# ANTIHYPERTENSIVE DRUGS EFFECTS ON GLUCOSE, INSULIN METABOLISM, LEFT VENTRICULAR MASS: A RANDOMIZED,DOUBLE−BLIND, CONTROLLED STUDY

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*Background*—Glucose and insulin levels are associated with left ventricular mass (LVM) in insulin-resistant individuals .The association between obesity and cardiovascular disease is well established, and up to 60% of overweight or obese patients have hypertension. Dietary interventions associated with modest weight loss are effective in controlling blood pressure and in reducing use of antihypertensive drug therapy in overweight and obese patients. However, long-term maintenance of weight loss is achieved only in a small proportion of patients. Antihypertensive drugs have different effects on glucose and insulin metabolism (GIM) and on LVM. . Consequently, antihypertensive drug therapy is often necessary in addition to weight loss interventions. Few studies have investigated different antihypertensive drugs, specifically in overweight and obese patients with hypertension. To evaluate whether the effects of antihypertensive therapy on LVM are associated with its effects on GIM, we compared the effects of telmisartan and aliskiren on these parameters in a group of insulin-resistant, obese hypertensives. *Methods and Results*—A total of 41 obese, nondiabetic hypertensives who were aged 55±6 years, had a body mass index of 32.8±5.0 $kg/m^2$, were free of coronary or valvular heart disease, and had normal LV function were randomized to treatment with telmisartan (n=21) or aliskiren(n=20). Echocardiographic LVM corrected for height (LVM/height) , GIM (3-hour intravenous glucose tolerance test) and albuminuria were measured after 4 to 6 weeks of washout and 6 months of treatment. Baseline characteristics were similar in both groups. Telmisartan and aliskiren effectively reduced blood pressure (from 149±13/98±4 to 127±8/82±6 mm Hg and from 148±9/98±4 to 129±9/82±6 mm Hg, respectively, for the telmisartan and aliskiren groups; $P$=0.002). Telmisartan significantly worsened GIM parameters, fasting glucose levels (5.3±0.9 to 6.0±1.5 mmol/L; $P$=0.003), fasting insulin levels (121±121 to 189±228 pmol/L; $P$=0.03), and most other relevant metabolic measures ($P$<0.05 for all). Aliskiren did not affect GIM. Telmisartan did not affect LVM/height (119±12 to 120±17 g/m; $P$=0.8), whereas aliskiren significantly reduced LVM/height (120±13 to 111±19 g/m; $P$=0.04). Upon BP control, microalbuminuria was markedly decreased in both group ($P$=0.002). *CONCLUSIONS*: In the absence of weight loss, most patients required combined antihypertensive therapy to control their BP, regardless of their body fat distribution pattern. Optimal target BP and normal albuminuria were achieved in the group as a whole and in both obese patient groups, while benefits to cardiac structure were of a smaller magnitude. High-risk, overweight/obese patients with hypertension and type 2 diabetes, Telmisartan provides significantly greater BP lowering versus Aliskiren throughout the 24-hour dosing interval, particularly during the hazardous early morning hours. Therefore In obese, hypertensive individuals, adequate and similar blood pressure control was achieved with telmisartan and aliskiren ;however, aliskiren but not telmisartan was associated with a more favorable GIM profile and led to a significant regression of LVM.

# Utility of B-natriuretic peptide levels in identifying elderly diabetic hypertensive patients with left ventricular systolic or diastolic dysfunction, as an Early Manifestation of Diabetic Cardiomyopathy .
## -Reversal by Chronic Angiotensin II Type 1A Receptor Blockade-

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**Background** We attempted to test the hypothesis that chronic angiotensin II type 1A receptor blockade (ARB)alters myocardial collagen turnover leading to an improvement of diastolic dysfunction in diabetic patients. While the mechanisms underlying it and the changes in left ventricular systolic function, diastolic function, and mitral regurgitation during long-term therapy remain unclear. On the other hand although echocardiography is important for making the diagnosis of left ventricular dysfunction, its cost and lack of availability limit its use as a routine screening test. B-natriuretic peptide(BNP) levels accurately reflect ventricular pressure, and preliminary studies with a rapid assay have found that levels are sensitive and specific for diagnosing heart failure in patients with dyspnea. We hypothesized that BNP levels obtained through the use of a rapid assay should correlate with echocardiographic abnormalities of ventricular function **.Objective** To identify the clinical and functional effects of telmisartan, focusing on diastolic function , mitral regurgitation variations.and and Plasma BNP Level .**Methods and Results** Fifty two type 2 diabetic hypertensies who were aged 67±5 years ,were divided into 2 groups: 30 treated with telmisartan for 6 months, and 22 without telmisartan, as controls. Doppler mitral flow velocity pattern and biomarkers of BNP levels were measured by a point-of-care immunoassay; cardiologists assessing left ventricular function were blinded to the assay results. They were assessed before and after ARB telmisartan during a 6-month period .Patients were grouped into those with normal ventricular function, systolic dysfunction only, diastolic dysfunction only, and both systolic and diastolic dysfunction. After 6 months of treatment with telmisartan, left ventricular ejection fraction had increased from 24% ± 7% to 29% ± 9% ($P < .0001$); this change was caused by a reduction in end-systolic volume index (106 ± 41 vs 93 ± 37 ml/m$^2$; $P < .0001$). Deceleration time of early diastolic filling increased (134 ± 74 vs 196 ± 63 ms; $P < .0001$). Seventeen of the 28patients with demonstrated improvement of left ventricular diastolic filling moved from having a restrictive filling pattern to having a normal or pseudonormal left ventricular filling pattern. In the control group, no signigicant changes in deceleration time of early diastolic filling were found (139 ± 74 vs 132 ± 45 ms; $P$ = not significant). The effective regurgitant orifice area decreased significantly in the telmisartan group but not in the control group. These changes were associated with a significant reduction of the mitral regurgitant stroke volume in the telmisartan group (50 ± 25 vs 16 ± 13 ml; $P < .0001$) but not in the control group (57 ± 29 vs 47 ± 24 ml; $P$ = not significant). These changes of mitral regurgitation were closely associated with significant improvement of forward aortic stroke volume ($r = -.57$, $P < .0001$). These findings were not observed in patients in the control group. The mitral E/A ratio increased from 0.65±0.11 to 0.75±0.19 following ARB. Mean (± SD). BNP concentration was 416 ± 413 pg/ml in the 28 patients diagnosed with abnormal left ventricular function, compared with 30 ± 36 pg/ml in the 20 patients with normal left ventricular function. 2 Patients with both systolic and diastolic dysfunction had the highest levels (675 ± 423 pg/ml). BNP levels were unable to differentiate systolic vs. diastolic dysfunction. In patients with symptoms of heart failure and normal systolic function, BNP levels >57 pg/ml had a positive predictive value of 100% for diastolic abnormalities. The plasma BNP concentration slightly decreased following chronic ARB, but the difference did not reach the statistical significance. The change in left ventricular chamber stiffness did not correlate with the change in BNP level(r=0.08, p=NS), **Conclusions** Chronic ARB improves diastolic dysfunction in diabetic hypertensives. A simple, rapid test for BNP levels can reliably predict the presence or absence of left ventricular dysfunction on echocardiogram.