

Impact of Pericardial Effusion on Cardiac Mechanics in Patients with Dilated Cardiomyopathy

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Keywords: Finite Element Analysis, Cardiac Mechanics, Cardiomyopathy, Pericardial Effusion.

Abstract: Dilated cardiomyopathy (CDM) is a degenerative disease of the myocardium accompanied by left ventricular (LV) remodeling, resulting in an impaired pump performance. Differently, pericardial effusion (PE) is a liquid accumulation in the pericardial cavity, which may inhibit blood filling of heart chambers. Clinical evidence show that PE may improve pump performance in patients with CDM. Therefore, this study aims to assess wall stress and global function of patients with CDM, PE as compared to healthy patient. These findings suggests that CDM has an important implication in the mechanical changes of LV and right ventricle by increasing wall stress and reducing pump function. Conversely, PE determines lowering myocardial fiber stress and improves global function as compared to those of CDM.

1 INTRODUCTION

Dilated cardiomyopathy (CDM) is a degenerative disease of the myocardial tissue accompanied by left ventricular (LV) remodeling (Nakayama et al., 1987). The histologic characteristics of CDM include hypertrophy of myofibers, myofibrillar lysis, nuclear changes and vacuolization of myocardial fibers and interstitial fibrosis of the myocardium (Hayashida et al., 1990). LV remodeling is a multistep process that involves acute dilation of the infarcted area, increase of LV volume, lengthening of the LV perimeter, and decrease of LV curvature. Natural history studies show that progressive LV remodeling is directly related to future deterioration of LV performance and a poor clinical course (Cohn et al., 2000) (Swynghedauw, 1999).

Pericardial effusion (PE) is a pathological accumulation of fluid within the pericardial space (Mirhosseini et al., 2013). Usually, such disease do not influence clinical decision-making as long as the PE is not considered haemodynamically compromising cardiac functionality (Frohlich et al., 2013). PE fluid accumulation can be attributed to an underlying systemic or local inflammatory process such as cancer or myo-/pericarditis or might occur

after surgery or can be secondary to congestive, severe heart failure. However, the mechanism of PE development and its prognostic value in heart failure remain elusive. A persistent PE at echocardiographic follow-up was associated with unfavourable outcome when compared with patients with resolved PE. Indeed, patients with PE exhibit worse right ventricular (RV) function, larger right atrial dimensions, more pronounced tricuspid regurgitation as well as a higher prevalence of pulmonary hypertension. A recent study shows that patients with PE have significantly elevated RA filling pressures and an increased mean arterial pulmonary pressure, whereas the left ventricular filling pressure and wedge pressure did not differ between PE and control group (Frohlich et al., 2013).

Mathematical modeling of the cardiovascular system using the finite element (FE) approach is an useful too to estimate the cardiac mechanics and wall stress, likely inhibiting CDM and PE. A few FE modeling studies of the LV have validated stress calculations by showing good agreement with myocardial strain measured with implanted markers (McCulloch et al., 1992); (Omens et al., 1993); (Vetter and McCulloch, 2000). Guccione et al. have

successfully modeled end-isovolumic systole in an ovine model of myocardial infarction and determined material parameters that reproduced circumferential stretching (as measured with 2D tagged MRI) in the infarcted border zone (Guccione et al., 2001).

The key role of wall stress in the progression of LV remodeling was studied in DCM (Quarterman et al., 2002); (Ratcliffe et al., 1998); (Zhong et al., 2009). An increase in wall stress is known to reduce myocardial fiber shortening, and increases in LV wall stress have been reported in DCM. LV wall stress is in part determined by the local curvature of the ventricular wall (i.e., decreased curvature will increase wall stress). In addition to increasing LV size, CDM can alter myocardial properties and normal LV shape curvature. The border zone will have a higher stress, which makes it more susceptible to ischemia and infarction and may accelerate the remodeling process.

Therefore, the purpose of present study was to assess the key role of wall stress and global function of patients with CDM, PE. Cardiac mechanics was thus compared to that of healthy patients with normal wall thickness. We also tested the hypothesis that pump function and wall stress in CDM can be positively affected by the presence of a PE liquid.

2 MATERIALS AND METHODS

2.1 Imaging Procedure

We retrospectively identified patients with CDM and PE who underwent magnetic resonance imaging (MRI) from radiologic records of Mediterranean Institute for Transplantation and Advanced Specialized Therapies (ISMETT) and Ospedale Riuniti Trieste. Patients underwent MRI as part of their care, and not for the purpose of our study.

A series of long- and short-axis images of the heart were obtained performing MR imaging synchronized to the R wave of the electrocardiogram signal. Short -axis slices were taken sequentially every 6 mm until complete scanning of heart chambers.

2.2 Heart Reconstruction

Endocardial and epicardial MRI surfaces of LV and RV were segmented by contour lines using the vascular modeling toolkit VMTK (<http://www.vmtk.org>). Specifically, LV and RV geometries were reconstructed at end-diastole (ED)

and end-systole (ES), which are defined as the images with the maximum and minimum cross-sectional area, respectively. Patients with PE required also segmentation of the outer pericardial layer. After segmentation process, endocardial and epicardial surfaces of LV and RV were obtained by loft protrusion of segmented contour lines.

2.3 FE Model

The space between the endocardial and epicardial surfaces was meshed with 8-node brick elements to generate a volumetric mesh in ABAQUS FE code. Cardiac myofiber angles at the epicardium and endocardium were assigned to be -60 degrees and 60 degrees, respectively (counterclockwise positive when viewed from the epicardium).

Nearly incompressible, transversely isotropic, hyperelastic constitutive laws for passive and active myocardium was implemented in ABAQUS/Explicit using a VUMAT subroutine (Ratcliffe et al., 1998). Myocardial material parameters were estimated comparing MRI measured and computationally derived LV and RV volumes at ED and ES, respectively. Manual iteration was used rather than formal optimization. Similarly, PE was modeled as isotropic, hyperelastic material which mechanical properties were empirically found to match ED and ES volumes of PE.

The basal node of LV were constrained along long axis direction. The endocardial wall was loaded at ED and ES pressure occurring at LV and RV. For LV, ED pressure (P_{ED}) was 100 mmHg while ES pressure (P_{ES}) was 25 mmHg. For RV, P_{ED} was 15 mmHg while P_{ES} was 30 mmHg.

2.4 Pressure-volume Relationships and Stroke Volume

Chamber ED and ES volume (V_{ED} and V_{ES}) solutions were used with the corresponding P_{ED} and P_{ES} to plot the ED and ES pressure-volume relationships (ESPVR and EDPVR, respectively), which were then fit to appropriate polynomial equations. The following linear equation was used to estimate the ESPVR:

$$P_{ES} = E_{ES}(V_{ED} - V_0) \quad (1)$$

where E_{ES} is the end-systolic elastance and V_0 is the volume intercept of the ESPVR, each determined by linear regression of the data.

The polynomial equation used to estimate the EDPVR was as follows:

$$P_{ED} = E_{0,ED} + E_{1,ED}V_{ED} + E_{2,ED}V_{ED}^2 \quad (2)$$

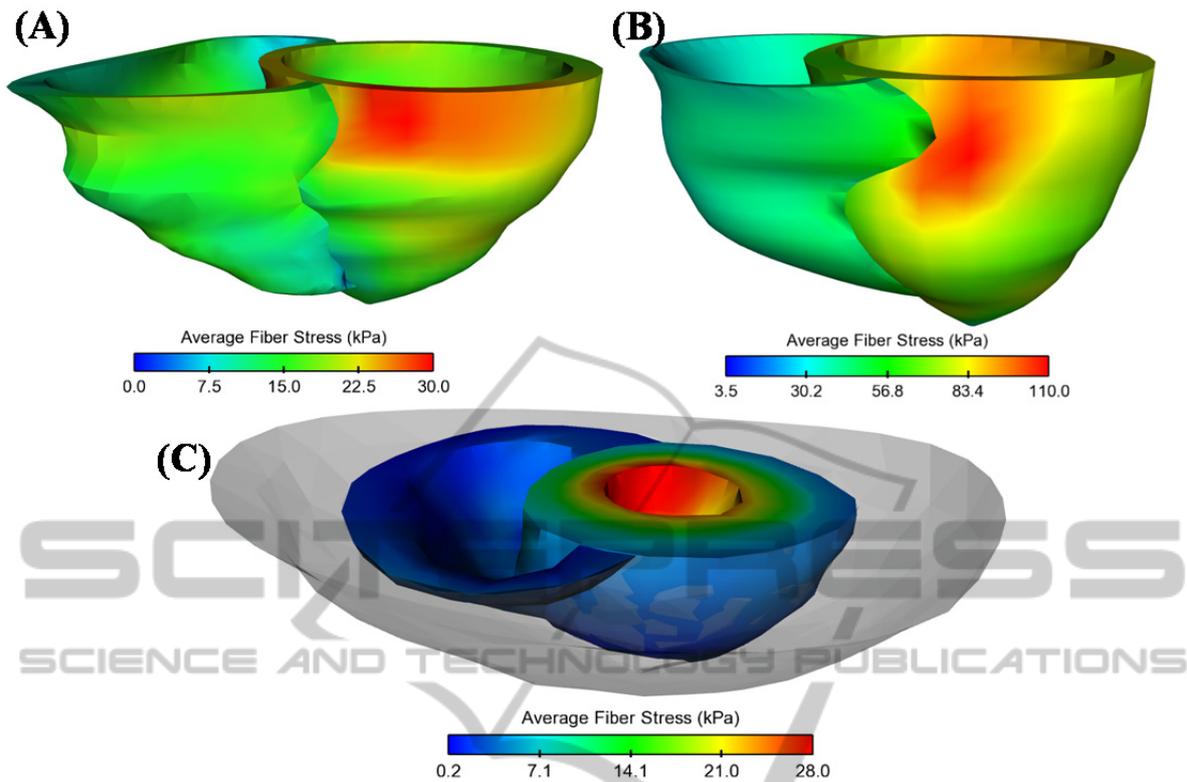


Figure 1: Representative map of average wall stress for (A) healthy patient, (B) CDM and (C) PE (solid grey indicates liquid volume); models are not at same scale.

where $E_{0,ED}$, $E_{1,ED}$ and $E_{2,ED}$ represent stiffness of the LV diastolic compliance, again determined by linear regression.

To determine global changes to pump function, the stroke volume (SV)/ P_{ED} and SV/V_{ED} relationships were calculated and plotted, assuming that arterial elastance (E_A) was constant. SV was calculated according to the following equation:

$$SV = \frac{V_{ED} - V_0}{1 + E_A/E_{ES}} \quad (3)$$

2.5 ED and ES Fiber Stress

For each simulation, stress in the local muscle fiber direction was computed throughout the LV and RV walls at end-diastole and end-systole of the pressure-volume load. Thus, we evaluated the average fiber stress has the mean value between the longitudinal fiber stress and the cross-fiber stress.

3 RESULTS

Figure 1 shows representative distribution of

average fiber stress for patients with PE and CDM as compared to the healthy patient. It can be observed that ES LV stress is higher than that of RV, and this occurs in the lateral side of LV chamber. Differently, the patient with PE show higher ES wall stress at the endocardial surface a cause of the liquid constraining LV wall motion.

Maximum values of ES average fiber stress was found markedly higher for patients with CDM (105.5 kPa, n=3) compared to that of healthy patient (20.9 kPa, n=2) and PE patient (42.9 kPa, n=2) as shown by Figure 2. For both healthy and CDM cases, maximum value of ED average fiber stress was found drastically lower that those exhibited at end-systolic phase (i.e., 13.5 kPa for healthy and 12.2 kPa for CDM). In contrast, ES fiber stress of PE cases decreased up to 19.1 kPa.

For LV, CDM caused a leftward shift of both EDVPR and ESPVR whereas PE induced a rightward shift of these relationships as shown by Fig. 3. Similar results are shown by RV. Starling curve for CDM lies on the left compared to that of both PE and healthy patients. Indeed, stroke volume (Starling law) was reduced in CDM because the decrease in diastolic compliance was not sufficiently

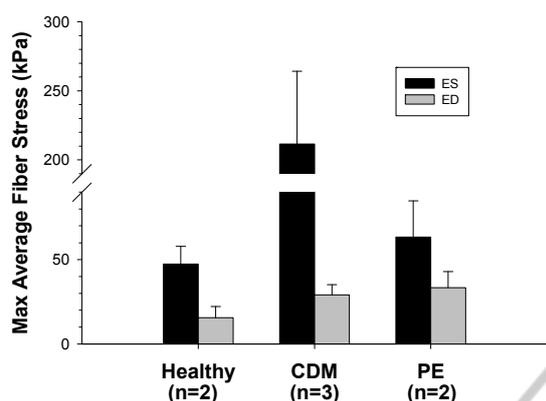


Figure 2: Comparison of maximum average wall stress among patients with CDM and PE. Control, healthy patient is also shown. Data are mean±SEM.

compensated by the improvements in end-systolic elastance.

4 DISCUSSION

The present research demonstrates clearly that CDM and PE alter differently both wall stress and cardiac function when compared to healthy subject. Indeed, the most striking finding is that the patient with PE exhibits lower myocardial fiber stress and better global function than those of the patient with CDM. Therefore, both CDM and PE have important implications in the mechanical changes of both LV and RV chambers.

There are few studies on the wall stress and cardiac function in CDM. Among these, Zhong et al. investigated LV remodeling in ischemic CDM using FE modeling (Zhong et al., 2009). They suggested that LV remodeling in ischemic CDM is a multistep process, which determines loss of contractile function followed by acute dilatation of the infarction area, increase of LV volume, lengthening of the LV perimeter, and blunting of the normal curvature. Wall stress were found increased in each region of LV wall and has been shown to be a measure of the afterload following infarction. These findings are in agree with our distribution of wall stress in CDM. Nevertheless, we found that ES wall stress are 72% higher than that of healthy and PE subjects, suggesting adverse clinical outcome for this cardiac disease.

FE modeling has been widely used to study cardiac diseases, and this has led to an improved integrative understanding of the heart system. For instance, Wenk et al. evinced that residual stress

produced by ventricular volume reduction surgery has a little effect on the LV function and cardiac mechanics (Wenk et al., 2010). Another study suggests that surgical anterior ventricular restoration reduces myofiber stress in the akinetic infarct at the expense of a reduction in the Starling relationship (Jhun et al., 2010). FE analysis also demonstrated that aneurysm implication decreases fiber stress without depressing stroke volume (Guccione et al., 2001); (Walker et al., 2005). Recently, Carrick et al. highlighted that Coapsys procedure decreases myofiber stress at ED and ES, and that the improvement in myofiber stress may contribute to the long-term effect of Coapsys on LV remodeling (Carrick et al., 2012).

In tissue engineering approach, FE simulation indicated that the addition of non-contractile material to a damaged LV wall has important effects on cardiac mechanics, with potentially beneficial reduction of elevated myofiber stresses, as well as confounding changes to clinical left ventricular metrics (Wall et al., 2006). This study therefore supports our hypothesis that that pump function and wall stress in CDM may be improved by surrounding the epicardial layer with liquid as it occurs in PE. This is also confirmed by clinical evidence in patients with liquid accumulation for which the global pressure-volume relationships is shift further to the left as suggested by our computational model.

6 MODEL LIMITATIONS

Although this model captures many aspects of LV and RV mechanics in both CDM and PE, limitations still exist. One significant limitation is that wall thickness between patients with CDM and PE were different.

This likely influences the wall stress which is given by the ratio of the pressure exerted on the LV endocardio on wall thickness. Indeed, patient with PE had a LV wall thickness of 8.5 mm which is higher than that of CDM (i.e., 5.7 mm). Future study needs patient comparison at matched values of LV wall thickness.

Other limits include calculation of regional myocardial material properties as well as restricted number of patients. In spite of this limitations, these findings provide relevant insight on the cardiac mechanics of patients with CDM and PE.

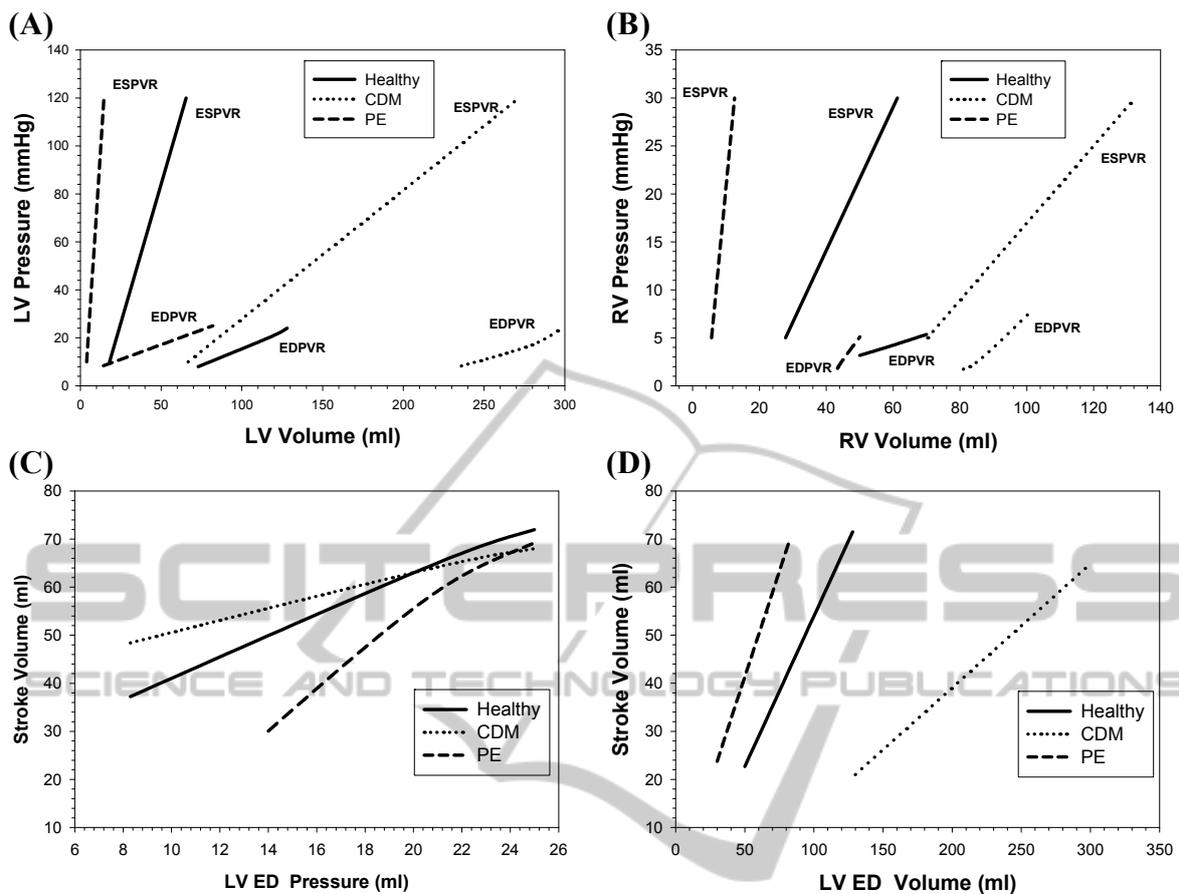


Figure 3: Representative cardiac function for a patient of each group: (A) LV pressure-volume relationships, (B) RV pressure-volume relationships, (C) LV stroke volume on ED pressure and (D) LV stroke volume on ED volume.

7 CONCLUSIONS

This study suggests that CDM and PE conversely alter both wall stress distribution and global cardiac function. The reduction in the myofiber stress caused by liquid accumulation on the pericardial layer may contribute to the long-term clinical outcome of patient with PE.

ACKNOWLEDGEMENTS

The authors thank Mr. Armando Pasta of ISMETT for his technical assistance with image acquisition. This study was funded in part by a grant from Fondazione RiMED provided to Dr. Pasta.

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