JACC: CARDIOVASCULAR IMAGING VOL. 6, NO. 4, 2013

ISSN 1936-878X/$36.00
PUBLISHED BY ELSEVIER INC. http://dx.doi.org/10.1016/j.jcmg.2012.10.022

ORIGINAL RESEARCH

The Slope of the Segmental Stretch-Strain Relationship as a Noninvasive Index of LV Inotropy

Ruta Jasaityte, MD,* Piet Claus, PhD,* Arco J. Teske, MD, PhD,*†
Lieven Herbots, MD, PhD,*‡ Bart Verheyden, PhD,§ Ruxandra Jurcut, MD, PhD,*‖
Frank Rademakers, MD, PhD,* Jan D'hooge, PhD*

Leuven and Hasselt, Belgium; Utrecht, the Netherlands; and Bucharest, Romania

OBJECTIVES The aim of this study was to test the hypothesis that the noninvasively constructed slope of the relationship between left ventricular (LV) regional systolic strain and stretch during atrial contraction represents LV inotropic state.

BACKGROUND LV systolic response to a changing preload depends on its inotropic state. Changing the preload has allowed constructing the slope of the end-systolic pressure-volume relationship that is used as an invasive measurement of LV inotropy. We assumed that the slope of the relationship between regional systolic LV strain (total_S) and stretch during atrial contraction (preS) depends on the LV inotropic state as well and can thus be used as a LV inotropy index.

METHODS Strain curves (tissue Doppler) were extracted from 27 healthy individuals to determine the normal stretch-strain relationship at rest, during a low-dose dobutamine (LD) challenge and during passive leg-lift (LL). The method was also applied in 7 patients with breast cancer before and after chemotherapy with anthracyclines.

RESULTS PreS and total_S correlated closely in all subjects ($r = 0.82$). Total_S values increased ($p < 0.05$) with LD (–20.44 ± 3.89% vs. –24.24 ± 5.55%) and LL (–19.65 ± 3.77% vs. –24.05 ± 3.67%), whereas preS increased only with LL (5.96 ±1.72% vs. 8.61 ± 2.18%), but not with LD (6.83 ± 2.34% vs. 7.29 ± 2.24%). No changes of total_S or preS were observed after the exposure to chemotherapy (–21.23 ± 2.93% vs. –21.49 ± 2.89% and 8.11 ± 1.03% vs. 8.59 ± 1.73%, respectively). The slope of stretch-strain relationship got steeper with LD (–1.47 ± 0.36 vs. –2.34 ± 0.36, $p < 0.05$), declined after the chemotherapy (–1.68 ± 0.15 to –0.86 ± 0.23, $p < 0.05$) and did not change with LL (–1.39 ± 0.57 vs. –1.51 ± 0.38, $p = NS$).

CONCLUSIONS The slope of the regional stretch-strain relationship can be regarded as a noninvasive index of myocardial inotropic state. It gets steeper with increasing inotropy, does not change with preload induced changes of LV systolic function, and flattens after the exposure to a cardiotoxic drug. (J Am Coll Cardiol Img 2013;6:419–28) © 2013 by the American College of Cardiology Foundation

From the *Department of Cardiovascular Sciences, Division of Cardiovascular Imaging and Dynamics, Catholic University of Leuven, Leuven, Belgium; †Department of Cardiology, University Medical Center Utrecht, Utrecht, the Netherlands; ‡Heart Center Hasselt, Jessa Hospital, Hasselt, Belgium; §Department of Cardiovascular Sciences, Division of Experimental Cardiology, Catholic University of Leuven, Leuven, Belgium; and the ‖Department of Cardiology, "Prof. Dr. C. C. Iliescu" Institute of Emergency for Cardiovascular Diseases, Bucharest, Romania. Dr. Verheyden is currently working as a product manager for Boston Scientific. Dr. D'hooge has received research grants from GE Healthcare, Siemens Medical Solutions, and Philips Healthcare. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Manuscript received July 5, 2012; revised manuscript received October 2, 2012, accepted October 18, 2012.

JACC: CARDIOVASCULAR IMAGING, VOL. 6, NO. 4, 2013
APRIL 2013:419–28

Inotropy describes the intrinsic ability of myocardium to generate force independent of loading conditions. Clinically applicable measurements of inotropy could be very useful in various clinical settings such as chronic heart failure and valvular heart disease. However, this remains a difficult task as noninvasive estimates of the left ventricular (LV) inotropic state are limited by their load dependency.

See page 429

Currently, only invasive measurements, such as the end-systolic pressure-volume relationship and preload recruitable stroke work, give a good estimate of myocardial inotropy. They both use the Frank-Starling mechanism, which is known as a phenomenon where at a given inotropic state active force developed by the ventricle increases with increasing preload. As this systolic LV response to preload is also modulated by the inotropic state, varying preload and measuring the LV response to this intervention can be used to assess LV inotropy. Unfortunately, this approach towards an estimation of the cardiac inotropic state cannot be easily applied in the daily routine as it requires simultaneous invasive recordings of LV pressures and volumes under changing preload conditions. Moreover, varying preload and invasively measuring the LV pressure and volume response cannot be applied in heart failure patients that do not tolerate volume challenges.

ABBREVIATIONS AND ACRONYMS

Δ_preS = change of left ventricular stretch during atrial contraction with leg lift

Δ_total_S = change of left ventricular strain with leg lift

BL = baseline, resting state

EDV = end-diastolic volume

EF = ejection fraction

ESV = end-systolic volume

FU = follow-up

LD = low-dose dobutamine challenge

LL = passive leg lift

MRI = magnetic resonance imaging

preS = left ventricular stretch during atrial contraction

SI = sphericity index

TDI = tissue Doppler imaging

total_S = left ventricular systolic shortening

WS = wall stress

A similar relationship between diastolic preload and systolic LV response may be present on a regional level as well. It is known that regional myocardial stretch during atrial contraction and systolic LV strain are inhomogeneous and related to each other (1). We therefore hypothesized that the slope of this intraventricular stretch-strain relationship could be measured by myocardial deformation imaging and used as an estimate of global LV inotropy in analogy to the invasive approaches.

METHODS

Study population. Thirty-five healthy individuals and 7 patients with breast cancer undergoing chemotherapy with cardiotoxic anthracycline were recruited to the study. All study participants were free from cardiovascular disease. The baseline echocardiographic examination in those individuals showed a sinus rhythm, normal LV systolic and diastolic function, and ruled out any structural heart disease. Individuals with signs of myocardial infarction, arrhythmias, LV hypertrophy, or conduction disturbances on the electrocardiogram were also not included in the study. Other exclusion criteria were: significant (≥50%) coronary artery stenosis on angiography in the previous 4 years, signs of relevant ischemic heart disease on perfusion and delayed enhancement magnetic resonance imaging (MRI) or single-photon emission computed tomography, previous hospital admission with signs suggestive of myocardial ischemia or with elevated cardiac enzymes. All study subjects signed an informed consent before inclusion. The study complied with the Declaration of Helsinki and the local ethical committee approved the study protocol.

The study population of healthy subjects was split in 3 groups: 1) the normal stretch-strain relationship was defined in 19 individuals; 2) to test the effect of increased inotropy on the slope of the stretch-strain relationship LV inotropy was modulated pharmacologically in a subset of 8 individuals from this first group; and 3) the third group consisted of the remaining 16 subjects in whom an acute increase of LV preload was induced by passive leg lifting to test its effect on the stretch-strain relationship.

Finally, the effect of the decreasing contractility on the slope of stretch-strain relationship was tested in patients with breast cancer before and after 3 cycles of standard chemotherapy with anthracycline.

Study protocol. An echocardiographic examination was performed with an ultrasound scanner (GE Vingmed Ultrasound, Vivid 7 or E9, Horten, Norway), equipped with 2.5 MHz M3S and M5S transducers. B-mode acquisitions of 4-chamber and 2-chamber views, pulsed wave Doppler recordings of the LV outflow tract and the mitral valve inflow were acquired. In addition, the sector size was reduced in order to obtain narrow sector tissue Doppler imaging (TDI) acquisitions (frame rate [FR] 180 to 210 Hz) of properly aligned LV walls (inferoseptal, anterolateral, anterior, inferior, inferolateral, and anteroseptal). This protocol was followed in the first group of healthy individuals and in the breast cancer patients, where it was used both at baseline (BL) (i.e., within 4 weeks before the start of a standard chemotherapy protocol with anthracycline) and at follow-up (FU) (i.e., within 7 to 14 days after the third chemotherapy cycle).