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Effect of Moxonidine on Left Ventricular Hypertrophy in Hypertensive Patients

J. Haczynski¹, A. Spring², M. Przewlocka-Kosmala², J. Flasiński³

The objective of the present study was to investigate the effect of moxonidine in left ventricular hypertrophic remodeling and to check the possible association between the moxonidine dose, blood pressure and the decrease in left ventricular mass assessed by transthoracic echocardiography in a nonrandomized prospective study.

Twenty patients completed the study (15 males = 75 %, and 5 females, mean age 47 ± 10 years). After the titration period, 8 patients (40 %) were treated with 0.6 mg, 8 patients (40 %) with 0.4 mg and 4 patients (20 %) with 0.2 mg moxonidine daily.

After the 9 month therapy period, the systolic blood pressure had decreased from 154.3 ± 10.3 to 136.2 ± 10.3 mmHg ($p < 0.001$), and the diastolic blood pressure from 99.3 ± 3.6 to 84.1 ± 5.0 mmHg ($p < 0.001$). The echocardiography showed a significant decrease in interventricular septum thickness (1.38 ± 0.1 vs 1.25 ± 0.05 mm, $p < 0.05$). The left ventricular posterior wall end-diastolic thickness and the left ventricular end-diastolic diameter did not change. The left ventricular mass decreased significantly during the moxonidine treatment period (309.7 ± 39 vs 264.6 ± 44.9 g, $p = 0.006$). There was a tendency toward an association between the dose of moxonidine and degree of left ventricular mass decrease, but the level of significance was not attained. Similarly, the decrease in systolic and diastolic blood pressure was not related to the moxonidine dose.

In conclusion, we have shown that moxonidine monotherapy effectively reduces the arterial systolic and diastolic pressure and significantly decreases the left ventricular mass. *J Clin Basic Cardiol 2001; 4: 61–65.*

Key words: arterial hypertension, blood pressure, left ventricular hypertrophy, left ventricular mass, echocardiography

Left ventricular hypertrophy (LVH) is a cardiac adaptation response to arterial hypertension in an attempt to overcome the enhanced peripheral vascular resistance. LVH has been proven to be a major independent risk factor for cardiovascular morbidity and mortality [1–6]. The exact mechanism leading to the increased occurrence of cardiac events in patients with LVH is not fully understood; it is probably multifactorial, including an increased oxygen consumption, a decreased coronary blood flow reserve, and susceptibility to malignant atrial and ventricular arrhythmias [7–12]. Cardiac hypertrophy comprises cardiomyocyte hypertrophy, interstitial fibrosis, and consequent structural alterations in the coronary microcirculation with a decreased coronary flow reserve, which results in impairment of the diastolic and systolic function of the left ventricle despite the normal anatomy of the epicardial coronary arteries [13]. Doppler-echocardiographic studies have demonstrated that the impairment of the left ventricular (LV) diastolic function precedes the development of the systolic dysfunction in patients with systemic arterial hypertension [14, 15].

It is currently considered that antihypertensive treatment can result not only in blood pressure normalization but also in an improvement of hypertensive cardiac remodeling via reversing myocyte hypertrophy, restoring the myocardial structure, and improving the coronary flow reserve [16].

Since the sympathetic nervous system is of main importance in the control of the function of the cardiovascular system and the development of hypertensive complications, the blocking of the sympathetic activity may prevent and reverse unfavorable consequences of high blood pressure. The classic centrally acting antihypertensive agents lower blood pressure by reducing excessive sympathetic tone; however, their clinical use is limited by an adverse effect profile resulting from α_2 -adrenoceptor agonism. Moxonidine is a central-

ly acting agent with selective agonism of imidazoline I1 receptors, but with very little α_2 -adrenoceptor agonism [17, 18]. Moxonidine reduces peripheral sympathetic nerve activity via blockade of the catecholamine secretion in the adrenal medulla too, and cause peripheral vasodilatation with mild bradycardia [19, 20]. Furthermore, moxonidine also blocks the release of renin in the kidneys, decreases albuminuria and improves glucose tolerance in humans [21–25]. The clinical efficacy and safety of moxonidine in the treatment of hypertension have been investigated and proven in over 70 clinical studies [26].

Moxonidine significantly decreases cardiac fibrosis, the activation and proliferation of interstitial cells, the media hypertrophy of small arteries and the focal degeneration of myocytes in spontaneously hypertensive rats [21, 27]. Using magnetic resonance tomography Eichstädt et al. demonstrated a cardiac hypertrophy regression after a 6 month treatment with moxonidine [28, 29]. A study on a small number (12) of patients revealed significant decreases in LV and septal wall thickness and a reduced ventricular volume, similar to the effects of nifedipine [30].

The objective of the present study was to investigate the effect of moxonidine in LV hypertrophy and to check the possible association between the moxonidine dose, the blood pressure and the decrease in left ventricular mass (LVM) assessed by transthoracic echocardiography in a nonrandomized prospective study.

Methods

Between April 1996 and November 1997, 25 patients at 2 cardiac centers (Cardiology Clinic, Wrocław University of Medicine, and Marine Institute, Gdynia, Poland) were prospectively included in the study. The patients had mild to moder-

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ate essential hypertension (diastolic blood pressure between 95 and 114 mmHg as an average of 3 consecutive measurements in sitting position with 2 minute time differences) and LVH assessed by transthoracic echocardiography. LVH was defined according to the criteria of the American Society of Echocardiography (interventricular septum and posterior wall end-diastolic diameter [IVS, PW and EDD, respectively] ≥ 13 mm) [31]. The patients had none of the following exclusion criteria: haemodynamically significant coronary artery stenosis, unstable angina, chronic heart failure stage at least NYHA III, left ventricular dilatation as assessed by echocardiography, age ≤ 18 year, pregnancy, clinically relevant cardiac rhythm disturbances, concomitant cardiac valve diseases, decreased systolic function, regional wall motion disturbances, renal and liver insufficiency or present concomitant antihypertensive therapy.

All clinical and echocardiographic examinations were in accordance with institutional guidelines. The research protocol was approved by the locally appointed ethics committee and the informed consent of the subjects was obtained.

The moxonidine (Cynt®) treatment included 8 week titration and a 36 week therapy period. The titration period was started (visit 1) with 0.2 mg moxonidine daily in the morning. After 3 weeks (visit 2), if the treatment was not efficacious (systolic blood pressure > 140 mmHg and/or diastolic blood pressure > 90 mmHg), the daily dose was increased to 0.4 mg in the morning. After the next 3 weeks (visit 3), if the dose of 0.4 mg had not normalized the blood pressure, it was increased to 0.6 mg daily (0.4 mg in the morning and 0.2 mg in the evening) for the next 2 weeks. In the event of ineffectiveness at visit 4, (0.6 mg moxonidine daily did not normalize the blood pressure), the moxonidine therapy was supplemented with another antihypertensive agent and the patient was excluded from the study ($n = 3$). Besides the 3 patients in whom moxonidine monotherapy was ineffective, 1 patient discontinued the moxonidine therapy due to headache, and 1 patient discontinued it without giving any reason. The remaining 20 patients continued the next 9 month therapy period with their optimal individual dose as established in the titration period. All patients were clinically evaluated at 3 month intervals (visits 5, 6 and 7), and echocardiography was performed.

The left ventricular dimensions (IVS, PW and LV EDD) were measured in the supine position in the transthoracic longitudinal axis view, using 2-dimensional echocardiographic images. The echocardiographic measurements were checked by using transthoracic short axis views and apical 4-chamber views. In the evaluation of the echocardiograms, the standard views were used after the recommendations of the American Society of Echocardiography [31].

The LVM calculated according to the formula of Devereux and Reichek [32]:

$$\text{LVM} = 1.04 \times [(\text{IVSEDD} + \text{PWEDD} + \text{LVEDD})^3 - (\text{LVEDD})^3] - 13.6 \text{ [g]}$$

All data on systolic and diastolic blood pressures and heart rate (average of 2 measurements in sitting position), drug-

related adverse events and clinical symptoms and echocardiographic results were recorded at each visit for all patients.

Statistics

The continuous variables of the group at each visit were expressed as means $\pm$ standard deviation. The differences between the values at visits 5, 6 and 7 were tested by using one-way analysis of variance with repeated measurements, supplemented with Tukey-Kramer post-hoc analyses. A difference was considered significant if $p < 0.05$.

Results

Baseline data

Twenty patients completed the study (15 males = 75 % and 5 females, mean age 47 ± 10 years). After the titration period, 8 patients (40 %) were treated with 0.6 mg, 8 patients (40 %) with 0.4 mg and 4 patients (20 %) with 0.2 mg moxonidine daily.

Table 1 lists the baseline clinical and echocardiographic data on the 20 patients.

Effectivity of moxonidine monotherapy

After the 9 month therapy period, the systolic blood pressure had decreased from 154.3 ± 10.3 to 136.2 ± 10.3 mmHg ($p < 0.001$), and the diastolic blood pressure from 99.3 ± 3.6 to 84.1 ± 5.0 mmHg ($p < 0.001$). The systolic and diastolic blood pressures had normalized already by visit 5, and remained constantly in the normal range during the further treatment period. The heart rate did not change during the study (Table 2).

The echocardiography already showed a significant decrease in IVS thickness at visit 5 (from 13.8 ± 1.0 to 13.2 ± 0.4 mm, $p < 0.05$), though it was still in the pathological range. Further gradual decreases in the IVS were observed at visits 6 and 7. At the end of the treatment period the septum thickness was already in the normal range (12.5 ± 0.5 mm) (Figure 1).

A tendency of the PW end-diastolic thickness to decrease was observed, but the change did not reach the level of sig-

Table 1. Baseline characteristics of the study patients

	Clinical data
Risk factors	
Smoker	7 (35 %)
Diabetes mellitus	1 (5 %)
Hyperlipidaemia	16 (80 %)
Family history of hypertension	16 (80 %)
ECG	
Left ventricular hypertrophy without strain	13 (65 %)
Left ventricular hypertrophy with strain	1 (5 %)
Left bundle branch block	2 (10 %)
Right bundle branch block	4 (20 %)
Echocardiography	
Enlargement of the left atrium	2 (10 %)
Mitral valve prolapse	3 (15 %)
Mild mitral insufficiency	1 (5 %)
Diastolic function disturbances	16 (80 %)

Table 2. Systolic and diastolic blood pressure with heart rate at baseline (visit 1), after 3 months (visit 5) 6 months (visit 6) and 9 months (visit 7) moxonidine monotherapy. BP=blood pressure

	Baseline (visit 1)	Visit 5	Visit 6	Visit 7	p value
BP systolic [mmHg]	154.3 ± 10.3	137.4 ± 4.4	136.8 ± 9.5	136.2 ± 10.3	< 0.001
BP diastolic [mmHg]	99.3 ± 3.6	85.7 ± 4.5	83.7 ± 4.9	84.1 ± 5.0	< 0.001
Heart rate [bpm]	71.8 ± 9.4	73.9 ± 6.4	73.5 ± 5.7	74.6 ± 5.8	n.s.

nificance (from 11.6 ± 1.08 to 10.5 ± 0.17 mm, $p = 0.208$) (Figure 2).

The moxonidine treatment did not influence the LVEDD (from 50.7 ± 3.0 to 50.2 ± 2.4 mm, $p = 0.937$) (Figure 3).

The LVM decreased significantly during the moxonidine treatment period ($p=0.006$), though it reached the level of significance only at visit 6 (6 month treatment period) (from baseline: 309.7 ± 39.0 g to 268.3 ± 43.1 g, $p < 0.05$), then remained constant until the end of the study (264.6 ± 44.9 g; decrease of 14.6 %) (Figure 4).

There was a tendency toward a relationship between the dose of moxonidine and degree of LVM decrease, but the level of significance was not attained (Table 3). Similarly, the decrease in systolic and diastolic blood pressure did not relate to the moxonidine dose (Table 3).

During the 9 month moxonidine treatment, 2 patients (10 %) reported dry mouth, 2 patients (10 %) suffered from headache, eye haemorrhagia developed in 1 patient (5 %), and in another patient (5 %) temporary hypotension was ob-

served. A serious drug-related adverse event, a transient cerebral ischaemic attack with transient left hemiparesis, occurred in 1 patient (5 %) in the eighth month of moxonidine treatment, but after a few weeks, all the neurological symptoms had disappeared; the moxonidine treatment was replaced with another antihypertensive treatment. No other drug-related serious adverse event was recorded.

After the 9 month effective moxonidine monotherapy, no ECG changes were seen.

Table 3. Effect of different moxonidine doses on decrease in left ventricular mass, systolic and diastolic blood pressure. BP= blood pressure

	Decrease in left ventricular mass [g]	Decrease in systolic BP [mmHg]	Decrease in diastolic BP [mmHg]
0.2 mg	22.9 ± 14.6	13 ± 10	16 ± 4
0.4 mg	48.4 ± 50.8	24 ± 10	15 ± 7
0.6 mg	58.8 ± 63.4	42 ± 60	32 ± 36

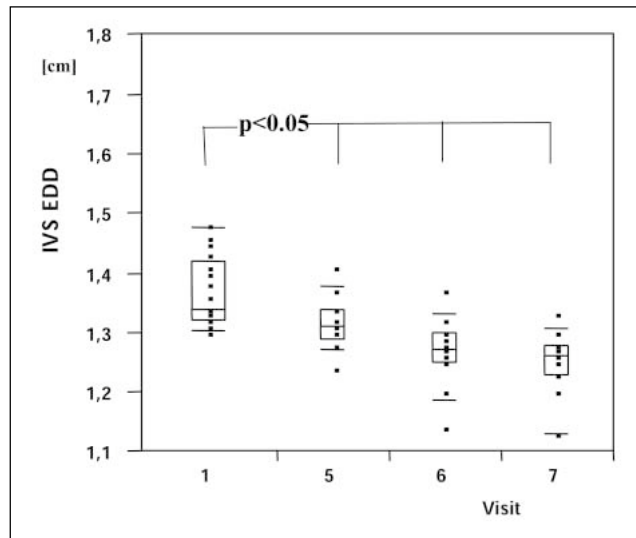


Figure 1. Interventricular septum end-diastolic diameter (IVS EDD) at baseline (visit 1) and after 3 month (visit 5), 6 month (visit 6) and 9 months (visit 7) moxonidine monotherapy.

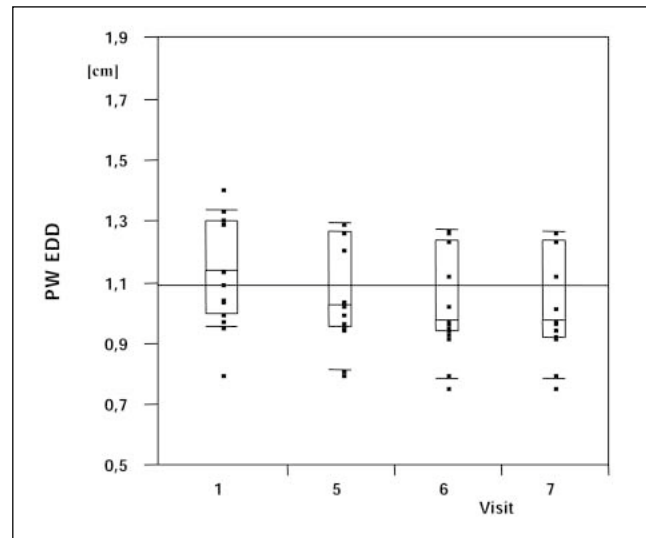


Figure 2. Left ventricular posterior wall end-diastolic diameter (PW EDD) at baseline (visit 1) and after 3 month (visit 5), 6 month (visit 6) and 9 month (visit 7) moxonidine monotherapy.

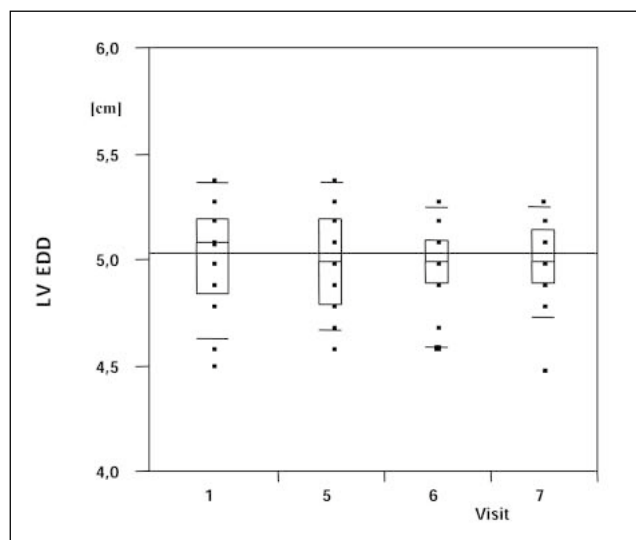


Figure 3. Left ventricular end-diastolic diameter (LV EDD) at baseline (visit 1) and after 3 month (visit 5), 6 month (visit 6) and 9 month (visit 7) moxonidine monotherapy.

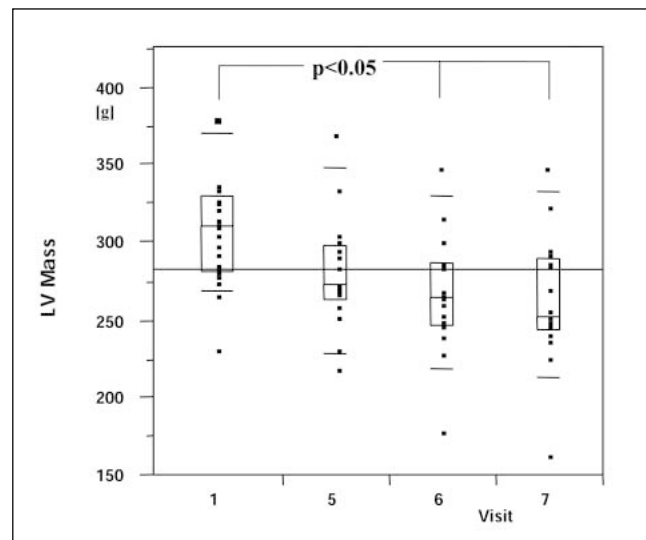


Figure 4. Left ventricular (LV) mass at baseline (visit 1) and after 3 month (visit 5), 6 month (visit 6) and 9 month (visit 7) moxonidine monotherapy.

Discussion

This prospective clinical study has shown that moxonidine monotherapy effectively reduces the arterial systolic and diastolic pressure and consequently results in a significant decrease in LVM. The moxonidine was well tolerated and, apart from some mild, possibly drug-related complaints, only one serious adverse event (a transient cerebral ischaemic attack) occurred, with transient neural symptoms but without any serious lasting damage.

Sympathetic overstimulation plays an important role in myocardial hypertrophy. Trimarco et al. demonstrated an association between changes in left ventricular mass and sympathetic activity in humans [33]. It has also been found that addition of noradrenaline to isolated cultured myocytes can provoke a growth response and an increment in protein synthesis [19–23]. Neurohumoral factors involved in the induction of LVH include activation of the renin-angiotensin system and an increased sympathetic tone [19]. Additionally, experimental studies suggest that angiotensin II may stimulate cardiac protein synthesis too, through induction of proto-oncogenes and growth factors [34, 35]. Consequently, prolonged antihypertensive therapy may reverse LVH through favorable hemodynamic changes, while antisymphomimetic therapy decreases the left ventricular mass directly, even after only a short treatment period [36–38].

Together with ventricular remodeling in LVH, structural remodeling of the coronary arteries occurs, causing a decrease in coronary vasodilator reserve. The maximal coronary blood flow in hypertensive patients is reduced by about 30–50 % and is thought to be the main reason for the coronary insufficiency, despite normal epicardial coronary artery morphology. It could be expected that the antihypertensive treatment may prevent or even reverse the unfavorable left ventricular and coronary vascular remodeling, which can lead to a decrease in mortality and morbidity in hypertensive patients.

The most important question from an epidemiological point of view is whether the regression of LVH improves the patient's outcome and overall prognosis. Evidence is emerging that the diastolic and even the systolic cardiac function may improve after the regression of cardiac hypertrophy, which could be followed by restoration of the myocardial compliance and coronary vascular reserve. Yurenev et al. showed that the progression of LVH in spite of a 4 year course of antihypertensive treatment was related to a higher incidence of cardiovascular event [39]. Similar results were reported by Koren et al., who found that an increase in left ventricular mass during treatment of systemic hypertension seems to be a negative prognostic factor [6]. A report from the Framingham Study verified an association between the incidence of cardiovascular disease and LVH determined by ECG during a 2 year follow-up period [40]. Similarly Muiesan et al. noted that a reduction in LVH was accompanied by a decrease in the risk of adverse cardiovascular events [41]. We observed only one major cardiac event in one patient, who suffered a transient cerebrovascular event with transient neurological symptoms. Unfortunately, the relatively small number of the included patients does not allow a statement about a possible correlation between a decrease in LVH and the infrequent occurrence of cardiovascular events in our patients.

Drugs that centrally inhibit sympathetic stimulation are known to produce a higher regression of LVH than those that only lower the blood pressure via other channels [20]. It has been demonstrated that antihypertensive treatment with other central sympathomimetic blockers (clonidine and rilmenidine) was followed by a marked decrease in left ventricular mass [22, 36]. Erichstädt et al. studied the influence of a

6 month treatment with moxonidine in a daily dose of 0.2–0.4 mg in 20 hypertensive patients, and found a significant regression of LVH as assessed by magnetic resonance imaging [28, 29]. Similarly, in our study, we have also demonstrated a significant decrease in left ventricular mass reaching a significance after a 6 month treatment period documented by echocardiography. There was a tendency for left ventricular mass decrease as the dose of moxonidine was increased, but it did not reach the level of significance. In contrast, there was no association between the moxonidine dose and the improvement in blood pressure.

Moxonidine proved to be a safe and generally effective drug. No patient died during the study, and only one serious adverse event (a transient ischaemic attack without a lasting neurological deficit) was reported. The most common adverse events were dry mouth (10 %) and headache (10 %) which were usually only transitory. Moxonidine administration was well tolerated over a broad dose range (0.2–0.6 mg) and a therapy duration of up to 11 months.

Limitations

This was a nonrandomized prospective study, with clear disadvantages resulting from the lack of a randomized control group. However, patients with essential hypertension and LVH in echocardiography can not be treated with placebo from an ethical point of view. The solution of this problem could be a randomization setup into two arms, moxonidine versus some other antihypertensive drug. However, our study was planned to establish the effect of moxonidine treatment in LVH in a self-control study. Thus, differences between baseline and follow-up data were compared. The significance of the changes in arterial blood pressure and echocardiographic findings is convincing.

The major limitation of the study is the relatively small number of patients. However, the very strict inclusion and exclusion criteria meant that a relatively homogeneous group of patients were enrolled allowing a much better evaluation of the study.

Unfortunately, the left ventricular diastolic parameters were not quantified, although an improvement in diastolic dysfunction could be expected after the decrease in left ventricular mass. However, measurement of the left ventricular diastolic parameter was not the aim of the study.

Similarly, determinations of the plasma adrenaline, noradrenaline, angiotensin, and other hormones involved in the regulation of blood pressure could enhance the value of the investigation.

In conclusion, the present study has shown that long-term moxonidine treatment can efficiently decrease both the systolic and diastolic blood pressures without changing the heart frequency. In parallel with the constant blood pressure reduction, the left ventricular concentric hypertrophy regressed, the interventricular septum thickness and, consequently, the left ventricular mass decreased significantly. Thus, moxonidine can effectively prevent the unfavourable left ventricular remodeling. Beside some mild, probably drug-related complaints, only one drug-related serious adverse event occurred. The present study proves the safety and efficacy of moxonidine treatment in patients with essential hypertension.

References

1. Grossman W, Jones D, McLaurin LP. Wall stress and patterns of hypertrophy in the human left ventricle. *J Clin Invest* 1975; 56: 56–64.
2. Ganau A, Devereux RB, Pickering TG. Relation of left ventricular hemodynamic load and contractile performance to left ventricular mass in hypertension. *Circulation* 1990; 81: 25–36.
3. Kannel WB, Gordon T, Castelli WP, Margolis JR. Electrocardiographic left

- ventricular hypertrophy and risk of coronary heart disease: the Framingham Study. *Ann Intern Med* 1970; 72: 813–22.
4. Levy D, Garrison RJ, Savage DD, Kannel WB, Castelli WP. Prognostic implication of echocardiographically determined left ventricular mass in the Framingham Heart Study. *N Engl J Med* 1990; 322: 1561–6.
 5. Sullivan JM, Vander Zwaag RV, el-Zeky F, Ramanathan KB, Mirvis DM. Left ventricular hypertrophy: effect on survival. *J Am Coll Cardiol* 1993; 33: 508–13.
 6. Koren MJ, Devereux RB, Casale PN, Savage DD, Laragh JH. Relation of left ventricular mass and geometry to morbidity and mortality in uncomplicated essential hypertension. *Ann Intern Med* 1991; 114: 345–52.
 7. Pichard AD, Gorlin R, Smith H, Ambrose J, Meller J. Coronary flow studies in patients with left ventricular hypertrophy of the hypertensive type. *Am J Cardiol* 1981; 47: 547–54.
 8. Houghton JL, Frank MJ, Carr AA, von Dohlen TW, Prisant M. Relations among impaired coronary flow reserve, left ventricular hypertrophy and thallium perfusion defects in hypertensive patients without obstructive coronary artery disease. *J Am Coll Cardiol* 1990; 15: 43–51.
 9. Strauer BE, Schwartzkopf B, Motz W, Vogt M. Coronary vascular changes in the progression and regression of hypertensive heart disease. *J Cardiovasc Pharmacol* 1991; 18 (Suppl): S20–S27.
 10. McLenachan JM, Henderson E, Morris KL, Dargie HJ. Ventricular arrhythmias in patients with hypertensive left ventricular hypertrophy. *N Engl J Med* 1987; 317: 787–92.
 11. Garrañ H. Vulnerability to ischemic ventricular arrhythmias in left ventricular hypertrophy. Editorial comment. *J Am Coll Cardiol* 1989; 14: 1374–5.
 12. Varizi SM, Larson MG, Benjamin EJ, Levy D. Echocardiographic predictors of nonrheumatic atrial fibrillation. The Framingham Heart Study. *Circulation* 1994; 89: 724–30.
 13. Motz W, Vogt M, Scheler S, Schwartzkopf B, Strauer BE. Coronary circulation in arterial hypertension. *J Cardiovasc Pharmacol* 1991; 17 (Suppl 2): S35–S39.
 14. Miyazaki S, Guth BD, Miura T, Indolfi C, Schulz R, Ross J. Changes of the left ventricular diastolic function in exercising dogs without and with ischemia. *Circulation* 1990; 81: 1058–70.
 15. Miura T, Miyazaki S, Guth BD, Indolfi C, Ross J. Heart rate and force-frequency effects on diastolic function of the left ventricle in exercising dogs. *Circulation* 1994; 89: 2361–8.
 16. Amann K, Greber D, Gharehbaghi H, Wiest G, Lange B, Ganten U, Mattfeld T, Mall G. Effects of nifedipine and moxonidine on cardiac structure in spontaneously hypertensive rats. Stereological studies on myocytes, capillaries, and cardiac interstitium. *Ann J Hypertens* 1992; 5: 76–83.
 17. Elliott HL. Moxonidine: pharmacology, clinical pharmacology and clinical profile. *Blood Press* 1998; Suppl 3: 23–7.
 18. Schachter M. Moxonidine: a review of safety and tolerability after seven years of clinical experience. *J Hypertens* 1999; 17: S37–S39.
 19. Swedberg K, Bergh CH, Dickstein K, McNay J, Steinberg M. The effects of moxonidine, a novel imidazoline, on plasma norepinephrine in patients with congestive heart failure. Moxonidine Investigators. *J Am Coll Cardiol* 2000; 35: 398–404.
 20. Prichard BNC, Graham BR, Owens CWI. Moxonidine: a new antiadrenergic antihypertensive agent. *J Hypertens* 1999; 17: S41–S54.
 21. Prichard BN, Owens CW, Graham BR. Pharmacology and clinical use of moxonidine, a new centrally acting sympatholytic antihypertensive agent. *J Hum Hypertens* 1997; 11: S29–S45.
 22. Bousquet P, Feldman J. Drugs acting on imidazoline receptors. A review of their pharmacology, their use in blood pressure control and their potential interest in cardioprotection. *Drugs* 1999; 58: 799–812.
 23. Van Zwieten PA, Peters SLM. Central 11-imidazoline receptors as targets of centrally acting antihypertensive drugs. *Clinical pharmacology of moxonidine and rilmenidine*. *Ann NY Acad Sci* 1999; 881: 420–9.
 24. Hansson L. Therapy of hypertension and metabolic syndrome: today's standard and tomorrow's perspectives. *Blood Press* 1998; Suppl 3: 20–2.
 25. Haenni A, Lithell H. Moxonidine improves insulin sensitivity in insulin-resistant hypertensives. *J Hypertens* 1999; 17: S28–S35.
 26. Schachter M, Luszyk J, Jäger B, Verboom C, Sohlke E. Safety and tolerability of moxonidine in the treatment of hypertension. *Drugs Saf* 1998; 19: 191–203.
 27. Mall G, Greber D, Gharehbaghi H, Wiest G, Amann K, Mattfeld T. Effects of nifedipine and moxonidine on cardiac structure in spontaneously hypertensive rats (SHR) – stereological studies on myocytes, capillaries, and cardiac interstitium. *Basic Res Cardiol* 1991; 86: 33–44.
 28. Eichstaedt H, Schroeder RJ, Auffermann W, Richter W. Regression of left ventricular hypertrophy. *J Cardiovasc Pharmacol* 1992; 19: S55–S61.
 29. Eichstaedt H, Richter W, Bäder M. Demonstration of hypertrophy regression with magnetic resonance tomography under the new adrenergic inhibitor moxonidine. *Cardiovasc Drugs Ther* 1989; 3: S583–S587.
 30. Hüting J, Mitrovic V, Bahavar H. Vergleich der Wirkungen von Moxonidine und Nifedipine auf die linksventrikuläre Funktion bei Monotherapie der essentiellen Hypertonie. *Herz Kreislauf* 1992; 24: 132–6.
 31. Sahn DJ, DeMaria A, Kisslo J, Weymann A. The Committee on M-mode standardisation of the American Society of Echocardiography. Recommendations regarding quantitation in M-mode echocardiography: results of a survey of echocardiographic measurements. *Circulation* 1978; 58: 1072–83.
 32. Devereux RB, Reichek N. Echocardiographic determination of left ventricular mass in man: anatomic validation of the method. *Circulation* 1977; 55: 613–20.
 33. Trimarco B, Ricciardelli B, De Luca N, De Simone A, Cuocolo A, Galva MD, Picotti GB, Condorelli M. Participation of endogenous catecholamines in the regulation of left ventricular mass in progeny of hypertensive patients. *Circulation* 1985; 72: 38–46.
 34. Katz AM. Angiotensin II: hemodynamic regulator or growth factor? *J Mol Cell Cardiol* 1990; 22: 739–47.
 35. Sadoshima JI, Izumo S. Molecular characterization of angiotensin II-induced hypertrophy of cardiac myocytes and hyperplasia of cardiac fibroblasts: critical role of AT1 receptor subtype. *Circ Res* 1993; 73: 413–23.
 36. Hüting J, Mitrovic V, Thormann J, Bahavar H, Schlepper M. Left ventricular muscle mass and diastolic function in patients with essential hypertension under long-term clonidine treatment. *Clin Cardiol* 1991; 14: 134–40.
 37. Dahlöf B, Pennert K, Hansson L. Reversal of left ventricular hypertrophy in hypertensive patients. A metaanalysis of 109 treatment studies. *Am J Hypertens* 1992; 5: 95–110.
 38. Motz W, Vogt M, Scheler S, Strauer BE. Hypertensive coronary microcirculation effects of the imidazoline-receptor-agonist moxonidine. *Cardiovasc Risk Factors* 1995; 5: 28–32.
 39. Yureniev A, Dyakonova H, Navikov I, Vitols A, Haynemann P. Management of essential hypertension in patients with different degrees of left ventricular hypertrophy: multicenter trial. *Am J Hypertens* 1992; 5 (Suppl): S182–9.
 40. Levy D, Salomon M, D'Agostino, Belanger AJ, Kannel WB. Prognostic implications of baseline electrocardiographic features and their serial changes in subjects with left ventricular hypertrophy. *Circulation* 1994; 90: 1786–93.
 41. Muiesan M, Salvetti M, Rizzoni D, Castellano M, Donato F, Agabiti-Rosei E. Association of change in left ventricular mass with prognosis during long-term antihypertensive treatment. *J Hypertens* 1995; 13: 1091–5.

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