CARDIAC MR ELASTOGRAPHY REVEALS INCREASED STIFFNESS OF THE LEFT VENTRICULAR MYOCARDIUM IN AGE AND PATHOLOGY.

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Background: The elasticity of the cardiac wall is synonymous for myocardial contraction and relaxation and presents therewith an important parameter for cardiac function. Increased myocardial stiffness is associated with diastolic dysfunction [1]. MR Elastography (MRE) is capable of measuring elasticity changes of the heart during the cardiac cycle using different approaches [2,3,4]. The alteration of myocardial elasticity can be derived from a change in the amplitudes of externally induced shear vibrations such that wave amplitudes are reciprocally correlated with myocardial elasticity and ventricular pressure [5]. Consequently, it is expected that diastolic dysfunction yields significantly lower wave amplitudes than asymptomatic myocardium [6].
Problem: Myocardial elasticity increases with age within a normal range [7]. Therefore, age may present a confounding variable in cardiac MRE.
Purpose of the study: To determine if cardiac MRE can serve to differentiate elastic parameters in aged volunteers and patients with diastolic dysfunction.

Methods: Cardiac MRE was performed in four groups on a clinical 1.5 T scanner (Siemens): young volunteers (n=17, mean age 32 years), older volunteers (n=5, mean age 55 years), and two groups with mild (n=11, mean age 58 years) and severe (n=4, mean age 58 years) relaxation abnormalities as identified by transthoracic echocardiography. Wave-amplitude sensitive ECG triggered steady-state GRE-MRE was performed using a 25 Hz stimulation transmitted by an extended piston driver attached to the anterior chest wall [2]. Shear wave components were encoded in the MRI phase signal in all three Cartesian components of the MR scanner. From these wave components the total deflection amplitude *U* was derived. Magnitude images were employed for measuring the cross-sectional area of the left ventricle. A dilation of this area was defined as diastole while a diminution of this area was referred to as systole. The delay between the decrease in amplitude *U* and onset of ventricular contraction was determined in all subjects and assigned to the time of isovolumetric elasticity contraction (*IVEC*). Conversely, the delay between the increase in wave amplitude and ventricular dilatation was used for measuring the time of isovolumetric elasticity relaxation (*IVER*). Furthermore, the following amplitude-related parameters were derived: 1) *U_mean*: the mean wave amplitudes averaged over the measure time and the left ventricular area; 2) *U_sys*: The systolic wave amplitudes averaged over time of systole and left ventricular area; 3) *U_dia*: The diastolic wave amplitudes averaged over time of diastole and left ventricular area; 4) *U_ref*: Reference amplitudes averaged over the entire measure time and a reference area anterior to the heart and adjacent to the right ventricle. The global left ventricular ejection fraction (*LV-EF(3D)*) was calculated from additionally acquired Cine –SSFP images. Wilcox rank sum test for equal medians was used to test for statistical significant differences between the groups.

Results: The results are summarized in table 1. A change in wave amplitude could be observed in the left ventricle with lower wave amplitudes during systole (*U_sys*) and higher wave amplitudes during diastole (*U_dia*). In all experiments the changes of wave amplitude occurred ahead of morphological changes of the left ventricle and resulted in distinct *IVER* and *IVEC*-time intervals. *IVER* increased significantly (p = 0.03 for mild diastolic dysfunction) in diastolic mild dysfunction compared to normals (young and old). *IVEC* increased in the group of severe diastolic dysfunction (p = n.s.), which had also a lower LV EF, indicating systolic dysfunction.
The normalized wave amplitude in the left ventricle (*U_mean/U_ref*) decreased from young to old volunteers (p= 0.02) and even stronger in mild (p< 0.001) and severe (p< 0.01) diastolic dysfunction. The time resolved amplitude variations (*U_sys, U_dia*) were observed on a lower level of wave amplitude variation.

Table 1 Group	*sys-tole [ms]*	*dia-stole [ms]*	*RR-interv [ms]*	*IVEC [ms]*	*IVER [ms]*	*U_ref [mm]*	*U_ mean [mm]*	*U_ mean/ U_ref*	*U_sys [mm]*	*U_sys/ U_ref*	*U_dia [mm]*	*U_sys/ U_dia*	*U_dia/ U_ref*	*LV-EF (3D) [%]*
young (n=17)	325 ±54	612 ±128	946 ±116	152 ± 43	73 ±43	0.3451 ±0.112	0.2091 ±0.068	0.6243 ±0.158	0.2992 ±0.090	0.8883 ±0.166	0.2082 ±0.058	1.43 ±0.13	0.6277 ±0.140	62.4 ±4.0
old (n=5)	317 ±80	596 ±157	923 ±167	160 ±73	79 ±36	0.4414 ±0.109	0.2293 ±0.090	0.5150 ±0.104	0.3059 ±0.076	0.6974 ±0.086	0. 206 ±0.041	1.48 ±0.14	0.4776 ±0.092	59.6 ±8.9
mild (n=12)	327 ±83	534 ±117	868 ±137	172 ±67	105 ±51	0.4900 ±0.113	0.1697 ±0.067	0.3457 ±0.095	0. 268 ±0.081	0.5686 ±0.189	0. 191 ±0.067	1.43 ±0.18	0.4064 ±0.155	60.4 ±10.5
severe (n=4)	363 ±78	505 ±74	862 ±105	247 ±134	153 ±81	0.4211 ±0.102	0.1327 ±0.032	0.3267 ±0.091	0. 230 ±0.046	0.5570 ±0.099	0. 161 ±0.038	1.45 ±0.21	0.3873 ±0.067	49.0 ±9.2

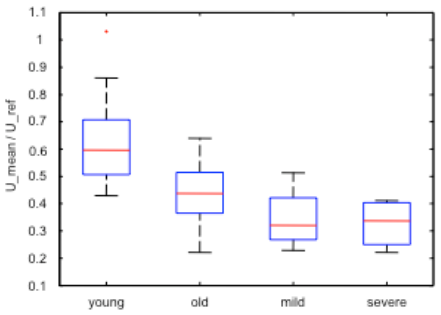

Figure 1: Boxplot displaying the normalized wave amplitude in the left ventricle *U_mean/U_ref* of the four groups. Significant differences can be found between young and old volunteers (p=0.02) and between young volunteers and diseased (p< 0.001-0.01). Only a trend towards lower normalized wave amplitudes between old volunteers and diseased (p=0.15-0.24) can be found.

Discussion and conclusion: Cardiac MRE is uniquely capable of measuring changes in myocardial elasticity in humans without intervention. Our results present the first indication that an increase in myocardial elasticity with age and disease can be measured by a clinical imaging modality using harmonic shear waves. We derived for the first time different MRE parameters as IVEC, IVER and wave amplitude ratios in different groups of diastolic dysfunction. In the group of severe diastolic dysfunction wave amplitudes were lower compared to mild diastolic dysfunction which indicates a further increase in myocardial stiffness due to disease progression. Further studies including more patients are necessary for defining normal values and cutoff limits for group separation.

References:

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