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TRANSFORMING GROWTH FACTOR -β1: A MARKER OF LEFT VENTRICULAR HYPERTROPHY IN HYPERTENSION
Jesús L. Almendral, Vladislav L. Shick, Steven A. Atlas, Clive Rosendorff, Department of Medicine, Bronx VA Medical Center, Bronx, NY; Department of Medicine, Mount Sinai School of Medicine, New York, NY.

Left ventricular hypertrophy (LVH) develops in approximately 15-20% of patients with hypertension and is an independent risk factor for subsequent cardiovasculard morbidity and all-cause mortality. Factors such as age, gender, weight and blood pressure explain only 41% of LV mass variability. Non-hemodynamic factors have been postulated to play a role in LVH development. Transforming growth factor-β1 (TGF-β1), a cytokine produced by virtually all cell types, has been implicated as a key mediator in cardiovascular hypertrophy in animal studies. Its over-production stimulates collagen synthesis and inhibits collagen degradation, leading to extracellular matrix proliferation and excess fibrosis. We therefore investigated the determinants of ventricular hypertrophy and compliance in a cohort of patients with hypertension and LVH diagnosed by the electrocardiographic criteria of S in V1 or R in V5/V6 > 35 mm or R in AVL > 11 mm. Sixty-seven patients enrolled in the Echocardiographic study of the effect on Cardiovascular Hypertrophy of Olmesartan (ECHO) were investigated. Demographic, clinical, and laboratory data obtained at study entry after at least one week off anti-hypertensive therapy were compared to the patient’s baseline LV mass and ventricular compliance measured by 2-D echocardiography. Using linear regression analysis, serum TGF-β1 correlated significantly with LV mass indexed to body surface area (r = 0.67, p = 0.246, r² = 0.246). This correlation was enhanced in patients with concentric hypertrophy (r = 0.58, p = 0.009). The strongest correlation was seen in patients with concentric hypertrophy who were not on hydroxyethylmethyluracil-coenzyme A (HMG-CoA) reductase inhibitors at study entry (r = 0.335, p = 0.0075). We therefore conclude that serum TGF-β1 predicts severity of LVH in hypertension, particularly in patients with concentric hypertrophy not taking HMG-CoA reductase inhibitors.

Key Words: Hypertension, Left Ventricular Hypertrophy, Transforming Growth Factor Beta-1

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AUGMENTED ACE2 EXPRESSION IN ISCHEMIC CARDIOMYOPATHY
David B. Averill, Jewell A. Jessap, Yuichiro Ishiyama, Carlos M. Ferrario. Hypertension and Vascular Disease Center, Wake Forest University School of Medicine, Winston-Salem, NC.

Previously, we showed that myocardial ischemia increased angiotensin (Ang)-(1-7) in cardiac myocytes. Since angiotensin converting enzyme 2 (ACE2) has been implicated in the production of Ang-(1-7) we investigated whether cardiac remodeling post myocardial infarction was also associated with elevated ACE2 expression. Experiments were performed in Lewis rats that were subjected to ligation of the left main coronary artery (LIG) or sham (SHAM) ligation. Rats were given a 4 week recovery period during which time cardiac hypertrophy associated with cardiac dysfunction was characterized by significant elevations in left ventricular end-diastolic pressure (p<0.01) and heart weight to body weight ratio (p<0.05) in the LIG group. At the end of this 4 week period the rats were sacrificed and heart tissue processed for ACE2 immunoreactivity. ACE2 immunoreactivity was evident in cardiac myocytes and coronary vessels. However, there was markedly less ACE2 immunoreactivity in the infarcted region of the heart. The intensity of ACE2 immunoreactivity in septal tissue was quantified using algorithms in Photoshop™. This analysis revealed significantly greater ACE2 immunoreactive staining in the LIG versus the SHAM group.

These results support the hypothesis that augmented ACE2 expression contributes to increased Ang-(1-7) production in the remodeled myocardium. The increased ACE2 staining may be a post-transcriptional event since we have previously reported that ACE2 mRNA was not increased in this model of cardiomyopathy.

Key Words: Cardiac Remodeling, Cardiomyopathy, Myocardial Ischemia

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UTILITY OF CORNELL VOLTAGE-DURATION PRODUCT FOR DETECTION OF LEFT VENTRICULAR HYPERTROPHY. THE ELECTROTENS STUDY
Vivencio Barrios, Alberto Calderon, Leandro Ribas, Carlos Escobar, Alejandro Amador, Enrique Asin. Cardiology, Hospital Ramon y Cajal, Madrid, Spain; Primary Care, CS Rosa Luxemburgo, Madrid, Spain; Medical Department, Boehringer Ingelheim Spain, Barcelona, Spain.

Since echocardiography is usually not feasible in primary care for detection of left ventricular hypertrophy (LVH), the interest on new ECG criteria for diagnosis of LVH is markedly increasing. Of them, the most relevant criterion, mainly due to its application in LIFE trial, is Cornell voltage-duration product (VDP). In fact, this criterion has been included in the European guidelines on Hypertension 2003 as an elective method to detect LVH. With the aim to determine the utility of this method in daily clinical practice we performed the ELECTROTENS study.

For this multicenter trial five consecutive hypertensive patients >18 years who attended a Cardiologic outpatient clinic were recruited. An ECG was performed to all the patients and all the records were sent to a core lab for a central VDP calculation. 1624 patients were initially recruited, but after a strict clean up procedure only 782 patients were finally evaluated. Population: 51% males; age 66.1±10.4 yrs; BMI 28.2±6.1 kg/m²; BP 155.7±7.7/90.8±10.6 mmHg (48% grade Hypertension, 39% grade II, 13% grade III). History of hypertension: 6.3±5.9 years.

Results: LVH was detected by VDP in 23.4% of the patients. Some factors were predictive of LVH by ECG-VDP: age, male gender, systolic BP and presence of hypertensive retinopathy.

Conclusions: Almost one of four hypertensive patients who daily attend a Cardiologic outpatient clinic exhibit LVH detected by VDP. This rate is significantly higher than that observed when other classical ECG voltage criteria, such as Sokolow-Lyon or Cornell, are used. Therefore, the VDP criterion appears to be a very useful method to detect LVH in daily clinical practice. Since echocardiography is not always easily feasible, the new ECG criteria, not only based on QRS voltage, should be considered a very useful tool to improve the detection of LVH, mainly in primary care medicine.

Key Words: Cornell Voltage-Duration Product, Electrocardiography, Left Ventricular Hypertrophy

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EFFECTS OF Candesartan ON LEFT VENTRICULAR GEOMETRY AND DIASTOLIC FUNCTION IN HYPERTENSIVE PATIENTS WITH LEFT VENTRICULAR HYPERTROPHY. THE VIPE STUDY
Vivencio Barrios, Alberto Calderon, Juan P Tomas, Soledad Ruiz, Jose L Moya, Alicia Megias, Luis M Molinero, Onofre Vesago, Raúl Fernandez, Enrique Asin. Cardiology, Hospital Ramon y Cajal, Madrid, Spain; Primary Care, CS Rosa Luxemburgo, Madrid, Spain; Statistics, Alce Ingenieria, Madrid, Spain; Medical Department, AstraZeneca, Madrid, Spain.

The VIPE study was designed to assess the efficacy of candesartan on hypertensive echocardiographic left ventricular hypertrophy (LVH) at

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short term. In this work we report the effects of the drug on the ventricular geometric pattern and the diastolic function. 97 hypertensive patients (70% females (F) and 30% males (M), age 68.9±9.5 years, BMI 29.3±4.7 kg/m²) with LVH diagnosed by echo were included. LVH criteria were left ventricular mass index (LVMI) ≥134 g/m² or ≥110 (M or F). The patients were treated with a candesartan-based regimen (8mg, 16mg, + HCTZ 12.5mg, + add-on drugs to target BP <140/90) during a 6-month follow up. Blood pressure (BP): 160.4±11.8/90.4±8.7 mmHg. LVMI: 165.5±32 (M) and 144.6±30.7 g/m² (F). Relative wall thickness (RWT): 0.46±0.08. Ventricular geometric pattern: 54% concentric LVH (cLVH), 46% eccentric LVH (eLVH). Doppler diastolic parameters: E peak velocity (E) 0.70±0.17 m/second; A peak velocity (A) 0.87±0.23 m/second; E/A ratio 0.78±0.21; E wave deceleration time (DT) 223.2±63.1 ms; Isovolumic relaxation time (IVRT) 114.7±21 ms.

Results: At 6 months, BP lowered to 141.1±16.8/81.1±10.7 (p<0.001 vs baseline). LVMI reduced 11.3±9.3%. RWT 0.44±0.08 (p<0.05 vs baseline). Ventricular geometry: 32% cLVH, 40% eLVH, 8.5% concentric remodeling and 19.5% normal (p<0.0025 vs baseline).

No significant changes were observed in diastolic parameters: E, A, E/A ratio, DT or IVRT. No significant changes were observed in ejection fraction. The drug was very well tolerated and no serious adverse events was reported.

Conclusions: The LVH regression observed with a short-term treatment based on candesartan is associated with a significant improvement in ventricular geometry. In almost one fifth of the patients the left ventricular pattern was normalised at six months. No significant changes in diastolic function parameters were observed. These data may suggest that the cardioprotective effects of candesartan could be observed earlier on LVH regression than on diastolic function improvement, what maybe needs more time.

Key Words: Angiotensin Receptor Blocker, Diastolic Function, Left Ventricular Hypertrophy

P-313 TREATMENT WITH CANDESARTAN SIGNIFICANTLY REDUCES ECHOCARDIOGRAPHIC LEFT VENTRICULAR HYPERTROPHY AT SHORT TERM. The VIPE STUDY

Vivencio Barrios, Alberto Calderon, Juan P Tomas, Soledad Ruiz, Jose Luis Moya, Alicia Megias, Luis M Molinero, Onofre Vegazo, Raúl Fernandez, Enrique Asín. Cardiology, Hospital Ramon y Cajal, Madrid, Spain; Primary Care, CS Sosa Luxemburgo, Madrid, Spain; Statistics, Alce ingeniera, Madrid, Spain; Medical Department, AstraZeneca Spain, Madrid, Spain.

Left ventricular hypertrophy (LVH) is the most frequent target organ damage in hypertension. Since regression of LVH significantly improves the prognosis, this should be a major target in hypertensive population with LVH. Because not all the antihypertensive drugs are equally efficacious in this point, we aimed to perform a study to assess the effect of candesartan in hypertension with LVH controlled by echocardiography. In almost one fifth of the patients the left ventricular pattern was normalised at six months. No significant changes in diastolic function parameters were observed. These data may suggest that the cardioprotective effects of candesartan could be observed earlier on LVH regression than on diastolic function improvement, what maybe needs more time.

Key Words: Angiotensin Receptor Blocker, Diastolic Function, Left Ventricular Hypertrophy

P-314 REGRESSION OF LEFT VENTRICULAR HYPERTROPHY INDUCED BY CANDESARTAN DETECTED BY CORNELL VOLTAGE DURATION PRODUCT IN DAILY CLINICAL PRACTICE: THE VIPE STUDY

Alberto Calderon, Vivencio Barrios, Juan Pablo Tomas, Jose Luis Moya, Angela Megias, Luis Miguel Molinero, Onofre Vegazo, Raül Fernandez, Enrique Asin. C.S. Rosa Luxemburgo, 5th Area Imsalud, San Sebastian de los Reyes, Madrid, Spain; Cardiology Institute, Ramon y Cajal Hospital, Madrid, Madrid, Spain; Medical, AstraZeneca, Madrid, Madrid, Spain.

Voltage-duration product (VDP) have shown in randomized controlled mega-trials (LIFE, VALUE) to be the most sensitive ECG criteria to detect and quantify changes in LVH. Nevertheless, no information is available about the usefulness of this criterion in daily clinical practice. We aimed to evaluate the utility of different ECG criteria for the detection of LVH in the population of VIPE study. This is a trial designed to assess the effect of candesartan in hypertension with LVH controlled by echocardiography. The VIPE study included 97 uncontrolled hypertensive patients with echocardiographic LVH: 70% females, age 68.9±9.5 years, BMI 29.3±4.7 kg/m². Blood pressure (BP): 160.4±11.8/90.4±8.7 mmHg. The patients were treated with a candesartan-based regimen (8mg, 16mg, + HCTZ 12.5mg, + add-on drugs to target BP <140/90) during a 6-month follow up. Voltage and VDP for Sokolow and Cornell criteria were compared.

Results: Only Cornell voltage and Cornell VDP (C-VDP) decreased at end-study: -1.2 mm (CI 95%: -0.03, -2.53; p=0.04) and -194.9 mVxmsc (CI 95%: -54.3, -335.5; p=0.007), respectively. Only C-VDP detected a significant change in LVH. In 12.8% of the patients with baseline LVH by C-VDP were not hypertrophic by C-VDP at end-study (p=0.02), while 28% showed complete LVH regression by echo. The main factors to determine LVH regression by C-VDP were: C-VDP at baseline, age, and BMI. The overall concordance of C-VDP with echocardiography was 44.16 (41.1 for no-LVH and 46.9 for LVH).

Conclusions: Our data support that C-VDP is the most valid ECG criterion for detection and follow up of LVH regression in daily clinical practice. This method may detect changes at a short time as six months and may even quantify the improvement in LVH. The reduction of C-VDP induced by candesartan in this study results clinically relevant.

Key Words: Angiotensin Receptor Blocker, Left Ventricular Hypertrophy, Voltage-Duration Product