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Effects of Nifedipine on Carotid and Femoral Arterial Wall Thickness in Previously Untreated Hypertensive Patients

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Background: Experimental and clinical evidence suggests that calcium-channel blockers may retard the atherosclerotic process after long-term treatment. Whether these effects exist after intermediate-term treatment in hypertensive patients is mainly unknown. **Objective**: To determine the 26-week effects of the long-acting calcium-channel blocker nifedipine on intima media thickness (IMT) in newly found hypertensive patients. **Design:** Open-label study with blinded end-point analysis. **Methods:** From a population survey, 131 previously untreated mild hypertensives (4× systolic blood pressure between 160 and 220 mmHg and/or diastolic blood pressure between 95 and 115 mmHg) were included. Patients were treated with long-acting nifedipine 30–60 mg targeted to reach a predetermined drop in blood pressure. Prior to and after 26 weeks of treatment, IMT was measured by ultrasonography in the carotid and femoral artery. The combined mean maximal far wall IMT was used as primary endpoint. Change from baseline was evaluated by paired *t*-test in an intention-to-treat analysis. **Results:** The mean maximal far wall IMT at baseline was 1.03 ± 0.23 mm, and decreased by 0.078 mm (95% confidence interval, CI 0.044–0.111) after treatment. Regression analysis, including baseline IMT and changes of blood pressure, showed that reduction of IMT was mostly influenced by baseline IMT ($p < 0.001$; model $R^2 = 0.11$). **Conclusion:** Our observations show that 26 weeks of nifedipine treatment inhibits IMT progression in these newly found hypertensive patients. This effect was mostly seen in arterial walls with highest IMT before treatment, suggesting that patients with highest cardiovascular risk benefit most of antihypertensive treatment. *Key words: intima media thickness, long-acting nifedipine, previously untreated hypertensive.*

INTRODUCTION

Many studies have shown cross-sectional associations between carotid intima media thickness (IMT), measured by ultrasonography, and cardiovascular risk factors [1–4], the prevalence of cardiovascular disease [5, 6] and the presence of atherosclerosis in other arterial beds [7]. Changes in IMT have been used as surrogate endpoint in determining the success of interventions that lower the levels of low-density lipoprotein cholesterol [8]. So far, few studies have looked at the effects of antihypertensive drugs on carotid IMT in hypertensive patients [9].

The possibility that antihypertensive drugs, in particular calcium-channel blockers, exert an anti-atherosclerotic action that is at least partly independent of their blood pressure-lowering effect is supported by evidence obtained from several experimental models of atherosclerosis [10–12]. Three clinical, randomized trials have used B-mode carotid ultrasound to compare long-term treatment of a calcium-channel blocker with a diuretic agent in assessing vascular changes in hypertensive patients. The Multicenter Isradipine Diuretic Atherosclerosis Study (MIDAS) [13] concluded that isradipine and the diuretic hydrochlorothiazide had similar effects on progression of carotid artery wall lesions, whereas the Verapamil Hypertension Atherosclerosis Study (VHAS) [14] concluded that the calcium-channel blocker verapamil had a greater effect on the progression of carotid artery wall than the diuretic chlorthalidone. Recently, the International Nifedipine GITS Study (INSIGHT) [15] reported a difference in early carotid wall changes in favor of the calcium-channel antagonist nifedipine compared to co-amilorizide after 4 years of treatment in hypertensive patients. Little is known about the short- and intermediate-term effects of dihydropyridines calcium-channel blockers on peripheral arterial walls in hypertensive patients. Furthermore, whether the above-mentioned long-term effects of antihypertensive drugs on arterial

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walls exist already after intermediate-term treatment is mainly unknown.

Therefore, the aim of our study was to determine the intermediate-term (26 weeks) effects of the long-acting dihydropyridine calcium-channel blocker nifedipine on carotid and femoral IMT in previously untreated asymptomatic hypertensive patients.

METHODS

Patients

Subjects were drawn from a population survey performed in two rural municipalities in the northern part of the Netherlands. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured in sitting position after 5 min of rest using the right arm. Those with previously untreated hypertension (to be defined as four measurements of SBP between 160 and 220 mmHg and/or DBP between 95 and 115 mmHg derived from multiple measurements made on three occasions over a period of 4 weeks) were included in the study. Exclusion criteria were all forms of secondary hypertension (tested by history and physical examination), mean sitting DBP greater than 115 mmHg, total cholesterol greater than 8 mmol/l, clinically significant heart failure or valvular heart disease with hemodynamic consequences; cardiac arrhythmias, pacemaker and myocardial infarction within the last 6 months; concomitant disease of the liver (liver function test > twice the upper limit of normal), kidneys (creatinine >160 μmol/l), angina pectoris, insulin-dependent diabetes mellitus, use of antilipemic drugs, alcohol or drug abuse, any therapy known to affect absorption and the inability to give consent to participate in the study.

Treatment regimen

Treatment was started with long-acting nifedipine 30 mg. After 4 weeks, the dose was uptitrated to 60 mg, unless SBP had fallen to ≤140 mmHg and/or DBP ≤90 mmHg with a minimum decrease of 10 mmHg. If patients adjusted to the higher dose developed symptoms related to hypotension, their dose was adjusted. In patients with inadequate therapeutic response to 60 mg nifedipine (defined as a SBP > 180 mmHg or a DB*P* > 105 mmHg) 12.5 mg hydrochlorothiazide was added. If response was still inadequate after another 4 weeks, the hydrochlorothiazide dose was doubled to 25 mg, as a last titration step. When response was still inadequate after this last titration step, patients were excluded from the study. Blood pressure and heart rate were measured at baseline and after 4, 8, 18 and 26 weeks of treatment.

Office blood pressure measurements

At each visit, blood pressure was measured twice with at least a 2-min interval in the sitting position. The arm in which the higher blood pressure values were measured at the start of the study was used for further measurements. The heart rate was taken immediately after the first blood pressure measurement in the sitting position by counting the pulse for at least 1 min.

Ambulatory blood pressure monitoring

Ambulatory blood pressure (ABP) was measured at baseline and after 6 months of treatment using SpaceLabs 90207 equipment (SpaceLabs Inc. Redmond Washington, USA). ABP was recorded every 30 min during the daytime (07.00–22.59 h) and every 60 min during nighttime (23.00–06.59 h). A cuff-size suitable to the arm circumference was selected. Patients were instructed to keep the arm still at the time of measurement and to carry out normal activities during the 24 h of measurement. Ambulatory recordings were performed only on working days, and the blood pressures were not displayed on the monitor. ABP data were analyzed without data editing using time-weighed means. At least 80% of readings must be successful; otherwise, the measurement was repeated if possible.

B-mode ultrasound

The B-mode ultrasound imaging of the carotid and the femoral arterial walls was done with an Acuson 128 (Acuson Corp., Mountain View, California, USA), equipped with a 7.0-MHz L7384 linear array transducer by two experienced and certified sonographers, who were unaware of the clinical data. The methods used to record and analyze B-mode ultrasound images have been described in detail before [16]. In short, 10 prespecified right and left carotid and femoral arterial wall segments were imaged. In the carotid artery, the arterial segment 1 cm proximal to the carotid dilatation (the common carotid artery), the arterial segment between the carotid dilation and carotid flow divider (carotid bulb) and a 1-cm-long arterial segment distal to the flow divider (internal carotid artery) were measured. In the femoral artery, a 1-cm arterial segment proximal to the femoral dilation (common femoral artery) and a 1-cm arterial segment distal to the femoral flow divider (superficial femoral artery) were measured. Of each arterial segment, 5-s real-time image sequences were stored on S-VHS. B-mode ultrasound video images were analyzed offline (S-VHS Panasonic NV-FS 100 HQ; VCR; Sony GVM-1400 QM multisync monitor; IDEN IVT-7p time base correctors, IPC 80486 personal computer equipped with DT2861 and DT2862 frame grabbers) by one reader. Image analysis software was developed in cooperation with Selzer *et al.* [17]. The IMT of the far wall was evaluated as the distance between the luminal–intimal interface and the medial–advential interface. Six carotid

and four femoral IMT data were aggregated to a single IMT value for each subject. The mean of the maximum IMT of up to 10 combined far walls was the primary endpoint of the study. The mean of the mean IMT and the mean of the minimum IMT of up to 10 combined far walls were secondary endpoints. In case macrovascular lesions were obvious and IMT was not measurable, lesions were considered plaques. Also, when IMT exceeded 1.2 mm, lesions were considered plaques. Plaques were scored as a dichotomous variable in the 10 predefined arterial segments in both the near and far walls. From repeated measurement procedures, the measurement error of variation in the population studied was calculated as 0.04 mm for the primary, combined carotid and femoral far wall IMT endpoint.

Echocardiography

Echocardiographic examinations were recorded by the same sonographer in the course of the study. An Acuson 128XP/10 (Acuson Corp., Mountain View, California, USA) with a 2.5–4.0-MHz transducer was used. Left ventricular dimensions were measured in two-dimensional mode according to the Penn Convention in the left lateral decubitus position. Three recordings were made of end diastolic left ventricular wall (LVPW), interventricular septum (IVS) and left ventricular end diastolic diameter (EDD). To estimate left ventricular mass the cube formula of Devereux & Reichek [18] was used. The left ventricular mass index was calculated by dividing left ventricular mass by body surface area.

Diastolic filling abnormalities were measured by using pulsed Doppler echocardiography. Measurements were done in the standard apical four-chamber view, with the patient in the left decubitus position. The Doppler sampling volume was placed between the tips of the mitral valve leaflets to obtain maximal filling velocities. Three recordings were made at the end of expiration. Early peak (E-peak) and atrial peak (A-peak) filling velocities were measured and their ratio (E/A ratio) calculated.

Statistical analysis

All statistical analyses (SAS software package, Cary, North Carolina, USA) were done by an independent statistical center (Trial Coordination Center, University Hospital Groningen, The Netherlands). The primary endpoint for treatment efficacy was the change in mean maximal far wall IMT. One of the secondary endpoints of the study was the change in mean mean far wall IMT and the change in mean minimum far wall IMT. Data are expressed as means $\pm$ standard error of the mean (SEM) or mean $\pm$ standard deviation (SD). Paired *t*-test or Wilcoxon sign-rank test was used to test for changes of IMT after treatment, as appropriate. Results are of the intention-to-treat type of analysis. Before the start of the study, power calculations were performed. An IMT difference of 0.12 mm was detectable (using an SD of 0.251 mm, which we found in the REGRESS study), with a power of 0.83 and an alpha of 0.05 [19]. Calculations were based on power calculations by de Groot *et al.* [19] and Salonen *et al.* [20]. To determine whether relations existed between maximum IMT, left ventricular mass, ABPs and their changes after treatment, Spearman correlations were used. To analyze which factors contribute to regression of mean maximum IMT after treatment, regression analysis was performed. The independent variables included baseline maximum IMT, change of ambulatory SBP, DBP and pulse pressure after 26 weeks of treatment. All statistical tests were two-sided with a significance level of $p < 0.05$.

RESULTS

Patients

In the population survey, 5107 inhabitants between 25 and 60 years of age had their blood pressure measured. After three serial blood pressure measurements, a total of 228 persons without antihypertensive drug treatment had DBP $\geq$95 mmHg, and 150 previously untreated persons had SBP $\geq$160 mmHg and were considered hypertensive. A check of their cholesterol levels and measurement of their blood pressure (for a fourth time) were offered. Of this remaining group, 131 patients gave written consent for the study and were included. They were treated with long-acting nifedipine, as described above, and advised to take a cholesterol-lowering diet. The population characteristics at baseline are summarized in Table I. After 26 weeks of treatment, 116 patients were still in the study, whereas 15 patients dropped out, mostly due to adverse events. A total of 23 patients had their dose reduced to 30 mg, merely because of adverse events. Reasons for not completing the 26 weeks of treatment with nifedipine were: adverse events (10), withdrawal of informed consent (two), protocol violation (two) and other (one). A total of 102 patients (78%) reported side-effects or adverse events during the study, resulting in 10 patients (8%) discontinuing the treatment with this as a primary reason. Most common side-effects probably related to drug treatment were headache ($n = 39$), ankle edema ($n = 27$) and flush ($n = 23$).

Effect of treatment on blood pressure, heart rate and metabolic variables

In the study treatment plan, nifedipine significantly reduced office blood pressures, 24-h SBP and DBP, while mean heart rate remained unchanged, as seen in Table II. Lipid profile did not change after 26 weeks of

Table I. *Baseline characteristics of 131 patients*

	Mean (range)
Age (years)	52 (27–60)
Sex (% male)	47
Smoking	
None (%)	44
Current (%)	32
Past (%)	24
Body mass index (kg/m^2)	28.5 (19.3–44.4)
SBP (mmHg)	173 (138–224)
DBP (mmHg)	100 (78–114)
24-h mean SBP (mmHg)	134 (108–165)
24-h mean DBP (mmHg)	84 (58–110)
Heart rate (beats/min)	74 (46–108)
Total cholesterol (mmol/l)	6.2 (5.0–8.0)
HDL cholesterol (mmol/l)	1.30 (0.59–2.28)
LDL cholesterol (mmol/l)	4.10 (2.47–5.61)
Triglycerides (mmol/l)	1.80 (0.32–11.07)
Glucose (mmol/l)	4.4 (3.3–13.4)
Potassium (mmol/l)	4.5 (3.7–5.7)
Creatinine (μmol/l)	84 (60–132)

SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

Table II. *Blood pressure and cholesterol levels after 26 weeks of treatment*

	Week 0	Week 26	*p*-value
24-h ABP in mmHg			
SBP	133.8 (1.0)	126.8 (0.9)	<0.0001
DBP	84.1 (0.8)	80.0 (0.7)	<0.0001
Office blood pressure in mmHg			
SBP	173 (16)	144 (12)	<0.0001
DBP	100 (7)	89 (7)	<0.0001
Total cholesterol (mmol/l)	6.2 (0.7)	6.3 (0.8)	0.391
HDL cholesterol (mmol/l)	1.30 (0.35)	1.29 (0.35)	0.774
LDL cholesterol (mmol/l)	4.10 (0.65)	4.22 (0.78)	0.152
Triglycerides (mmol/l)	1.80 (1.21)	1.75 (1.05)	0.641

Values are mean (standard deviation).

ABP, ambulatory blood pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

treatment. A total of 38 patients (28%) had blood pressures below 140/90 mmHg; 10 patients needed additional diuretic treatment to get their blood pressure below 180/105 mmHg. No patient used antilipemic drugs. Body mass index did not change after 26 weeks of treatment.

Effect of treatment on IMT

The change of mean max far wall IMT was −0.078 mm (95% confidence interval, CI −0.111 to −0.044) with $p < 0.0001$). For the secondary endpoint, the change of mean mean far wall IMT was −0.055 mm (95% CI −0.080 to −0.031) with $p < 0.0001$. The change of mean max far wall IMT and the change of mean mean far wall IMT did not differ when only participants with both baseline and 6-month measurements available (matched couples) were calculated, so the dropouts did not affect the outcome (Table III). The greatest reduction in far wall IMT was seen in the common femoral artery, in which the highest baseline IMT was found, as seen in Table IV. Moreover, in the carotid bulb and the superficial femoral artery, no significant changes were observed. The minimum far wall IMT was reduced only in the common femoral artery, which exhibited also the highest baseline value (Table IV). At baseline, the majority of the arterial plaques was found in the common femoral artery (prevalence of 34%), followed by the carotid bulb (22%) and the internal carotid artery (15%). The minority of the arterial plaques was found in the superficial femoral artery (5%) and the common carotid artery (3%). At baseline, significant correlations were found between mean maximum far wall IMT and left ventricular mass ($r = 0.27$ with $p = 0.002$), ambulatory SBP and DBP ($r = 0.22$ with $p = 0.01$ and $r = 0.18$ with $p = 0.04$,

Table III. *Change in intima media thickness (IMT) after 26 weeks of treatment*

	Mean (SEM)	*n*
Mean max far wall IMT baseline, mm	1.03 (0.02)	131
Mean max far wall IMT after 26 weeks, mm	0.94 (0.02)	116
Matched mean max far wall IMT baseline, mm	1.02 (0.02)	116
Change of mean max far wall IMT, mm	−0.08 (0.02)	116
Mean mean far wall IMT baseline, mm	0.81 (0.01)	131
Mean mean far wall IMT after 26 weeks, mm	0.75 (0.01)	116
Matched mean mean far wall IMT baseline, mm	0.81 (0.01)	116
Change of mean mean far wall IMT, mm	−0.06 (0.01)	116

Values are mean (SEM, standard error of the mean).

Table IV. *Combined left and right far wall intima media thickness (IMT) per segment at baseline and after 26 weeks of treatment*

Segment	Week	*n*	Mean (mm)	Max (mm)	Min (mm)
CCA	0	261	0.756 (0.143)	0.939 (0.182)	0.578 (0.130)
	26	230	0.724 (0.136)[a]	0.904 (0.171)[a]	0.570 (0.112)
BUL	0	252	0.895 (0.273)	1.154 (0.418)	0.645 (0.225)
	26	221	0.880 (0.352)	1.098 (0.428)	0.665 (0.277)
ICA	0	226	0.778 (0.286)	0.992 (0.416)	0.553 (0.217)
	26	201	0.720 (0.222)[a]	0.911 (0.313)[a]	0.516 (0.189)
CFA	0	250	0.996 (0.518)	1.263 (0.669)	0.725 (0.420)
	26	213	0.830 (0.440)[b]	1.045 (0.561)[b]	0.643 (0.371)[a]
SFA	0	245	0.615 (0.168)	0.780 (0.220)	0.455 (0.145)
	26	223	0.610 (0.191)	0.767 (0.250)	0.463 (0.167)

[a] $p < 0.05$; [b] $p < 0.001$.

Data are expressed as means (SD). CCA, common carotid artery; BUL, bulbus of carotid artery; ICA, internal carotid artery; CFA, common femoral artery; SFA, superficial femoral artery; Mean, mean of all mean far wall IMT; Max, mean of all maximum far wall IMT; Min, mean of all minimum far wall IMT.

respectively). Change in mean maximum IMT was not correlated with change in left ventricular mass ($r = 0.02$ with $p = 0.87$), nor with changes in ambulatory SBP and DBP ($r = 0.05$ with $p = 0.62$ and $r = 0.009$ with $p = 0.92$, respectively). Regression analysis revealed, that the reduction of maximum IMT was mostly influenced by the baseline maximum IMT ($p < 0.001$; model $R^2 = 0.11$).

Reproducibility

Ten, randomly chosen patients were re-examined, in order to reveal the measurement of variation. The measurement error of variation of the mean max far wall IMT at baseline was 0.07 mm. After 26 weeks of treatment, a second reproducibility study with the same 10 patients revealed a measurement error of variation of 0.04 mm.

Echocardiography

The mean left ventricular mass index at baseline was 97.8 g/m^2 (SEM $\pm$ 1.9). The change of left ventricular mass index after 26 weeks of open-label nifedipine treatment was -8.9 g/m^2 (95% CI -11.5 to -6.4), with $p < 0.0001$. This is a reduction of 9.1%. The mean E/A ratio at baseline was 1.04 (SEM $\pm$ 0.02), and did not significantly change after 26 weeks (change of 0.028 with 95% CI -0.006 to 0.061).

DISCUSSION

Antihypertensive therapy with the dihydropyridine calcium-channel blocker nifedipine in a long-acting formulation significantly reduced IMT of the carotid and femoral arteries in these hypertensive patients with mild hypercholesterolemia after 6 months of treatment. This reduction in IMT is probably mainly due to blood pressure reduction, although a significant relationship between reduction of blood pressure and decrease in IMT could not be observed. Our patients were slightly obese, with 30% smokers, had mild to moderate hypertension and mild hypercholesterolemia and therefore exhibit at least two risk factors for cardiovascular morbidity. Our findings comply with the findings of the long-term VHAS [14], in which verapamil reduced carotid lesions after 4 years of treatment. The greatest reduction of IMT was seen in arterial walls with the highest baseline value, as in our study. However, the relatively short-term effects of treatment on IMT could not be studied, because in the VHAS the baseline IMT value consisted of the mean of two consecutive measurements with a time span of 3 months. Therefore, possible reduction of IMT after 3 months of treatment could not be assessed. In the VHAS, this design was done in order to minimize the regression to the mean effect.

It is unlikely that the regression of IMT, found in our study, is due to regression to the mean, as we used up to 10 IMT measurements to obtain the IMT max as the primary endpoint. Moreover, IMT was not a selection criterion for the study. Furthermore, the accuracy and reproducibility were checked regularly. We used two expert sonographers and one reader, who were unaware of the patient characteristics. Reproducibility of IMT measurements in our group of patients was well within acceptable range [21]. Recently, the INSIGHT study showed that nifedipine significantly slowed down the IMT progression rate compared to the diuretic co-amilorizide, while blood pressure reductions were similar [15].

Another study supporting our findings is the long-term PREVENT study in which the effects of amlodipine vs placebo on IMT were studied in patients with angiographically documented coronary artery disease. In PREVENT, amlodipine significantly reduced carotid artery IMT after 3 years of treatment [22]. The decrease in IMT in our intermediate-term study is considerably greater than that observed in the PREVENT. The reason for this difference in IMT reduction might be that all our patients were previously untreated, while the majority of the patients in PREVENT had antihypertensive drugs and were normotensive at baseline.

One might object that our IMT measurements were not corrected for possible effects of nifedipine on diameter changes in the carotid artery. Decreases in the carotid diameter have been reported after the start of antihypertensive treatment. Such a decrease in diameter might result in an increase in IMT and thus might mask an IMT reduction in progression of atherosclerosis. In the INSIGHT study, a decrease of 1.2% in carotid lumen diameter was found for nifedipine [15]. Such effects on carotid diameter occur early after drug initiation, when pressure is reduced, and remain relatively stable without progression as the IMT changes.

Whether this decrease in IMT is due to functional vasodilatation rather than structural changes remains unclear. Ultrasound imaging cannot discriminate between the intimal layer and the medial layer of the vessel wall to distinguish true atherosclerosis viewed as a disorder restricted to the intimal layer vs the adaptive response of the medial layer to changes in tensile stress such as during hypertension [23]. However, the common carotid artery is usually spared in atherosclerosis, in contrast to the carotid bifurcation [23]. In this view, the significant reduction of IMT in the CCA segment and not in the carotid bulb, suggest a reduction of the medial layer to a probably diminished tensile stress.

Boutouyrie *et al.* [24] suggested that this effect in the carotid artery is mainly due to a reduction in local pulse pressure. Theoretically, this would imply that not only calcium-channel blockers could affect IMT, but all antihypertensive drugs, provided local pulse pressure is lowered. On the other hand, a reduction in IMT of the radial artery, being a muscular artery, was not seen in the study by Boutouyrie *et al.* [24] that compared the effects of a beta-blocker with an ACE inhibitor. In our study, we found the greatest reduction of IMT in the femoral artery, being a muscular artery, suggesting that calcium-channel blockers affect the muscular arteries as well as the elastic arteries like the carotid artery. This reduction of IMT was mostly influenced by the baseline IMT. This implies that arterial walls with thicker IMT show the most marked treatment effects, as seen in the common femoral artery of our patients.

Why calcium-channel blockers reduce IMT already within 6 months of treatment, we can only speculate. Recently, it has been shown that nifedipine improves endothelial function in patients with hypercholesterolemia, independently of an effect on blood pressure or plasma lipids [25, 26]. This effect of nifedipine is thought to be realized by the enhancement of the bioavailability of endothelial nitric oxide, possibly via an antioxidative protection [27]. This increased nitric oxide availability might contribute to the antithrombotic, antiproliferative and antiatherosclerotic effects of the dihydropyridine calcium antagonist.

The study design of the study is consistent with clinical practice. Treatment of hypertension usually starts with monotherapy. This seems insufficient nowadays, because in more than 50% of patients, as has been demonstrated in most intervention trials [28] combination therapy is necessary. In our study, nearly 30% of patients with monotherapy had a blood pressure of 140/90 mmHg or lower, whereas 8% of patients required additional diuretic treatment to get their blood pressure below 180/105 mmHg. According to the recently published JNC IV [29] and WHO-ISH [30] guidelines, additional treatment currently seems justified.

The reduction of 9.1% of left ventricular mass that we found after 26 weeks of treatment is similar in studies performed in primary care setting [31, 32]. Regression of left ventricular mass is usually associated with improvement of diastolic filling. In this study, E/A ratio did not change significantly after treatment. This may be explained by the fact that E/A ratio was not markedly abnormal before the start of treatment.

CONCLUSIONS

Our observations extend those of previous longer-term studies showing that 26 weeks of antihypertensive treatment with nifedipine treatment inhibits IMT progression in previously untreated hypertensive patients. Although this is an open-label study, the endpoint measurements were done in a blinded fashion. Therefore, the IMT reduction can be considered to represent an effect of our initiation of blood pressure lowering treatment, because the natural course of IMT consists of an increase, or during our short study period, a stable value. The clinical significance of these changes in IMT is not fully clear, but the beneficial effects of calcium-channel blockers on IMT may announce a smaller incidence of complications in the longer term. This has to be confirmed by larger studies with longer follow-up.

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