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Received August 26, 1989; accepted in revised form February 22, 1990.

and no detectable coronary artery disease, with or without left ventricular hypertrophy.^{7,12} In fact, left ventricular hypertrophy¹³ or microvascular coronary disease¹⁴ might decrease flow reserve in hypertensive patients, even in the absence of epicardial coronary stenoses.^{15,16}

The aim of this study was to assess whether dipyridamole infusion might induce ischemiclike electrocardiographic changes in asymptomatic essential hypertensive patients and to describe the clinical and echocardiographic correlates possibly associated with this electrocardiographic response.

Methods

Selection of Patients

A control group of 20 young normotensive subjects (10 men and 10 women, 20–30 years old) was studied. All were asymptomatic with normal resting and exercise electrocardiographic findings, normal baseline echocardiographic findings, and no family history of hypertension or coronary artery disease.

Twenty-eight asymptomatic hospitalized patients (15 men and 13 women, 32–66 years old, mean 53 years) with mild-to-moderate essential hypertension were enrolled for the study. All met the following inclusion criteria: 1) two-dimensional echocardiographic images of acceptable quality in resting conditions; 2) off medications at the time of the study for at least 7 days (at least 15 days for patients on β -blockers); 3) no concomitant systemic disease or cardiac disease other than hypertrophy; 4) absence of diabetes, hyperlipemia, or family history of coronary artery disease; 5) normal regional and global left ventricular contraction, and 6) absence of a "strain" pattern in the baseline electrocardiogram. A strain pattern was considered to be present with a downsloping ST segment and an asymmetric, inverted T wave without terminal positivity exceeding the negative component in amplitude. All patients underwent a resting echocardiogram and a high dose DET.

Resting Electrocardiography

All patients had a resting 12-lead electrocardiogram. The criterion of hypertrophy was based on Sokolow and Lyon's precordial voltage (SV_1 and RV_5 or $V_6 > 35$ mm).¹⁷

Resting Echocardiography

Measurements were made by two-dimensional targeted M-mode tracings obtained from the parasternal long axis view. Left ventricular mass was calculated according to the Penn convention.¹⁸ Criteria of hypertrophy were a left ventricular mass index greater than 134 g/m² for men and greater than 110 g/m² for women.¹⁹

Dipyridamole-Echocardiography Test

Two-dimensional echocardiographic and 12-lead electrocardiographic monitoring were performed in combination with a dipyridamole infusion: 0.56 mg/

kg over 4 minutes followed by 4 minutes of no dose and then 0.28 mg/kg in 2 minutes. The cumulative dose was, therefore, 0.84 mg/kg over 10 minutes.⁵

Aminophylline, which promptly reverses the effects of dipyridamole, was readily available and was routinely given at the end of each test (80 mg over 1 minute). During the procedure, the blood pressure and a 12-lead electrocardiogram were recorded each minute. Electrocardiographic tracings were independently read by two experienced cardiologists blind to clinical and angiographic information. The tracings were considered diagnostic for myocardial ischemia when there was a horizontal or downsloping ST segment shift of at least 0.1 mV 0.08 second after the J point compared with baseline. The decision was unanimously reached in 46 cases; in the two split cases, a consensus was reached.

Two-dimensional echocardiograms were continuously recorded during and up to 10 minutes after dipyridamole administration.^{5,6} In the baseline studies, all standard echocardiographic views were obtained when possible. During the test, new areas of abnormal wall motion were looked for on multiple views (mainly parasternal, long and short axis, and apical, four, and two chamber view) by rapidly moving the ultrasound transducer through various positions.⁵

A commercially available, wide-angle, phased-array imaging system (model 77020, 2.5 and 3.5 MHz transducers, Hewlett Packard, Andover, Mass.) was used.

The videotapes were analyzed by two independent observers blinded to the clinical information. Segmental anatomy and wall motion were assessed in a qualitative manner as previously reported.⁵ Wall motion was graded as hyperkinetic, normal, hypokinetic, akinetic, or dyskinetic. Positivity of the test for ischemia due to angiographically assessed coronary artery disease was linked to the detection of a transient asynergy of contraction. A unanimous decision was reached in all studies.

In each study subject, percent fractional shortening was calculated as:

$$\frac{\text{end-diastolic diameter} - \text{end-systolic diameter}}{\text{end-diastolic diameter}} \times 100$$

This variable was measured during two conditions: baseline state and peak changes. Measurements were made by two-dimensional targeted M-mode tracings obtained from the parasternal long axis view.

Pulsed Doppler Examination

The Doppler diastolic transmitral flow velocity waveform, which is an index of diastolic function,²⁰ was recorded in resting conditions and every minute during dipyridamole stress according to a methodology previously described in detail.²¹

For each test, two time points were considered for quantitative evaluation: basal state and peak dipyridamole effect, when the maximal changes in transmitral flow were recorded. For each time point in each

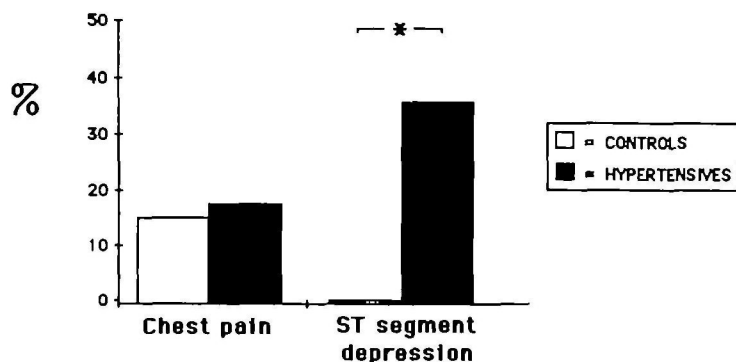


FIGURE 1. Bar graph showing incidence of chest pain and ST segment depression in normotensive control subjects and hypertensive patients during dipyridamole stress. Electrocardiographic changes are significantly more frequent in hypertensive patients.

test, left ventricular diastolic flow velocity waveforms from at least three cardiac cycles were characterized quantitatively and the values averaged. For each tracing, the following measurements were obtained: 1) peak velocity of early diastolic rapid inflow (E, in cm/sec), 2) peak velocity of late diastolic inflow due to the atrial contraction (A, in cm/sec), and 3) the ratio of the peak early to peak late velocity (E/A).

The Doppler study was attempted in all hypertensive patients. Interpretable Doppler tracings during control and at peak changes were obtained in 22 of 28 hypertensive patients (feasibility, 79%). A total of six hypertensive patients, four with and two without echocardiographically assessed left ventricular hypertrophy, had resting or stress-induced tachycardia that precluded the acquisition of readable Doppler tracings. Of these six, two were responders and four were nonresponders.

Coronary Arteriography

Fourteen hypertensive patients underwent coronary angiography for clinical diagnostic needs for one of the following reasons: 1) development of an atypical chest pain syndrome 8 months after the enroll-

ment into the study (one patient), 2) presence of a positive exercise electrocardiography stress test (seven patients), 3) presence of a "false positive" exercise Thallium scintigraphy (two patients) with transient reversible perfusion defect either in the apical (one patient) or anterolateral (one patient) wall, 4) strongly positive (ST segment depression >0.2 mV from baseline) dipyridamole-electrocardiography test (this response is believed to be highly suspect for presence of coronary artery disease²²) (four patients).

All patients underwent selective coronary arteriography using the Judkins technique. Multiple views of each vessel were filmed. A vessel was considered to have significant obstruction if its diameter was narrowed by 50% or more with respect to the prestenotic tract.

Statistical Analysis

Mean±SD are given for each value.

Differences were tested for significance by paired and unpaired Student's *t* test or by χ^2 test. A *p* value <0.05 was considered statistically significant.

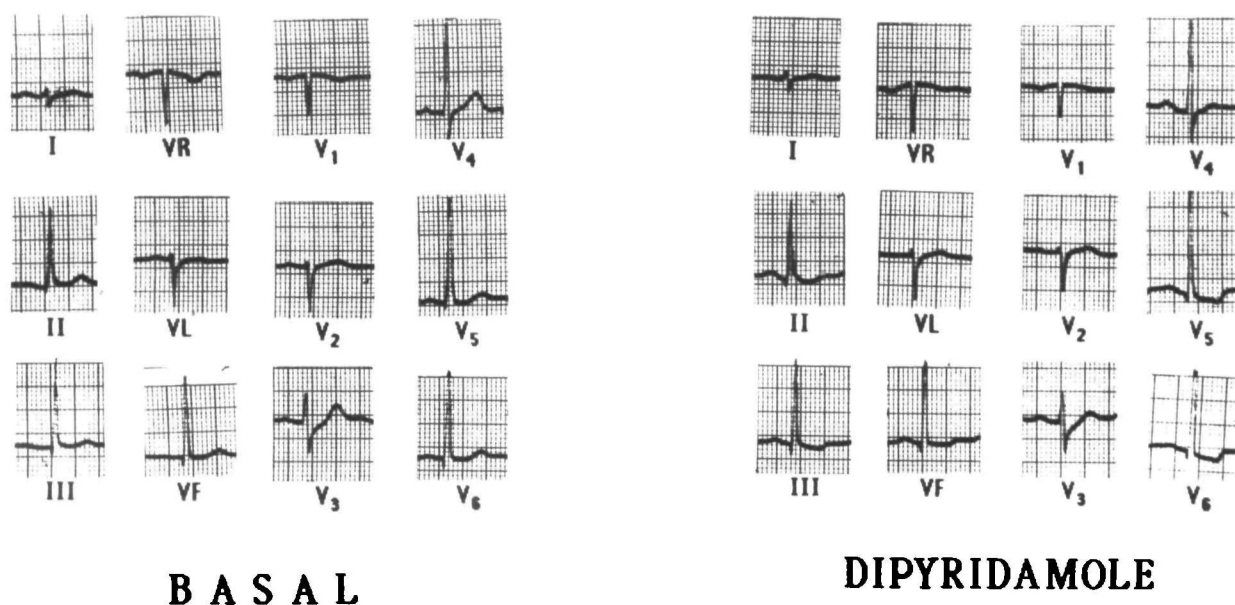


FIGURE 2. A representative example of tracings showing ST segment depression during dipyridamole stress (Dipyridamole) in a patient with no depolarization abnormalities in the resting electrocardiogram (Basal).

TABLE 1. Hemodynamic Findings During Dipyridamole Stress in Hypertensive Patients

	Basal		Dipyridamole		
	Responders	Nonresponders	Responders	Nonresponders	Nonresponders
Heart rate (beats/min)	76±10	NS 74±8	105±17	NS	99±12
Systolic arterial pressure (mm Hg)	164±14	NS 165±11	155±19	NS	155±10
Diastolic arterial pressure (mm Hg)	100±4	NS 103±8	96±4	NS	97±8
Rate pressure product (mm Hg×beats/min×1/100)	125±23	NS 122±16	163±29	NS	153±20

Values given are mean±SD. NS, p =not significant.

Results

Fifteen hypertensive patients had echocardiographic and 10 of these 15 also had electrocardiographic evidence of left ventricular hypertrophy.

DET was completed in all patients. Side effects appeared in 12 of 20 in the normotensive control group and 20 of 28 in the hypertensive group (60 versus 71%, p =NS). In order of frequency they were: headache (36%), flushing (19%), and nausea (7%). The side effects were always of mild severity, well tolerated by the patient, and reversed by aminophylline routinely given at the end of the test. None of the participants had severe hypotension, vomiting, or significant ventricular arrhythmias during the test. Three control subjects and five hypertensive patients had mild, atypical chest discomfort during DET (15 versus 18%, p =NS) (Figure 1). Regional wall motion

asynery during DET did not develop in any of the study subjects, either normotensive or hypertensive.

Electrocardiographic Findings

None of the control subjects and 10 of the hypertensive patients had diagnostic ST segment depression during DET (0% versus 36%, p <0.01) (Figures 1 and 2).

On the basis of the electrocardiographic response, two subsets of hypertensive patients were identified: "responders" (10 patients with dipyridamole-induced ST segment depression) and "nonresponders" (18 patients without dipyridamole-induced ST segment depression). The blood pressure values were similar in the two groups (systolic blood pressure: 165±15 versus 164±10 mm Hg, p =NS; diastolic blood pressure: 104±7 versus 104±7 mm Hg, p =NS); the duration of

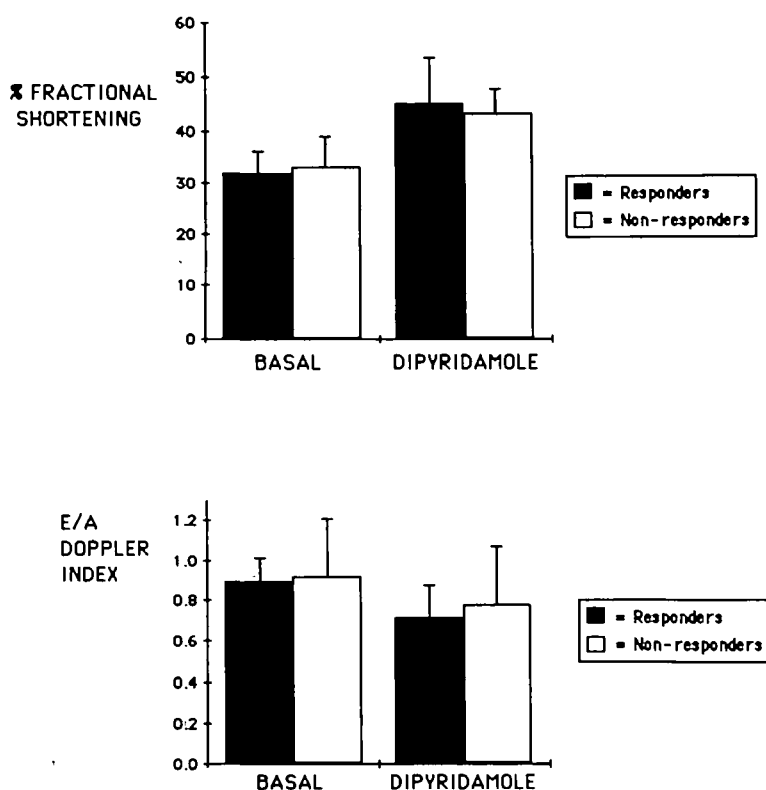


FIGURE 3. Bar graphs showing changes in percent (%) fractional shortening and E/A Doppler index in hypertensive patients with (responders) and without (nonresponders) ST segment depression during dipyridamole stress.

hypertension was longer in responders (11.0 ± 6.3 versus 5.5 ± 4.7 years, $p < 0.05$). The heart rate and blood pressure responses to dipyridamole infusion were similar in the two groups (Table 1).

Echocardiographic Findings

Responders and nonresponders could not be differentiated on the basis of resting or stress-induced global systolic (percent fractional shortening) or diastolic (E/A ratio) function indexes (Figure 3).

Echocardiographically assessed left ventricular hypertrophy was present in 7 of 10 responders and 8 of 18 nonresponders (70% versus 44%, $p = \text{NS}$). A greater value of left ventricular mass index was present in responders (149 ± 35 versus 124 ± 38 g/m², $p < 0.05$).

Coronary Angiographic Findings

Coronary angiography showed only minimal epicardial coronary artery lumen narrowing (<30%) in three patients (two responders and one nonresponder) and entirely normal vessels in 11 patients (eight responders and three nonresponders).

Discussion

The findings of this study are fully consistent with data previously obtained by our group in symptomatic hypertensive patients, showing that: 1) ST segment depression can frequently be elicited, together with chest pain, in patients with angiographically normal coronary arteries⁷; 2) this electrocardiographic response is not necessarily associated with left ventricular hypertrophy¹²; and 3) the specificity of the dipyridamole test for angiographically assessed coronary artery disease is dramatically low with electrocardiographic criteria, but it remains excellent with echocardiographic criteria.⁷

Two-Dimensional and Doppler Findings During Dipyridamole

In both responders and nonresponders, there was a similar, clear-cut modification induced by dipyridamole in indexes of global systolic and diastolic function. Percent fractional shortening increased significantly at peak dipyridamole in a way similar to what has been described in patients without coronary artery disease and normal mechanical response to dipyridamole infusion.²³ A transient hyperkinetic phase is usually detected during dipyridamole testing,⁵ and left ventricular hemodynamic monitoring showed a pronounced rise in dP/dt of contraction in patients without echocardiographic evidence of myocardial ischemia.²³

We have previously shown that during dipyridamole infusion there is a "pseudoischemic" pattern in transmitral inflow velocity curve that can be found even in the absence of coronary artery disease or dipyridamole-induced systolic dysfunction.²¹ This pseudoischemic pattern consists of a relative increase in the atrial component of the transmitral inflow velocity profile. This same pattern was found in hypertensive patients, possibly explained by the hemody-

namic changes induced by the drug (increase in heart rate and changes in loading conditions of the left ventricle), which may very well mimic the effect of left ventricular ischemia on transmitral flow pattern.²¹

Possible Pathophysiological Meaning of Dipyridamole-Induced ST Segment Depression

We speculate that the most likely explanation for ST segment depression induced by dipyridamole and reversed by aminophylline is a transient subendocardial underperfusion. Such underperfusion might be due to several possible causes: epicardial coronary artery stenosis, arterial hypotension, left ventricular hypertrophy, or microvascular coronary disease^{15,16}.

Significant epicardial coronary stenoses were unlikely to be present in our study population as all patients were free of anginal symptoms at the time of study, and we failed to detect significant stenoses in the 14 patients (including the 10 responders to dipyridamole testing) in whom coronary angiography was performed according to clinical and diagnostic needs. Furthermore, the lack of dipyridamole-induced ventricular dyssynergy carries a low probability that an anatomically severe²⁴ or physiologically important²⁵ epicardial coronary stenosis is present.

Another contributing mechanism can be arterial hypotension. Harrison et al²⁶ showed that left ventricular hypertrophy can profoundly impair the lower range of autoregulation in the subendocardial myocardium of hypertensive dogs. As suggested by Pepi et al,^{3,4} it is entirely possible that the high blood pressure becomes a physiological requirement in the myocardium of hypertensive patients so that adequate coronary perfusion pressure and blood flow can be maintained. The subendocardium will tend to suffer first when the coronary perfusion pressure is lowered.^{13,14} However, after dipyridamole, the mean decrease in blood pressure was mild, without significant differences between responders and nonresponders. Therefore, it appears likely that the hypotensive mechanism plays a minor role when compared with the coronary arteriolar dilation, which is provoked by dipyridamole through adenosine accumulation.⁸

From the theoretical viewpoint, the infusion of a coronary dilator can induce myocardial ischemia in the presence of a reduction in coronary flow reserve.⁸ In this situation, a vasodilator stimulus will decrease subepicardial resistance but will not alter subendocardial resistance because its vasodilator reserve is already exhausted in resting conditions (the myocardial oxygen demands of the subendocardium are greater than those of the subepicardium).⁹ In the absence of an epicardial coronary stenosis, the decrease in coronary flow reserve can be obtained through two main mechanisms: left ventricular hypertrophy or disease of small coronary vessels, or both. It is consistent with this interpretation that responders had higher levels of left ventricular mass.^{13,15} However, left ventricular hypertrophy was not a prerequisite for the development of dipyri-

damole-induced ST segment depression. This finding is in agreement with the documented possibility of a dissociation between left ventricular and vascular hypertrophy in hypertensive patients, determining the reduced coronary flow reserve in hypertensive patients with normal left ventricular mass.¹⁴ It can be considered consistent with this hypothesis that responders had a longer duration of hypertension, which is associated with more profound structural changes in the coronary resistance vessels.²⁷

The absence of mechanical changes does not contradict the "ischemic" interpretation of the dipyridamole-induced ST segment depression.⁸ In fact, presence or absence of abnormal wall motion appears to relate to the amount of subendocardial tissue rendered ischemic, with minor degrees of transmural involvement less likely to produce regional dysfunction.²⁸ As in Syndrome X, one must hypothesize that the dipyridamole-induced ischemia is large enough, in a horizontal or circumferential direction, to induce ST segment depression but not so deep, in a transmural or vertical axis, as to provoke wall motion abnormalities. In Syndrome X, this "echocardiographically silent" myocardial ischemia can be associated with a reduction in flow reserve possibly due to microvascular disease.^{9,22}

Limitations of the Study

The evidence reported above renders less likely the viewpoint that dipyridamole-induced ST segment depression might simply be a nonspecific response to drug infusion. In contrast to the exercise stress test, during dipyridamole testing there is no excessive tachycardia and hyperventilation that may easily induce nonspecific ST segment changes. However, the lack of a metabolic or coronary reserve evaluation during dipyridamole in these patients makes the results of this study mostly descriptive and the discussion largely speculative. We believe, therefore, that the ischemic nature of dipyridamole-induced electrocardiographic changes cannot be claimed on the basis of this investigation, and further studies are needed to convincingly demonstrate the pathophysiological and clinical correlates of dipyridamole-induced ST segment depression.

We conclude that a significant number of asymptomatic essential hypertensive patients show dipyridamole-induced ST segment depression in the absence of any detectable regional or global, systolic or diastolic, left ventricular dysfunction. This electrocardiographic finding is more frequent in the presence of left ventricular hypertrophy and longer duration of hypertension, both of which are factors possibly correlated to a reduction in coronary reserve and to the presence of microvascular disease.

Acknowledgments

We are very grateful to Claudia Taddei for secretarial assistance and to Dr. Nadia Simonini for reviewing the manuscript for the English language.

References

1. McMahon FG: *Management of Essential Hypertension*. New York, Futura Publishing Co, Inc, 1978, pp 229, 383-386
2. Yagil Y, Kobrin I, Lebsel B, Ben Ishay D: Ischemic ECG changes with initial nifedipine therapy of severe hypertension. *Am Heart J* 1982;103:310-311
3. Pepi M, Alimento M, Maltagliati A, Guazzi MD: Cardiac hypertrophy in hypertension repolarization abnormalities elicited by rapid lowering of pressure. *Hypertension* 1988;11:84-91
4. Pepi M, Alimento M, Maltagliati A, Tosi E, Guazzi MD: Electrocardiographic alterations suggestive of myocardial injury elicited by rapid pressure lowering in hypertension. *Eur Heart J* 1988;8:899-905
5. Picano E, Lattanzi F, Masini M, Distante A, L'Abbate A: High dose dipyridamole-echocardiography test in effort angina pectoris. *J Am Coll Cardiol* 1986;8:848-854
6. Picano E, Severi S, Michelassi C, Lattanzi F, Masini M, Orsini E, Distante A, L'Abbate A: Prognostic importance of dipyridamole-echocardiography test in coronary artery disease. *Circulation* 1989;80:450-457
7. Picano E, Lucarini AR, Lattanzi F, Distante A, Di Legge V, Salvetti A, L'Abbate A: Dipyridamole-echocardiography in essential hypertensive patients with chest pain. *Hypertension* 1988;12:238-243
8. Picano E: Dipyridamole-echocardiography test: The historical background and the physiologic basis. *Eur Heart J* 1989;10:365-376
9. Epstein SE, Cannon RO: Site of increased resistance to coronary flow in patients with angina pectoris and normal epicardial coronary arteries. *J Am Coll Cardiol* 1986;8:459-461
10. Picano E, Lattanzi F, Masini M, Distante A, L'Abbate A: Usefulness of a high-dose dipyridamole-echocardiography test for diagnosis of syndrome X. *Am J Cardiol* 1987;60:508-512
11. Picano E, De Pieri G, Salerno JA, Arbustini E, Distante A, Martinelli L, Montemartini C, Viganò M: Electrocardiographic changes during dipyridamole stress as potential markers of acute cardiac rejection. *Circulation* 1990;81:72-77
12. Lucarini AR, Lattanzi F, Picano E, De Prisco F, Distante A, L'Abbate A, Salvetti A: Dipyridamole-echocardiography test in essential hypertensives with chest pain and angiographically normal coronary disease. *Am J Hypertens* 1989;2:120-123
13. Strauer BE: Ventricular function and coronary hemodynamics in hypertensive heart disease. *Am J Cardiol* 1979;44:993-1008
14. Brush JE, Cannon RO, Schenke WH, Leon MB, Bonow RO, Maron BJ, Epstein SE: Angina due to coronary microvascular disease in hypertensive patients without left ventricular hypertrophy. *N Engl J Med* 1988;319:1302-1307
15. Marcus ML: Effects of cardiac hypertrophy on the coronary circulation, in Marcus ML (ed): *The Coronary Circulation in Health and Disease*. New York, McGraw-Hill Book Co, Inc, 1983, pp 285-306
16. Coronary artery disease in hypertension (editorial). *Lancet* 1988;2:1461-1462
17. Sokolow M, Lyon TP: The ventricular complex in left ventricular hypertrophy as obtained by unipolar precordial and limb leads. *Am Heart J* 1949;37:161-186
18. Devereux RB: Detection of left ventricular hypertrophy by M-mode echocardiography. Anatomic validation, standardization, and comparison to other methods. *Hypertension* 1987;9(suppl II):II-19-II-26
19. Devereux RB, Reichek N: Repolarization abnormalities of left ventricular hypertrophy. Clinical, echocardiographic and hemodynamic correlates. *J Am Coll Cardiol* 1984;4:1222-1230
20. Spirito P, Maron BJ, Bonow RO: Noninvasive assessment of left ventricular diastolic function: Comparative analysis of Doppler echocardiographic and radionuclide angiographic techniques. *J Am Coll Cardiol* 1986;7:518-526
21. Lattanzi F, Picano E, Masini M, De Prisco F, Distante A, L'Abbate A: Transmittal flow changes during dipyridamole-induced ischemia: A doppler-echocardiographic study. *Chest* 1989;95:1037-1042
22. Osterspey A, Jansen W, Tauchert M, Eigel J, Hopp H, Behrenbeck DW, Hilger HH: Stellenwert des dipyridamole-test in der

- diagnostik der koronaren herzkrankheit. *Dtsch Med Wochenschr* 1983;69:1469-1475
23. Picano E, Simonetti I, Carpeggiani C, Lattanzi F, Macerata A, Trivella MG, Marzilli M, L'Abbate A: Regional and global biventricular function during dipyridamole stress test: A hemodynamic and echocardiographic study. *Am J Cardiol* 1989;63:429-432
 24. Simonetti I, Picano E, Lattanzi F, Marzilli M: Dipyridamole echocardiography correlates with coronary lesion geometry (abstract). *Circulation* 1989;79:825
 25. Picano E, Parodi O, Lattanzi F, Marcassa C, Sambuceti G, Bellina R, Salvadori P, Camici P, L'Abbate A: Noninvasive assessment of regional coronary flow reserve by dipyridamole echocardiography: Correlation with ¹³N-Ammonia and positron emission tomography (abstract). *J Am Coll Cardiol* 1990;15:233A
 26. Harrison DG, Florentine MS, Brooks LA, Cooper SM, Marcus ML: The effect of hypertension and left ventricular hypertrophy on the lower range of coronary autoregulation. *Circulation* 1988;77:1108-1115
 27. Schneeweiss A, Sherf L, Lehrer E, Lieberman Y, Neufeld HN: Segmental study of the terminal coronary vessels in coarctation of the aorta: A natural model for study of the effect of coronary hypertension on human coronary circulation. *Am J Cardiol* 1982;49:1996-2002
 28. Weiss JL, Bulkley BH, Hutchins GM, Mason SJ: Two-dimensional echocardiography recognition of myocardial injury in man: Comparison with postmortem studies. *Circulation* 1981;63:401-408

KEY WORDS • ischemia • dipyridamole • echocardiography • essential hypertension