Received: 3 May 2021 | Accepted: 8 July 2022

DOI: 10.1111/cpf.12780

ORIGINAL ARTICLE

Clinical Physiology and Functional Imaging

Cardiac remodelling in association with left ventricular dyssynchrony and systolic dysfunction in patients with coronary artery disease

Hanna Hämäläinen[1,2] | Tiina M. Laitinen[1] | Marja Hedman[2,3] | Antti Hedman[4] | Antti Kivelä[4] | Tomi P. Laitinen[1,2]

[1]Department of Clinical Physiology and Nuclear Medicine, Kuopio University Hospital, Kuopio, Finland

[2]Institute of Clinical Medicine, University of Eastern Finland, Kuopio, Finland

[3]Department of Cardiothoracic Surgery, Kuopio University Hospital, Kuopio, Finland

[4]Heart Center, Kuopio University Hospital, Kuopio, Finland

Correspondence

Hanna Hämäläinen, Department of Clinical Physiology and Nuclear Medicine/Kuopio University Hospital, PO BOX 100, Kuopio FI-70029 KYS, Finland.
Email: hanna.hamalainen@kuh.fi

Funding information

Paavo Nurmen Säätiö; Suomen Lääketieteen Säätiö; Specified governments transfers to the Kuopio University Hospital, Grant/Award Number: 5031349; Aarne Koskelon Säätiö; Sydäntutkimussäätiö; Itä-Suomen Yliopisto, Grant/Award Number: Doctoral School; Finnish Cardiac Society; Suomen Kulttuurirahasto

Abstract

Background: In patients with coronary artery disease (CAD), ischaemic cardiomyopathy may result in progressive cardiac remodelling and left ventricular (LV) dysfunction. Myocardial perfusion imaging (MPI) can be used to quantify LV size and shape, mechanical dyssynchrony (LVMD) and ejection fraction (EF) as well as myocardial ischaemia and injury extents. We investigated the prevalence of LV remodelling (LVR) in patients with CAD and the relationship between LVR, LVMD and EF.

Methods: Three hundred twenty-six patients with CAD were evaluated. The EF and end-diastolic volume (EDV) were measured using MPI. LVMD was assessed using phase analysis. LVR was characterised according to LV dilatation or increased shape indices (systolic shape index [SIES] and diastolic shape index [SIED]).

Results: LVR were observed in 41% of CAD patients. EDV, SIES and SIED were larger in patients with LVMD or low EF. After adjustment for age, sex and infarct and ischaemia extents, phase histogram bandwidth correlated with EDV ($r = 0.218$) and SIES ($r = 0.266$) and EF correlated with EDV ($r = -0.535$), SIES ($r = -0.554$) and SIED ($r = -0.217$, $p < 0.001$ for all).

Conclusions: LVR is frequently seen in patients with CAD and may be detected even before the development of symptomatic heart failure. A large LV volume and a more spherical-shaped LV were associated with LVMD and low EF, highlighting the close relationships between remodelling and systolic dyssynchrony and dysfunction. MPI is useful for assessing LVR by providing information about LV size and shape, which changes from an ellipsoid towards a spherical form in the development of ischaemic cardiomyopathy.

KEYWORDS

coronary artery disease, ejection fraction, heart failure, left ventricular mechanical dyssynchrony, phase analysis, remodelling, shape index, single-photon emission computed tomography

1 | INTRODUCTION

A healthy left ventricle (LV) contracts symmetrically during systole and is more bullet-like in shape than spherical in three-dimensional geometry. In response to pathophysiological stimuli, such as ischaemia or excessive mechanical load, multiple molecular and cellular processes contribute to LV remodelling (LVR) (Burchfield et al., 2013). Adverse remodelling of LV volume and shape are commonly seen in patients with heart failure and LVR is known to predispose individuals to cardiovascular morbidity and mortality (Burchfield et al., 2013). LV mechanical dyssynchrony (LVMD) was also found to be a significant determinant of LV systolic dysfunction in patients with heart failure and it may occur even without signs or symptoms of heart disease (Miyachi et al., 2013). The interactions between LVR and LVMD are yet not completely known.

LVR is a complex of events that may take place under various pathological conditions. For example, after myocardial infarction, over time, LV may undergo significant volumetric dilatation leading to reduced LV function. Furthermore, chronic LV pressure overload can induce significant concentric LV hypertrophy that may also proceed to reduce LV contractile function. This LVR may also alter the shape of the LV into a more spherical-like shape, which may further impair LV function. These changes in LV geometry have been associated with adverse outcomes (Ambale-Venkatesh et al., 2017; Gimelli et al., 2019, 2020; Phan et al., 2016). On the other hand, in patients with symptomatic heart failure, cardiac resynchronisation therapy (CRT) may be an effective treatment, and it has been found to reverse remodelling in patients with heart failure (Bank et al., 2015; Bozyel et al., 2017; Itoh et al., 2015; St John Sutton et al., 2017; Zhang et al., 2015).

LV shape and its transition from a bullet- to a spherical-like shape has been measured with cardiac magnetic resonance imaging (Ambale-Venkatesh et al., 2017), echocardiography (Phan et al., 2016) and myocardial perfusion imaging (MPI) using single-photon emission computed tomography (SPECT) (Gimelli et al., 2019, 2020). Electrocardiography (ECG)-gated MPI SPECT offers a way to simultaneously measure LV perfusion, LV volume and function as well as quantitatively measure LVMD. It is also possible to measure LV shape more precisely with MPI SPECT with LV shape indices (Abidov et al., 2006; Gimelli et al., 2019, 2020). A greater shape index is associated with more spherical LV morphology.

The development of LVMD may be one of the mechanisms leading to the progression of heart failure. LVMD has also been found to be connected to myocardial infarct scarring and myocardial ischaemia (Hämäläinen et al., 2021). Enlargement of the LV and its transition to being more spherical may also be one factor in the development of LVMD. Our aim was to evaluate prevalence of LVR in a large sample of coronary artery disease (CAD) patients. Furthermore, to explore association between LVR and LVMD, these factors were assessed using the ECG-gated MPI SPECT with phase and shape analyses.

2 | METHODS

This study was approved by the Ethics Committee of Kuopio University Hospital.

2.1 | Subject selection

We retrospectively analysed medical records and MPI SPECT studies of 1191 patients who underwent MPI from January 2009 to May 2011 in the Department of Clinical Physiology and Nuclear Medicine, Kuopio University Hospital. Of this population, we included patients who had: (1) a diagnosis of CAD; (2) full MPI data (both rest and stress studies) available; and (3) a 12-lead electrocardiogram available from the MPI study. We excluded patients with atrial fibrillation to avoid bias of the LVMD measurements. There were 326 patients (128 women and 198 men) who fulfilled these criteria.

Basic characteristics (age, gender, weight, height and body mass index) of the patients were collected, as well as previous invasive cardiac procedures, such as percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG), chronic diseases, medications and history of smoking from the medical records. In addition, we analysed the ECG recordings and the MPI data and performed phase analyses.

The whole study population was recorded as the CAD group, which was further divided into subgroups: (1) having LVMD or (2) having a low ejection fraction (EF). Furthermore, subjects were classified according to the American College of Cardiology Foundation/the American Heart Association (ACCF/AHA) heart failure classification criteria in a four-step breakdown (A–B–C–D) (Yancy et al., 2013). Stage A represents high risk for developing heart failure but without structural heart disease or symptoms of heart failure, stage B represents structural heart disease but without signs or symptoms of heart failure, stage C represents structural heart disease with prior or current symptoms of heart failure, and stage D represents refractory heart failure requiring specialized interventions.

2.2 | MPI protocol

A 1-day adenosine MPI protocol was used for this study. Patients were instructed to avoid caffeine-containing beverages and medications for 24 h before MPI. Adenosine-stress MPI with 99mTc-tetrofosmin was performed and all the included patients underwent both stress and rest phases. At the stress phase, adenosine at a rate of 140 μg/kg/min (in case of adenosine-related symptoms, the dose was reduced to 98 or 70 μg/kg/min) was administered intravenously for 6 min. Intravenous 99mTc-tetrofosmin (300 MBq) was injected as a bolus at 4 min from the onset of adenosine infusion. Low-level bicycle exercise was used in combination with adenosine infusion when possible, to avoid extracardiac tracer accumulation. Thirty minutes after the tracer injection, ECG-gated MPI SPECT was

acquired. For the rest study, patients received another intravenous injection of tracer (99mTc-tetrofosmin, 700 MBq) and were imaged 45 min after the injection.

2.3 | Image acquisition

MPI scans were performed in the supine position with a dual detector SPECT/CT system (Philips Precedence; Royal Philips N.V., Amsterdam, the Netherlands). The image acquisition was carried on with detectors in 90° configurations using 180° body contour orbits with 64 projections. An energy window with a width of 20% was centred on 140 keV and images were acquired at a 128 × 128 matrix size. The gated data were acquired with 16 time bins at 25 or 30 s per angle depending on the patient's weight (if weight was <100 kg, 25 s/angle was used, and if weight was ≥100 kg, 30 s/angle was used). Reconstructions were made with HERMES Hybrid Recon Cardiology (Hermes Medical Solution AB).

2.4 | Perfusion analysis

LV perfusion analyses were carried out retrospectively for reconstructed rest and stress images using automated QPS/QGS2012 software (Cedars-Sinai Medical Centre, 2011). The perfusion defect area relative to the total LV area (injury %) and the reversible perfusion defect area relative to the total area (ischaemia %) were measured (Kang et al., 1997).

2.5 | Volume analysis

The volume parameters were collected from automated Quantitative Gated SPECT (QGS) algorithm (QGS2012, QGS software, Cedars-Sinai Medical Centre), in which the mid-myocardial LV surface was first computed and endo and epicardial surfaces were computed subsequently. The LV end-diastolic volume (EDV), end-systolic volume (ESV), stroke volume and EF were calculated by identifying the endocardial surface of the LV in different time frames of the cardiac cycle. For subgroup analysis, a low EF was characterised as EF ≤ 50%.

2.6 | Phase analysis

Phase analysis data were collected with reconstructed rest perfusion scanning from ECG-gated MPI SPECT data using the QGS2012-programme. Phase analysis assesses regional LV count changes throughout the cardiac cycle and records the time when each segment starts to contract (Hess et al., 2017). Phase analysis detects regional count changes in 16 time bins to observe the variation in LV wall thickness throughout the cardiac cycle. This was done for 1008 spatial points covering the whole LV area (myocardial surfaces were presented using two-dimensional ellipsoidal coordinate systems with 36 longitudes and 28 latitudes). The onset of mechanical contraction was assessed for each spatial point and the information was presented as a phase histogram, describing the distribution of the timing of LV regional onset of mechanical contraction as a function of the length of the RR-interval (Hess et al., 2017). The phase histogram reflects the heterogeneity of regional LV contraction over time: the greater the phase histogram bandwidth (PHBW), standard deviation (PHSD) and entropy (PHE) are, the more dyssynchronic the LV contraction is (Van Kriekinge et al., 2008). The definition of having LVMD is to have the values of PHBW, PHSD or PHE above the limit of the highest normal value based on our earlier defined reference material (PHBW > 63.7°, PHSD > 26.5°, PHE > 63.7%) (Hämäläinen et al., 2018).

2.7 | Definition of LVR

A shape index defines three-dimensional LV geometry derived from LV endocardial contours in end-systolic and end-diastolic phases and is defined as the ratio between the maximum dimension of the LV in all short-axis planes and the length of the midventricular long axis as shown in Figure 1 with arrows (Figure 1 shows one of many short-axis planes and the midventricular long axis). The QPS programme automatically measures the LV shape index in the end-systolic and end-diastolic phase (Cedars-Sinai Medical Centre, 2011; Nitta et al., 2020). First, for each short-axis plane on the end-diastolic images, the maximum dimension of the LV is found by using the endocardial surface as the boundary for distance between two endocardial points derived from the raw three-dimensional contours derived from gated SPECT. The maximum long-axis endocardial dimension is estimated from the distance between the most apical point of endocardial surface and the centre of the valve plane in the end-diastolic images (Nitta et al., 2020). The same measurements are also calculated using the end-systolic images, in the identical locations, to define the LV shape index at end-diastole and end-systole. The end systolic shape index (SIES) and end diastolic shape index (SIED) range from 0 (ellipsoid) to 1 (spherical) (Cedars-Sinai Medical Centre, 2011; Nitta et al., 2020).

LVR was characterised according to LV dilatation with EDV or SIES or SIED exceeding the limit of highest normal. Enlargement of the LV was characterised by overcrossing the reference values according to our previous report (EDV_{male} > 139.1 ml and EDV_{female} > 94.3 ml) (Hämäläinen et al., 2018). Reference values for normal LV shape indices were derived from the same reference group. The limit of highest normal was 0.548 for SIES and 0.792 for SIED.

2.8 | Statistical analysis

A one-sample Kolmogorov–Smirnov test was used to test the normality of distribution for continuous variables. Descriptive statistics for continuous variables were presented as mean ± SD. In

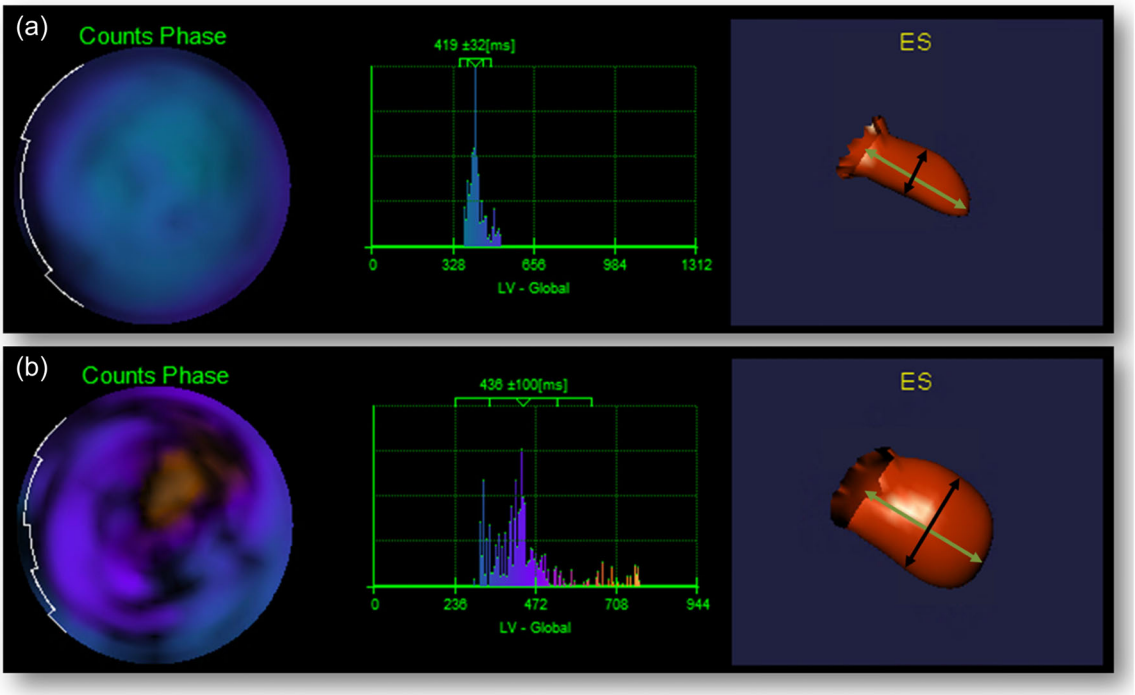

FIGURE 1 Two representative cases of an ellipsoid-shaped left ventricle (LV) (upper panels) and a spherical-shaped LV (lower panels). The upper panel (a) shows the phase histogram and the shape of the LV in a 76-year-old male with synchronous LV contraction (narrow phase histogram) and an ellipsoid-shaped LV with an end-diastolic volume (EDV) of 95 ml, an end-systolic shape index (SIES) of 0.42, an end-diastolic shape index (SIED) of 0.65, a phase histogram bandwidth (PHBW) of 30.0° and an ejection fraction (EF) of 75%. The lower panel (b) shows the case of a 66-year-old male with LV dyssynchrony (wide phase histogram) and spherical-shaped LV with an EDV of 269 ml, an SIES of 0.69, an SIED of 0.72, a PHBW of 153.0° and an EF of 16%. The righthanded red pictures represent the formation of an SIES that is defined using an end-systolic frame and measures the ratio of the maximum dimension of the LV along all short-axis planes (black arrows) to the maximum dimension of the midventricular long axis (green arrow). The SIED is measured based on the analogous principle from the end-diastolic frame.

the case of continuous variables, a *t*-test was used to assess the statistical significance between the two independent samples. Comparisons of the two categorical variables were carried out using a χ^2 test. Associations between LVMD, EF and LVR were analysed using the Pearson correlation analysis and the partial correlation analysis adjusted for either age and sex or age, sex, extent of myocardial scarring and extent of ischaemia. Statistical tests were two sided and significance was present if $p < 0.05$. All statistical calculations were performed with the SPSS for Windows programmes (SPSS 25.0).

3 | RESULTS

3.1 | Patient characteristics

Patient clinical characteristics are summarised in Table 1. In the CAD group ($n = 326$), the mean age was 68 ± 10 years and there were 198 males (61%) and 128 females. There were 250 patients (77%) who had hypertension, 106 patients (33%) who had diabetes, and 140 patients (43%) had previously diagnosed myocardial infarction. PCI had previously been made for 127 patients (39%) and CABG for 111 patients (34%). A left bundle branch block was found in 23 (7%) patients. Based on the ACCF/AHA heart failure classification criteria 225 patients (69%) were classified into stage B, 86 patients (26%) into stage C and 15 patients (5%) into stage D.

Abnormally high EDV, SIES and SIED were seen in 27%, 24% and 9% of patients, respectively. In 133 patients, any of these indicators of LVR were present, which means a prevalence of 41% in our population. Prevalence of LVR was 28% in ACCF/AHA heart failure stage B, 64% in stage C and 100% in stage D ($p < 0.001$ between the stages). Nearly one-third of the CAD patients had LVMD ($n = 94$, 29%); low EF (EF ≤ 50%) was found in 22% of the CAD patients.

The extents of myocardial injury and ischaemia were significantly larger in the LVMD and low EF groups as compared to those without LVMD and those with normal EF, as shown in Table 1. In the LVMD group 53 patients (56%) had LV EF < 50%. Correspondingly, in the low EF group 53 patients (74%) had LVMD. The LVMD group had statistically significantly lower EF, increased EDV, greater shape indices and higher perfusion scores compared with the non-LVMD group. In the LVMD group LVR was observed in 67 patients (71%). Furthermore, patients in the low EF group had a statistically significantly higher PHBW, PHSD, PHE as well as increased EDV

TABLE 1 Clinical characteristics of the study population

	CAD group (*n* = 326)	Non-LVMD (*n* = 232)	LVMD (*n* = 94)	Normal EF (>50%) (*n* = 254)	Low EF (≤50%) (*n* = 72)
Background information					
Age (years)	68 ± 10	68 ± 10	69 ± 11	68 ± 10	69 ± 11
Male	198 (61%)	133 (57%)	65 (69%)*	135 (53%)	63 (88%)###
Weight (kg)	83 ± 18	82 ± 17	84 ± 19	82 ± 17	84 ± 20
Height (cm)	167 ± 10	166 ± 9	169 ± 10*	166 ± 9	172 ± 9###
BMI (kg/m^2)	29.5 ± 5.4	29.6 ± 5	29.2 ± 5	29.8 ± 5.5	28.3 ± 5.2#
Systolic BP	145 ± 23	148 ± 23	140 ± 23**	148 ± 24	136 ± 18###
Diastolic BP	74 ± 10	74 ± 11	75 ± 9	74 ± 11	74 ± 9
Perfusion scores					
Ischaemia %	4.2 ± 2.6	3.8 ± 2.4	5.2 ± 2.9***	3.9 ± 2.4	5.1 ± 3.1##
Injury %	6.5 ± 9.3	4.2 ± 6.7	12.1 ± 12.1***	3.6 ± 5.9	16.6 ± 11.8###
Volume parameters					
EDV (ml)	112 ± 61	97 ± 47	149 ± 74***	92 ± 28	184 ± 86###
ESV (ml)	50 ± 50	35 ± 31	88 ± 66***	31 ± 16	119 ± 67###
EF (%)	62 ± 16	68 ± 12	47 ± 16***	68 ± 10	38 ± 10###
Shape indices					
SIES	0.49 ± 0.10	0.46 ± 0.09	0.56 ± 0.11***	0.46 ± 0.08	0.60 ± 0.11###
SIED	0.68 ± 0.08	0.68 ± 0.08	0.70 ± 0.09**	0.67 ± 0.08	0.72 ± 0.09###
Phase analysis					
PHBW (degrees)	48 ± 26	48 ± 21	77 ± 34***	48 ± 20	85 ± 36###
PHSD (degrees)	14 ± 7	14 ± 6	21 ± 9***	14 ± 6	23 ± 10###
PHE	60 ± 6	61 ± 5	67 ± 5***	61 ± 5	68 ± 5###

Note: Values are mean ± SD. Statistical significances between the non-LVMD and LVMD groups: *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$; and between the normal EF and low EF groups: #$p < 0.05$, ##$p < 0.01$, ###$p < 0.001$.

Abbreviations: BMI, Body mass index; BP, Blood pressure; CAD, Coronary artery disease; EDV, End-diastolic volume; EF, Ejection fraction; ESV, End-systolic volume; LVMD, left ventricular mechanical dyssynchrony; NS, not statistically significant; PHBW, Phase histogram bandwidth, PHE, Phase histogram entropy; PHSD, Phase histogram standard deviation; SIED, End-diastolic shape index; SIES, End-systolic shape inde.

and higher shape indices than in patients with normal EF. In the low EF group LVR was observed in 63 patients (88%).

3.2 | Association between LVMD, EF and LVR parameters

Figure 2 shows the correlations between PHBW, EDV and the shape indices. The greater the PHBW, the more spherical the LV and the larger the EDV were. According to the univariate analysis, similar correlations were found with PHSD and EDV ($r = 0.373$), SIES ($r = 0.486$) and SIED ($r = 0.207$) as well as with PHE and EDV ($r = 0.466$), SIES ($r = 0.492$) and SIED ($r = 0.208$), $p < 0.001$ for all. After adjustment for age, sex and extents of myocardial scarring and ischaemia, PHBW was associated statistically significantly with EDV ($r = 0.212$, $p < 0.001$), SIES ($r = 0.380$, $p < 0.001$) and SIED ($r = 0.189$, $p < 0.001$). Figure 3 shows the correlations between EF, EDV and the shape indices. The lower the EF, the more spherical the LV and the larger the EDV were. After adjustment for age, sex and extents of myocardial scarring and ischaemia, EF correlated significantly with EDV ($r = -0.538$, $p < 0.001$), SIES ($r = -0.554$, $p < 0.001$) and SIED ($r = -0.226$, $p < 0.001$).

4 | DISCUSSION

LVR is a long-term response to myocardial injury or chronic volume overloading, which, over time, changes the shape and function of the LV (Berti et al., 2011; Udelson, 2017). LVR has been found to occur even despite successful reperfusion after acute myocardial infarction (Berti et al., 2011; Goel et al., 2014), and it is one step in the development of heart failure. This study showed that LVR is

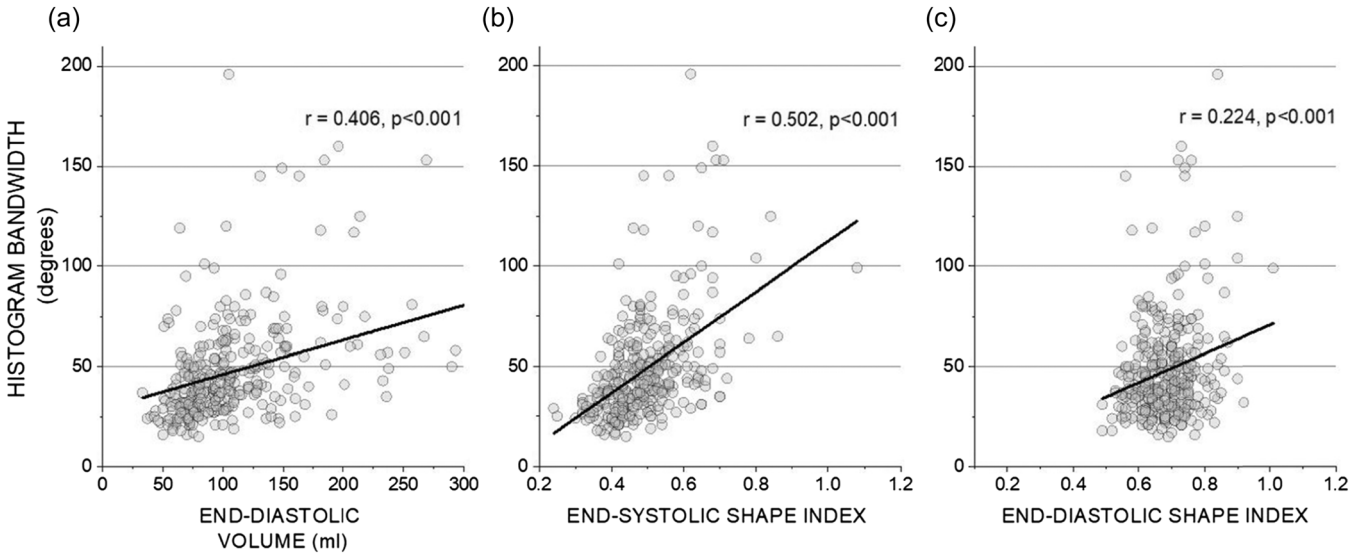

FIGURE 2 The correlation between the phase histogram bandwidth and (a) the end-diastolic volume, (b) the end-systolic shape index and (c) the end-diastolic shape index.

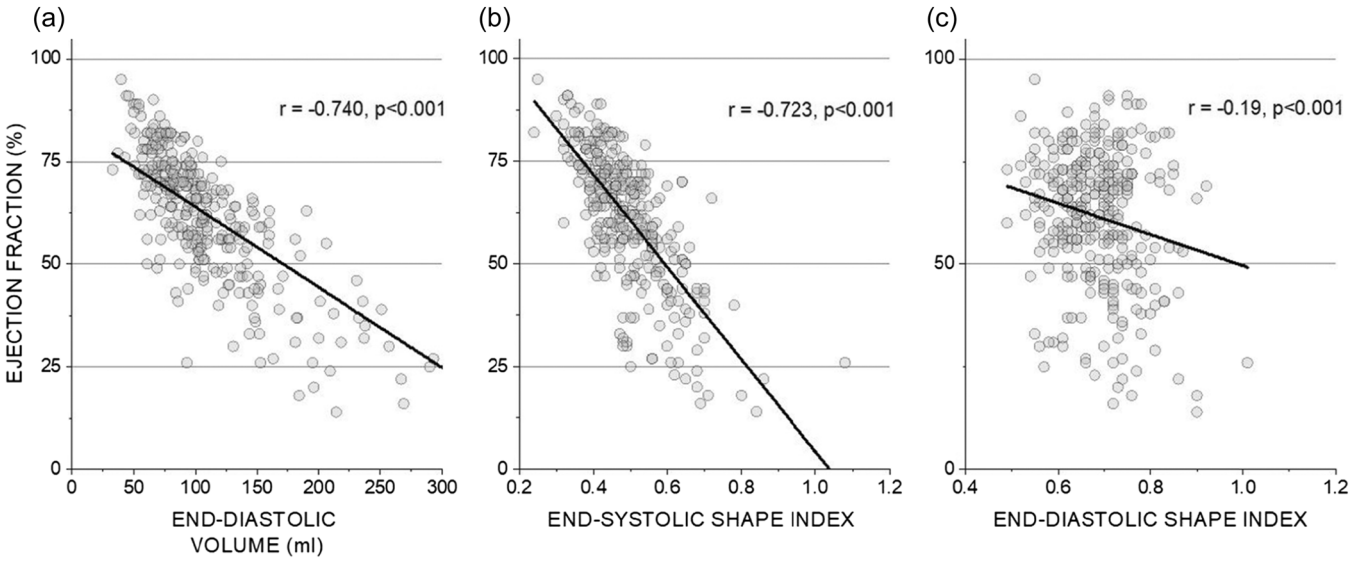

FIGURE 3 Correlation between left ventricular ejection fraction and (a) the end-diastolic volume, (b) the end-systolic shape index and (c) the end-diastolic shape index.

frequently seen in patients with CAD referred for MPI. A large LV volume and a more spherical-shaped LV were associated with LVMD and low EF.

The lack of a generally accepted definition of LVR makes it difficult to accurately assess prevalence of LVR and to compare prevalence rates between different studies. Therefore, previous information on the prevalence of LVR in different situations is incomplete and it is not unambiguous to examine the results of this study by comparing them with the prevalence rates presented in the literature. Our study was a cross-sectional study, and we defined LVR as a condition where either the left ventricular (LV) EDV or the LV end-systolic or end-diastolic shape index is greater than the upper limit of normal variation detected from the reference population. So far, we do not know if such definition of LVR would be predictive of outcomes and demonstration of its reliability and usability requires further investigation. We found that in CAD patients the prevalence of LVR was 41%. The highest prevalence rates were observed in patients belonging to the ACCF/AHA heart failure stages C and D. In patients with LV EF below 50% prevalence of LVR was 88%. In subjects with acute ST elevation myocardial infarction an increase in LV EDV of at least 12%–20% or an increase in ESV of at least 12% –15% from baseline to 3 months follow-up has been interpreted as evidence of advanced LVR (Legallois et al., 2022). Based on a meta-analysis, the prevalence rate of LVR after ST segment elevation

myocardial infarction has been about 23% (Legallois et al., 2022), which is a little lower than in our cross-sectional study with a different definition.

Currently, in clinical work, EDV may be the most usable clinical variable associated with diagnosis of LVR. Moreover, EF is a usable parameter in recognizing LVMD in clinical work: it reflects the function of LV and EDV, the volumetric load. This study showed that EF is strongly associated with LVMD and 74% of patients with LVMD had decreased EF. If the shape of the LV transforms into a more spherical shape, the EDV increases and the EF decreases because the synchronous contraction of LV suffers from altered three-dimensional structure. This study also showed that EDV as well as the shape indices (SIES and SIED) were associated with LVMD. SIES correlated more strongly with PHBW than SIED did.

We speculate that the SIES also partly reflects the systolic function of the LV because in a well-contracting LV, the diameter of the LV decreases more during contraction than the length of the LV. When contraction is deficient, the LV shape remains more spherical at the end-systolic phase. The SIED reflects more the shape of the LV in the diastolic phase when the shape of LV is at the initial state. The EDV is affected by many factors and it offers more than just predictions regarding the shape of LV, which the shape indices derived from MPI SPECT can also describe. We speculate that measuring the shape of the LV may provide additional important information when studying the pathophysiology and development of heart failure.

Recently, (Nitta et al., 2020) studied 167 patients with normal perfusion to investigate the associations of LV shape with LV volume and function and found that the SIES was associated with LV systolic and diastolic functions and age, ESV and EF were independently associated with the SIES. In their study, the mean SIES was 0.49 ± 0.07, which was close to our 326 CAD patients who had a mean SIES of 0.49 ± 0.10. In our study, the SIES was lower in the non-LVMD group (0.46 ± 0.09) and higher in the LVMD group (0.56 ± 0.11). The SIED was also comparable to Nitta et al. (2020): in our study, the mean SIED was 0.68 ± 0.88; in their study, the SIED was 0.67 ± 0.007. In our study, the SIES correlated with the extent of infarct scarring. Based on our results, the bigger the infarct scar was, the more spherical the LV shape was and the more pronounced the LVMD was. In another study, the spherical shape of the LV was also studied with the additional measurement of an eccentricity index (Gimelli et al., 2019, 2020). Thus, in multivessel CAD, the LV was found to be more spherical compared to patients without CAD (Gimelli et al., 2019, 2020). Nitta et al. (2020) excluded patients with summed stress score > 3 and they did not measure LVMD. Our study group was more versatile, but the results were still comparable. Adverse LVR in our study probably resulted mostly from perfusion defects and less from elevated hemodynamic load, such as valvular heart disease or arterial hypertension, that were more important factors in Nitta et al.'s (2020) study. In addition to reference group with normal perfusion or CAD patients, the LV shape indices have also been studied between diabetic and nondiabetic patients (Nappi et al., 2018) with the finding that diabetic patients had greater shape indices than nondiabetic patients.

Gaudieri and coworkers evaluated the added prognostic value of the LV shape index assessed by MPI SPECT in 674 patients without known CAD and with normal perfusion and EF (Gaudieri et al., 2019). In that study an SIES of ≤0.54 was considered normal, as shown by Abidov et al. (2006) previously. Survival of the patients with an abnormal shape index was lower in the follow-up study. In this context, the idea was raised that evaluation of the LV shape index may identify patients with early-stage LVR. In our study of CAD patients, the average SIES based on these limits was normal in the non-LVMD group (0.46 ± 0.09) but elevated (0.56 ± 0.11) in the LVMD group.

As a result of our findings, it seems that the shape of the LV is closely associated with volumetric and functional remodelling changes as well as with LVMD—and combined all these may indicate risk for the development of heart failure. This was also noted in a previous follow-up study (Stankovic et al., 2017), which indicated that the association between the correction of LVMD after CRT with survival was stronger than that of any volumetric cut-off value, even though volumetric response after CRT was strongly associated with long-term mortality. The point in time during the development of heart failure when the shape of the LV starts to become more spherical, when LVMD occurs and when the contractile function of LV starts to fail is not clear. We consider that early recognition of the factors predicting upcoming heart failure, including early remodelling changes, may help in preventing future heart failure.

The population of our study was large and the present data provide a representation of the actual population of subjects submitted for MPI. The study was retrospective, so all patients included in the study were sent for MPI SPECT for medical reasons and the selection was made based on previous medical records, while the analyses were made afterwards. All patients had previous clinical diagnosis of CAD. Only atrial fibrillation was the exclusion criterion. Therefore, some of the patients may have suffered from other chronic diseases in addition to CAD. By using MPI we are able to simultaneously and quantitatively assess enlargement of the LV and alteration in the shape of the LV as well as several major structural and functional disorders such as myocardial injury, myocardial ischaemia, decrease in EF and LVMD. Our study setting allows us to investigate their associations in a comprehensive way. Temporal resolution and robustness of this method are described in an article by (Chen et al., 2011).

5 | CONCLUSIONS

In patients with CAD, in addition to the extent of infarct scarring, a larger LV volume and a more spherical-shaped LV were associated with LVMD, suggesting that LVR is closely associated with the development of LVMD. MPI is a feasible method to simultaneously assess LVMD and LVR which may be helpful in early recognition of the factors predicting heart failure.

ACKNOWLEDGEMENTS

This study was financially supported by the Finnish Cultural Foundation, the Paavo Nurmi Foundation, the Finnish Medical Foundation, the Finnish Foundation for Cardiovascular Research, the Finnish Cardiac Society, specified governments transfers to the Kuopio University Hospital (5031349), the Aarne Koskelo foundation and the University of Eastern Finland's Doctoral School.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The datasets presented in this article are not readily available because permission to use this data is restricted by the General Data Protection Regulation (EU) 2016/679 and the Finnish authority (FINDATA) have defined the users and limited operating environment (THL/5431/14.02.00/2020). Output of Statistical analyses are available by request to the corresponding author.

ORCID

Hanna Hämäläinen http://orcid.org/0000-0001-5313-2689
Tomi P. Laitinen http://orcid.org/0000-0003-3553-9957

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How to cite this article: Hämäläinen, H., Laitinen, T.M., Hedman, M., Hedman, A., Kivelä, A. & Laitinen, T.P. (2022) Cardiac remodelling in association with left ventricular dyssynchrony and systolic dysfunction in patients with coronary artery disease. *Clinical Physiology and Functional Imaging*, 42, 413–421. https://doi.org/10.1111/cpf.12780