Journal of Hypertension

http://www.jhypertension.com Vol 44 Suppl 1 May 2026

ESH 2026 Abstract Book

Wolters Kluwer

Official Journal of the International Society of Hypertension and the European Society of Hypertension

DETERMINANT OF CARDIOPROTECTION IN OBESITY AND TYPE 2 DIABETES

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Journal of Hypertension. May 2026: 44(Suppl 1):e55

PREDICTORS OF BIOMARKER DYNAMICS IN CARDIOMETABOLIC PHENOTYPES ASSOCIATED WITH ARTERIAL HYPERTENSION, TYPE TWO DIABETES, AND OBESITY

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Journal of Hypertension. May 2026: 44(Suppl 1):e55

CARDIOMETABOLIC PHENOTYPES IN PATIENTS WITH ARTERIAL HYPERTENSION COMBINED WITH TYPE 2 DIABETES MELLITUS AND OBESITY AND THEIR EARLY CLINICAL AND BIOCHEMICAL MARKERS

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Journal of Hypertension. May 2026: 44(Suppl 1):e55-e56

2:LVMM – 263.5±46.05 vs 198.9±57.5 g/m2, p=0.001; LVMMI – 166.33±33.6 vs 135.13±43.8 g/m2, p=0.001. Patients with LVH had higher systolic blood pressure (SBP), and diastolic blood pressure (DBP): SBP - 136.87±18.8 vs 130.88±16.8 mm Hg, p<0.018 and DBP - 86,15±10,5 vs 82,56±10,09 mm Hg, p<0.014. LVEF was preserved in both groups, and no significant difference was found between the groups: 60.9±4.1% vs 59.7±5.58%, p=0.3). The left atrial index (LAI) was significantly higher in patients with LVH: LAI – 25.1±8.3 vs 13.8±12.1 cm, p=0.001. NT-proBNP levels were significantly higher in Group 1 (153 pg/mL [54.5-372.7] vs. 47 [26-200] pg/mL. A positive correlation was found between LVH and LAI (r=0.4, p=0.001) and NT-proBNP levels (r=0.2, p=0.042). A greater number of patients had concentric hypertrophy when analyzing the types of LV remodelling. Normal geometry comprised 8.5% of patients; concentric remodeling, 6.4%; concentric hypertrophy, 78%; eccentric hypertrophy, 7.1%; X2=211.48, p<0.001).

Conclusions: The development of LVH in patients with DM led to a significant increase in NT-proBNP levels.

BROWN ADIPOSE TISSUE CONNEXIN-43 DYSFUNCTION AS A NOVEL DETERMINANT OF CARDIOPROTECTION IN OBESITY AND TYPE 2 DIABETES

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Objective: Obesity and type 2 diabetes (T2D) markedly increase cardiovascular risk, particularly hypertension, cardiac hypertrophy, and diastolic dysfunction. Brown adipose tissue (BAT) is an active endocrine and metabolic organ with cardioprotective effects mediated by energy expenditure, glucose and lipid metabolism, and regulation of systemic inflammation. In obesity and T2D, BAT undergoes functional impairment and whitening, but mechanisms linking BAT dysfunction to hypertension-related cardiac remodeling remain unclear. Connexin 43 (Cx43), a key gap junction channel protein, is essential for electrical and metabolic coupling in cardiomyocytes and is also expressed in BAT, where it supports thermogenic and metabolic activity. We hypothesized that dysregulation of BAT Cx43 contributes to cardiometabolic imbalance and cardiac dysfunction in obesity-related T2D.

Design and method: Forty four-month-old male Zucker Diabetic Fatty rats (lean fa/+ and obese diabetic fa/fa) were divided into control or Cemtirestat-treated groups (2.55 mg/kg/day). After six months of treatment, cardiac structure and function were assessed by echocardiography with emphasis on diastolic function. Selected biometric and biochemical parameters were measured, and BAT and left ventricular (LV) myocardium were collected for analysis of Cx43 expression, inflammatory markers and related signaling pathways.

Results: Obese T2D rats exhibited increased body and heart weight, visceral adiposity, BAT mass, hyperglycemia, hyperinsulinemia, and dyslipidemia. Cx43 expression was increased in the LV but markedly reduced in BAT, accompanied by BAT whitening and a shift toward white-like adipocytes. Thermogenic and metabolic regulators (UCP1, UCP3, FGF21, GDF15, PPAR-gamma) were downregulated, while inflammatory mediators (IL-6, IL-10, TNF-alfa) were elevated. PKC epsilon was reduced and PKC delta increased in both BAT and LV tissue. Cemtirestat improved selected metabolic and inflammatory parameters and attenuated diastolic dysfunction without significantly affecting ventricular Cx43 expression.

Conclusions: Impaired BAT Cx43 signaling is associated with loss of BAT thermogenic and anti-inflammatory capacity and is associated with cardiac hypertrophy and diastolic dysfunction - hallmarks of hypertensive heart disease - in obesity-related T2D. BAT and Cx43 represent potential cardiometabolic and antihypertensive targets.

This study was supported by VEGA 2/0133/24, APVV 21-0410 and VV-MVP-24-0278 grants.

PREDICTORS OF BIOMARKER DYNAMICS IN CARDIOMETABOLIC PHENOTYPES ASSOCIATED WITH ARTERIAL HYPERTENSION, TYPE TWO DIABETES, AND OBESITY

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Objective: To assess the prognostic significance of changes in circulating biomarkers related to neurohumoral activation, myocardial remodeling, metabolic regulation, and renal function in patients with arterial hypertension complicated by type two diabetes and obesity, and to identify clinical and functional predictors associated with the formation of a favorable cardiometabolic phenotype during targeted pharmacological treatment.

Design and method: A total of 211 patients with arterial hypertension were enrolled and stratified into four clinical groups according to the presence of type two diabetes and obesity. Serum levels of catestatin, cardiotrophin one, beta two microglobulin, cystatin C, neutrophil gelatinase associated lipocalin, N terminal prohormone of brain natriuretic peptide, leptin, and insulin were measured using immunoassay methods. Comprehensive evaluation included echocardiographic assessment of cardiac structure and function, lipid profile, glycemic control, renal function parameters, and body mass index. Multivariate regression and logistic analyses were applied to identify independent predictors of biomarker dynamics and cardiometabolic phenotypes.

Results: Changes in biomarker levels demonstrated significant associations with structural and functional cardiac parameters, renal function, lipid metabolism, and glycemic control. Catestatin and cardiotrophin one were predominantly associated with favorable myocardial remodeling and improved diastolic function in isolated arterial hypertension. In patients with metabolic comorbidity, cystatin C, beta two microglobulin, neutrophil gelatinase associated lipocalin, leptin, and N terminal prohormone of brain natriuretic peptide showed strong correlations with left ventricular hypertrophy, dyslipidemia, impaired renal function, and subclinical cardiac dysfunction. The most consistent predictive value across cardiometabolic phenotypes was observed for catestatin, cardiotrophin one, cystatin C, beta two microglobulin, leptin, and N terminal prohormone of brain natriuretic peptide.

Conclusions: A multibiomarker approach provides significant prognostic information beyond traditional clinical parameters in arterial hypertension complicated by metabolic disorders. Specific biomarker patterns reflect distinct cardiometabolic phenotypes and are associated with myocardial remodeling, diastolic dysfunction, renal impairment, and metabolic imbalance. Integration of biomarker monitoring into routine clinical practice may improve risk stratification and support personalized therapeutic strategies in patients with arterial hypertension and metabolic comorbidity.

CARDIOMETABOLIC PHENOTYPES IN PATIENTS WITH ARTERIAL HYPERTENSION COMBINED WITH TYPE 2 DIABETES MELLITUS AND OBESITY AND THEIR EARLY CLINICAL AND BIOCHEMICAL MARKERS

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Objective: To determine cardiometabolic phenotypes and identify early clinical, biochemical, and instrumental markers associated with cardiovascular and renal impairment in patients with arterial hypertension combined with type 2 diabetes mellitus and obesity.

Design and method: A total of 211 patients with grade 1 arterial hypertension were examined and divided into four groups according to comorbidity: isolated arterial hypertension, arterial hypertension with obesity, arterial hypertension with type 2 diabetes mellitus, and arterial hypertension combined with obesity and type 2 diabetes mellitus. Clinical assessment, anthropometric evaluation, lipid and carbohydrate profiling, and renal function tests were performed. Circulating levels of cardiotrophin-1, catestatin, leptin, N-terminal brain natriuretic peptide, neutrophil gelatinase-associated lipocalin, cystatin C, and beta-2 microglobulin were measured using enzyme-linked immunosorbent assay. Cardiac structure and function were assessed by echocardiography. Statistical analysis included analysis of variance, Student's t-test, and multivariate regression analysis.

Results: Three distinct cardiometabolic phenotypes were identified depending on the pattern of comorbidity. Patients with isolated arterial hypertension demonstrated the most favorable cardiometabolic profile. The presence of obesity and type 2 diabetes mellitus was associated with progressive deterioration of metabolic, renal, and cardiac parameters. Cardiotrophin-1 and N-terminal brain natriuretic peptide levels were significantly higher in patients with type 2 diabetes mellitus, indicating increased myocardial stress and early heart failure risk. Neutrophil gelatinase-associated lipocalin showed the highest prognostic value for early renal impairment and increased consistently with metabolic burden. Echocardiographic findings revealed a cumulative effect of obesity and type 2 diabetes mellitus on left ventricular hypertrophy, chamber dilation, and systolic and diastolic dysfunction, with the most pronounced changes observed in patients with combined pathology.

Conclusions: Patients with arterial hypertension combined with obesity and type 2 diabetes mellitus exhibit distinct cardiometabolic phenotypes characterized by progressive cardiovascular and renal involvement. Cardiotrophin-1, N-terminal brain natriuretic peptide, and neutrophil gelatinase-associated lipocalin are promising early markers for risk stratification. Identification of cardiometabolic