Impact of Hypertension on Ventricular-Arterial Coupling and Regional Myocardial Work at Rest and during Isometric Exercise

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Background: To understand better the mechanism of left ventricular (LV) remodeling related to hypertension, it is important to evaluate LV function in relation to the changes in loading conditions. The aim of this study was to investigate changes in conventional ventricular-arterial coupling indexes, LV strain, and a new index reflecting regional myocardial work assessed noninvasively at rest and during isometric exercise in a random sample including participants with normal blood pressure and those with hypertension.

Methods: A total of 148 participants (53.4% women; mean age, 52.0 years; 39.2% with hypertension) underwent simultaneous echocardiographic and arterial data acquisition at rest and during increased afterload (handgrip exercise). End-systolic pressure was determined from the carotid pulse wave. Arterial elastance (Ea) and LV elastance (Ees) were calculated as end-systolic pressure/stroke volume and end-systolic pressure/end-systolic volume. Doppler tissue imaging and two-dimensional speckle tracking were used to derive LV longitudinal strain. Regional myocardial work (ejection work density [EWD]) was the area of the pressure-strain loop during ejection.

Results: At rest, with adjustments applied, Ees (3.06 vs 3.71 mm Hg/mL, $P = .0003$), Ea/Ees (0.54 vs 0.47, $P = .002$) and EWD (670 vs 802 Pa/m^2, $P = .0001$) differed significantly between participants with normal blood pressure and those with hypertension. During handgrip exercise, Ea and Ea/Ees significantly increased ($P < .0001$) in both groups. Doppler tissue imaging and two-dimensional LV strain decreased in participants with hypertension ($P \leq .008$). Only in subjects with normal blood pressure EWD significantly increased (+14.7%, $P = .0009$).

Conclusions: Although patients with hypertension compared with those with normal blood pressure have increased LV systolic stiffness and regional myocardial work to match arterial load at rest, they might have diminished cardiac reserve to increase myocardial performance, as estimated by EWD during isometric exercise. (J Am Soc Echocardiogr 2012;25:882-90.)

Keywords: Echocardiography, Hypertension, Ventricular-arterial coupling, Strain

The interaction of the heart with the systemic vasculature, ventricular-arterial coupling (VAC), is a key determinant of cardiovascular performance.[1] The capacity of the body to augment cardiac output, regulate systemic blood pressure (BP) and respond appropriately to elevations in heart rate and preload and afterload depends on the properties of both the heart and the vasculature into which the left ventricle ejects blood.[2] Hypertension is associated with the stiffening of the large arteries and left ventricle. Because a high arterial pressure opposes left ventricular (LV) ejection, it might lead in the short term to a reduction of LV stroke volume, which is compensated for by shifting the LV pump function to a higher energy level (the Frank-Starling mechanism) and by activating an autoregulation mechanism (the Anrep response). Thus, the heart responds to the greater afterload with an increase in LV stiffness.[3] In the long term, this chronically increased cardiac loading leads to LV remodeling (concentric hypertrophy), increases LV oxygen requirements, and eventually causes LV failure. Moreover, to expand stiffened arteries, the heart needs to generate greater forces. Pulse-wave velocity also increases in stiffening arteries, leading to an early return of the reflected wave, which in turn augments late systolic

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Abbreviations

BP = Blood pressure

CI = Confidence interval

DTI = Doppler tissue imaging

Ea = Arterial elastance

Ees = End-systolic elastance

ESP = End-systolic pressure

ESV = End-systolic volume

EWD = Ejection work density

FLEMENGHO = Flemish Study on Environment, Genes and Health Outcomes

LA = Limits of agreement

LV = Left ventricular

SV = Stroke volume

2D = Two-dimensional

VAC = Ventricular-arterial coupling

LV load. Further damage to the left ventricle might be caused by increasing time required for systole and shortening of diastole.

Matching the properties of the left ventricle to those of the arteries might preserve cardiac mechanic efficiency at rest, but not necessarily during LV loading. Measurement of VAC generally requires invasive registration of LV pressures and LV volumes, recorded over a wide range of LV loads.[3] Effective arterial elastance (Ea), commonly known as the ratio of LV end-systolic pressure (ESP) to stroke volume (SV), reflects the net arterial load imposed on the left ventricle.[4] LV end-systolic elastance (Ees) provides an estimate of LV performance and is calculated by measuring the slope of the relations between ESP and end-systolic volume (ESV) registered over a range of LV loads.[4] The Ea/Ees ratio is commonly used as an index of the interaction between the left ventricle and the arterial system. Some investigators have proven the feasibility of a noninvasive assessment of VAC in patients with hypertension.[5-7] For instance, Osranek *et al.*[6] measured LV volumes by echocardiography and estimated central aortic pressure from a tonometrically recorded pulse-wave signal at the radial artery at rest and during handgrip exercise.

Additional information about LV performance can also be derived from an assessment of myocardial deformation (strain). On the basis of Doppler tissue imaging (DTI) and two-dimensional (2D) speckle tracking, regional myocardial strain curves can be calculated.[8,9] Moreover, strain in combination with simultaneously measured LV pressure can be used to estimate regional myocardial work.[10] Thus, using the relation between regional LV deformation (strain) and loading, a measure of intrinsic myocardial performance can be obtained.

To understand better the mechanism of LV remodeling related to hypertension, it is important to evaluate LV function in relation to the changes in the loading conditions in subjects with normal BP and those with hypertension. Few studies[6,7] have examined noninvasively the changes in VAC components during exercise in patients with hypertension. To our knowledge, no population study thus far has described changes in LV myocardial deformation (strain) and/or regional myocardial work derived from simultaneously obtained estimates of LV ESP and strain under different loading conditions. In the present study, we investigated changes in conventional VAC indexes, LV longitudinal strain, and a new index reflecting regional myocardial work assessed noninvasively at rest and during isometric exercise in a random sample including participants with normal BP and those with hypertension.

METHODS

Study Participants

Study participants were from the Flemish Study on Environment, Genes and Health Outcomes (FLEMENGHO), consisting of a random population sample stratified by sex and age from a geographically defined area in northern Belgium.[11] Seven municipalities gave listings of all inhabitants sorted by address. Households, defined as subjects living at the same address, were the sampling unit. We numbered households consecutively and generated a random-number list using SAS (SAS Institute Inc., Cary, NC). Households with numbers matching the list were invited. The ethics committee of the University of Leuven approved the study, and participants provided informed consent. FLEMENGHO participants were repeatedly visited at home and examined at a local examination center. At each contact, standardized and validated questionnaires were administered to collect detailed information about each participant's personal and familial medical history, use of medications, and lifestyle. In 2009 and 2010, we reinvited 215 former FLEMENGHO participants for follow-up examinations at our field center, including echocardiography and the isometric exercise test (participation rate, 81.3%).

We excluded 26 subjects from statistical analysis because of myocardial infarction or coronary revascularization ($n = 6$), moderate to severe valvular abnormalities ($n = 9$), atrial fibrillation ($n = 5$), or symptomatic heart failure ($n = 6$). We excluded a further 41 subject, because DTI studies or 2D echocardiograms ($n = 15$) or carotid artery pressure waves ($n = 21$) were of insufficient quality, as well as participants who did not comply with the study protocol ($n = 5$). Thus, the number of participants statistically analyzed totaled 148.

Echocardiography

Participants refrained from smoking, heavy exercise, and drinking alcohol or caffeine-containing beverages for ≥3 hours before echocardiography.

Data Acquisition. One experienced physician (T.K.) performed the ultrasound examinations according to a standardized protocol as published elsewhere,[11] using a Vivid 7 Pro (GE Vingmed Ultrasound AS, Horten, Norway) interfaced with a 2.5-MHz phased-array probe. With the subject in the partial left decubitus position and breathing normally, the observer obtained images from the parasternal long and short axes and from the apical four-chamber and two-chamber and long-axis views. All recordings included at least five cardiac cycles and were digitally stored for offline analysis.

Using DTI, the observer recorded low-velocity, high-intensity myocardial signals at a high frame rate (>190 frames/sec), while adjusting the imaging angle to ensure parallel alignment of the ultrasound beam with the myocardial segment of interest. The Nyquist limit was set as low as possible avoiding aliasing.

Offline Analysis. The same observer (T.K.) analyzed recorded images, averaging three heart cycles for statistical analysis, using a workstation running EchoPAC version 4.0.4 (GE Vingmed Ultrasound AS). LV ESV and end-diastolic volume were measured offline from the apical four-chamber and two-chamber views, using the standard biplane Simpson's method.[12]

On the basis of color Doppler myocardial motion data, one-dimensional longitudinal regional strain rate and strain curves were calculated by comparing local myocardial velocity profiles, using dedicated software.[11] The SPEQLE package (version 4.6.2) allows M-mode tracking of the myocardium to ensure that the sample volume is maintained in the same anatomic position within myocardial image throughout the cardiac cycle. We positioned the sampling volume in the septal, lateral, inferior, and posterior walls at the level of the posterior chordae tendineae. To compute end-systolic strain, hereafter referred to as strain, we averaged three consecutive