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Assessment of left sided filling dynamics in diastolic dysfunction using cardiac computed tomography

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ABSTRACT

Background: Left ventricular (LV) diastolic dysfunction (DD) often accompanies coronary artery disease but is difficult to assess since it involves a complex interaction between LV filling and left atrial (LA) emptying.

Objective: To characterize simultaneous changes in LA and LV volumes using cardiac computed tomography (CT) in a group of patients with various grades of DD based on echocardiography.

Methods: We identified 35 patients with DD by echocardiography, who had also undergone cardiac CT, and 35 age-matched normal controls. LV and LA volumes were measured every 10% of the RR interval, using semi-automatic software. From these, – systolic, early-diastolic and late-diastolic volume changes were calculated, and additional parameters of diastolic filling derived. Conduit volume was defined as the difference between the LV and LA early-diastolic volume change.

Results: Patients with DD had significantly larger LV mass, and LA volumes, reduced early emptying volumes and increased conduit volume as percent of early LV filling (All $p < 0.001$). LA function, manifesting as total emptying fraction (LATEF), decreased proportionately with worsening grades of DD ($p < 0.001$). LA contractile function was maintained until advanced grade-3 DD. By receiver operating characteristic analysis, LATEF had an AUC of 0.88 to separate between normals and DD. At a threshold of <42.5%, LATEF has 97% sensitivity and 69% specificity to detect DD.

Conclusions: DD is characterized by reduced LA function and an alteration in the relative contributions of the atrial emptying and conduit volume components of early LV filling. In patients undergoing cardiac CT, it is possible to identify the presence and severity of DD.

Abbreviations: DD, diastolic dysfunction; TTE, transthoracic echocardiography; LV, left ventricle; LA, left atrium; EF, ejection fraction; LV-E, LV early filling volume; LV-A, LV late filling volume; LV-E/A, ratio of LV early to late filling volume; LVSV, LV stroke volume; LAEDV, LA end-diastolic volume; LAESV, LA end-systolic volume; LAMDV, LA mid-diastolic volume; LASFV, LA systolic filling volume (Reservoir volume); LAEEV, LA early emptying volume(Passive emptying volume); LALEV, LA late active emptying volume (Booster pump volume); LATEF, LA total emptying fraction; CV, Conduit volume= (LV-E – LA passive emptying volume); %CV/LVSV, % total LV filling passing through LA without affecting its volume; E, peak early mitral inflow velocity measured by pulsed Doppler; A, peak late mitral inflow velocity measured by pulsed Doppler; e′, peak mitral annulus velocity measured by pulsed tissue Doppler.

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1. Introduction

Evaluation of the diastolic function of the left ventricle (LV) is an essential part of the workup of patients with suspected heart disease. The gold standard is the invasive measurement of left heart pressures, however, in practice, evaluation of diastolic function is primarily carried out by echo-Doppler. Unfortunately, robust non-invasive evaluation remains elusive by current criteria, with a large percentage of patients having inconclusive results, especially among those with preserved ejection fraction (EF) [1,2]. Cardiac computed tomography (CT) is now regularly performed in the evaluation of the patient with suspected coronary artery disease, primarily to visualize the coronary arteries, although it is able to provide important functional information as well. The high resolution well contrasted 3-dimensional data-set is optimally suited for volumetric analysis of the cardiac chambers, with most studies concentrating on analysis of systolic function [3], however several studies have looked at evaluation of diastolic function too, mainly by attempting to mimic echo-Doppler indices [4]. On the other hand, magnetic resonance imaging (MRI) studies of diastolic function have shown that optimal evaluation of diastolic function requires analysis of LV-left atrial (LA) interactions [5,6], something that has not been clinically feasible due to the large amount of manual processing required. Recent advances in automatic segmentation of all cardiac chambers have now made the task of rapid processing of large datasets feasible [7,8].

We hypothesized that evaluation of simultaneous LV and LA volume changes during diastole, based on accurate 3D semiautomatic chamber measurements, would demonstrate characteristic physiological patterns through the various stages of DD. We thus aimed to analyze simultaneous LV and LA volume curves derived from 4D CT datasets to obtain a better understanding of LV-LA interactions in the setting of diastolic dysfunction (DD). We also aimed to assess the diagnostic accuracy of CT derived diastolic function compared to echo-Doppler, as the clinical reference standard.

2. Material and methods

2.1. Patient selection

The study was approved by the local Helsinki committee. We identified 385 patients who had undergone both transthoracic echocardiography (TTE) and cardiac CT within one month of each another (Fig. 1). The median time interval between these studies was 1 day (IQR 0-2 days). Most scans were performed to evaluate the coronary arteries in patients with chest pain. After excluding 134 patients, the remaining 251 patients were categorized as normal, abnormal or indeterminate diastolic function. Exclusion criteria are listed in Fig. 1. Based on American society of echocardiography (ASE) guidelines [2], Echo-Doppler can accurately determine diastolic functional grade, when certain conditions are met, however there is a large grey zone where it is more difficult to make the diagnosis. We thus, studied only those cases which clearly fitted the ASE definitions of normal and abnormal diastolic function, removing those cases which were indeterminate.

Since diastolic function is strongly affected by age, we performed 1:1 age matching, to achieve equal numbers of normal and DD. Eventually 2 matched groups of 35 patients were included for analysis. We also wished to compare DD patients with preserved systolic function, and patients with combined diastolic and systolic function, thus DD patients were divided into 2 groups, having preserved versus abnormal systolic function (EF < 45%). In order to ensure that the 2 groups contained patients with similar severity of DD, matching was performed for DD severity, resulting in 12 patients with DD and preserved systolic function and 12 patients with DD and reduced systolic function.

2.2. CT scan

Cardiac CT was performed using a Brilliance 64S scanner (Philips Healthcare, Cleveland, Ohio), using retrospective ECG gating with tube current modulation to reduce radiation during systole. Scan parameters were 64 slices × 0.625 mm, rotation time 0.42 s, pitch 0.2, tube voltage 120kVe, tube current 800–1000 mAS. CT angiography was performed, using 80 mL contrast medium at a rate of 5 mL/sec and 40 mL of saline wash-out. Reconstructions were performed every 10% of the cardiac cycle at a slice thickness of 1 mm, using a soft reconstruction filter. The number of phases/cycle needed was determined by a preliminary investigation comparing use of 10 versus 20 phases in 10 patients.

2.3. Echocardiography

Echocardiographic examinations were carried out in a high volume echocardiography laboratory, and interpreted by one of 4 experienced physicians. A full diastolic assessment was carried out according to ASE recommendations [2]. LV mass was calculated by the ASE M-mode formula [9]. LA diameter was measured at end-systole from the parasternal long axis view. LA area was measured from the 4-chamber view also at end-systole. Mitral inflow peak early (E) and late diastolic (A) velocities were measured by pulsed wave Doppler, placing the sample volume at the mitral leaflet tips in diastole. The deceleration time of the early filling velocity was also measured. Mitral annular velocities (e′) were measured using tissue Doppler imaging at the septal and lateral annuli. Pulmonary artery pressure was estimated from the peak tricuspid valve pressure gradient added to the right atrial pressure. The latter was estimated from the diameter of the IVC and the percent decrease in the diameter during inspiration [10].

Finally two experienced cardiologists reviewed all TTE reports and classified them as normal diastolic function, grade 1-3 DD, or indeterminate, based on ASE recommendations [2]. These recommendations are based on an integrative evaluation of several parameters, especially, E/A, E/e′, LA volume and estimated peak pulmonary artery pressure.

2.4. Analysis of CT datasets

All 10 cardiac phases (0–90% of the RR interval) were loaded to a commercial CT workstation (EBW 4.6, Philips Healthcare, Cleveland, Ohio). Based on the automatic volume curves (Fig 2), maximum LV volume or end-diastole, minimum LV volume or end-systole, and mid-diastole, the relatively isovolumic phase between early and late ventricular filling, were identified (Fig. 2). The workstation performs automatic segmentation of all cardiac chambers, and results of automatic LV and LA volumes and LV mass were recorded. The segmentation can either be performed offline, before loading the study, or while the user is evaluating the coronary arteries, and takes about 2 min. Segmentation quality was graded for each of the LV and LA, on a scale of 1–4 [8], where grades 1 and 2 indicate accurate segmentation and grades 3 and 4, inaccurate or failed segmentation. Manual editing was then performed as required, using the tools available and results recorded. The latter semiautomatic results were used in all analysis.

Based on these volumes which were indexed for body surface area (BSA), various parameters of LV diastolic function, LA function and parameters integrating LV and LA volume changes were calculated. Our aim was to obtain a complete description of the volumetric changes during diastole, including simultaneous LA emptying and LV filling volumes, to attempt to characterize the pro-