

Myocardial Strain Evaluation with  
Cardiovascular MRI: Physics,  
Principles, and Clinical Applications

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# INTRODUCTION



Early detection of cardiovascular disease facilitates prompt initiation of appropriate therapy and prevents the development of irreversible complication.



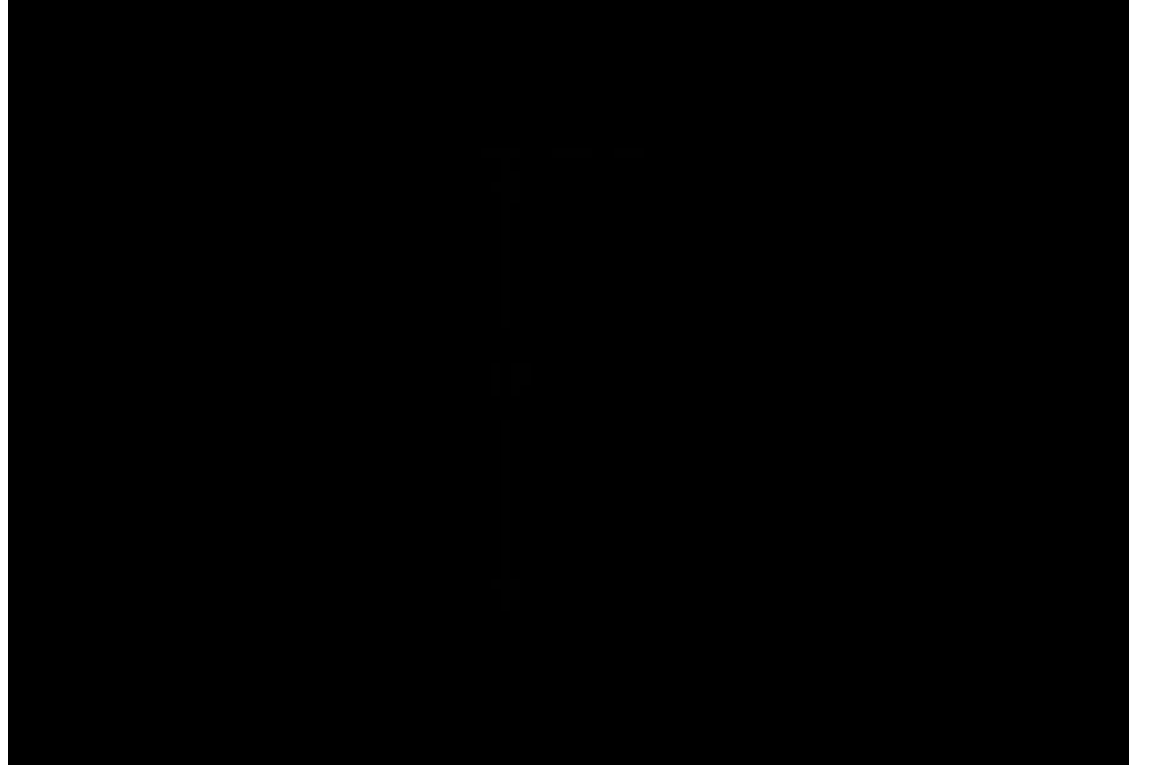
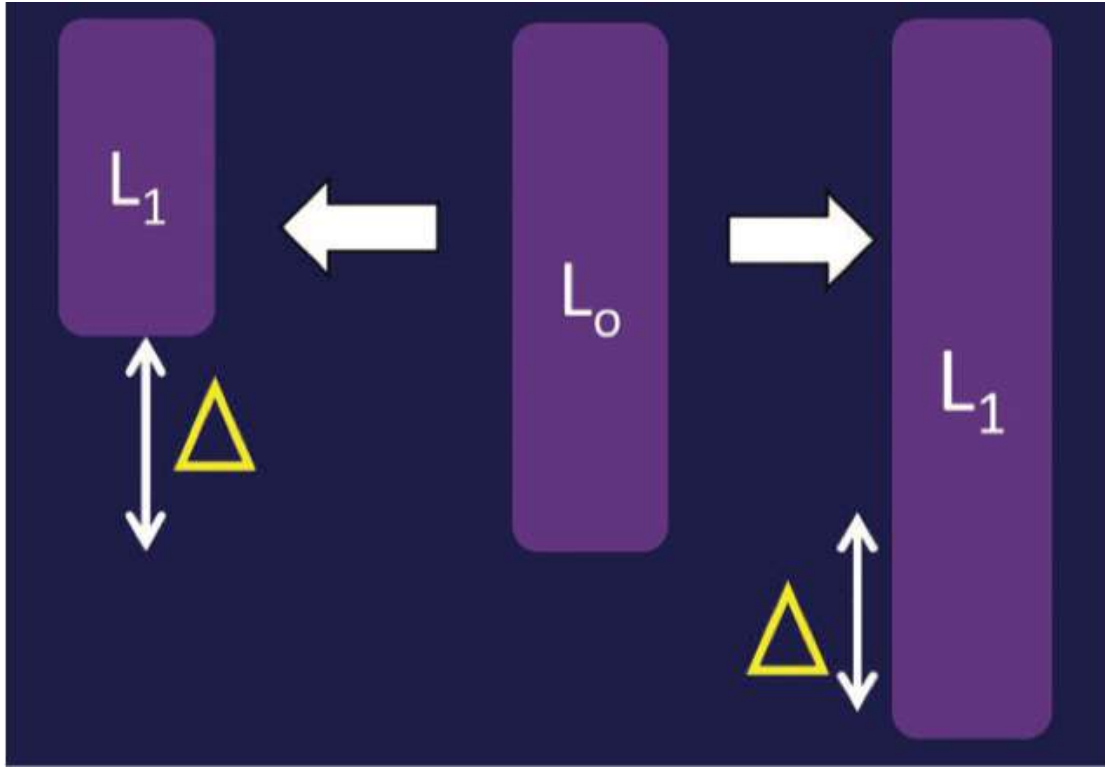
Ejection fraction is the most common imaging biomarker for myocardial systolic function but it is not a sensitive metric. 40% of patient with heart failure has normal EF (HFpEF). Abnormal EF usually implies a late potentially irreversible stage of underlying cardiovascular disease.

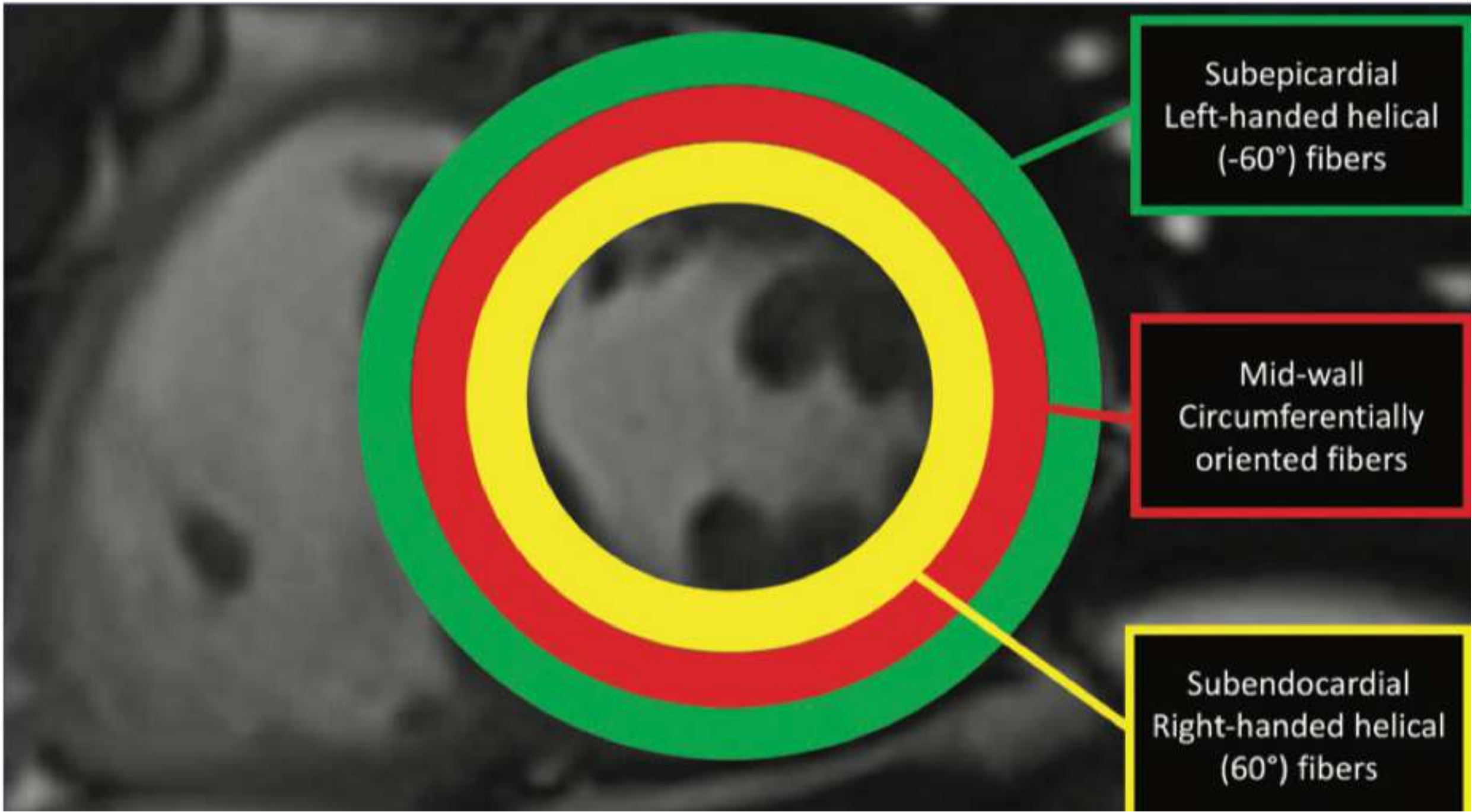


Myocardial strain is an indicator of myocardial deformation, which is a more sensitive imaging biomarker of myocardial disease than commonly used ventricular ejection fraction.



Although myocardial strain is commonly evaluated by using speckle-tracking echocardiography (STE) or tissue Doppler (TDI), cardiovascular MRI (CMR) is increasingly performed for this purpose.



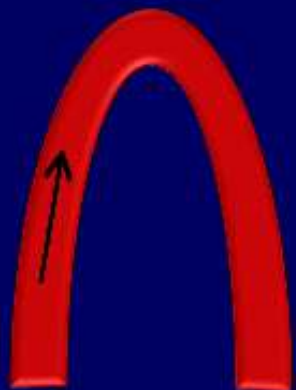


Subepicardial  
Left-handed helical  
(-60°) fibers

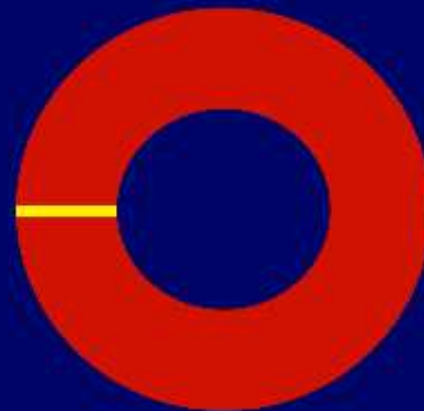
Mid-wall  
Circumferentially  
oriented fibers

Subendocardial  
Right-handed helical  
(60°) fibers

Longitudinal



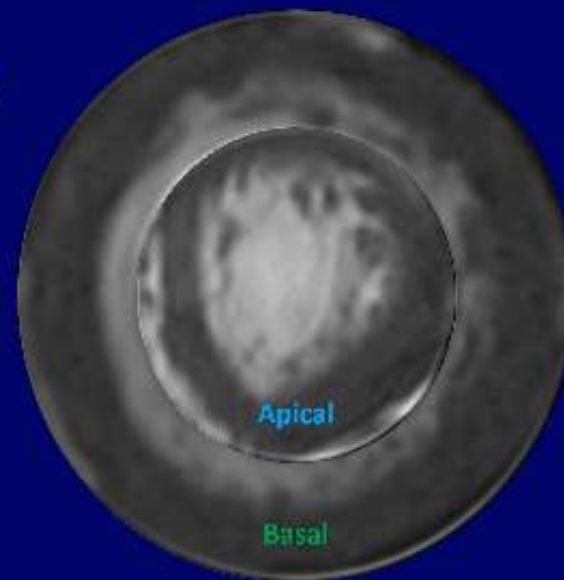
Radial



Circumferential



Torsion



# Strain Imaging Techniques

- Echocardiography is the most performed imaging technique for myocardial strain, either by using speckle-tracking echocardiography (STE) or tissue Doppler imaging (TDI).
- High temporal resolution of echocardiography is well suited to evaluate the rapid events such as myocardial activation and patient with high heart rates.
- STE uses dedicated postprocessing software to track the myocardial speckles produced by reflections of myofibres throughout the cardiac cycle, mainly at endocardial border.
- TDI helps evaluate velocity between two points in the myocardium, but limited to one direction along the ultrasound beam to evaluate global longitudinal strain (GLS) in the apical window (sensitive noise).
- Limitations: variable image quality, operator dependency, limited acoustic windows, and lower signal-to-noise ratio.
- CT can help in the evaluation of the myocardial strain using retrospective electrocardiographically-gated technique and feature-tracking technique. CT strain values correlate well with echocardiography.

# CMR Strain Techniques

- CMR, the current reference standard for myocardial function and volumes, can also be used for the evaluation of myocardial strain.
  - Several CMR strain techniques are available, with most requiring dedicated CMR sequences and some requiring dedicated postprocessing software.
- Myocardial Tagging
  - Strain-encoded Imaging
  - Displacement Encoding with Stimulated Echoes
  - Tissue Phase Mapping
  - Feature Tracking

**Table 1: Comparison of Advantages and Disadvantages of Various MRI Strain Techniques**

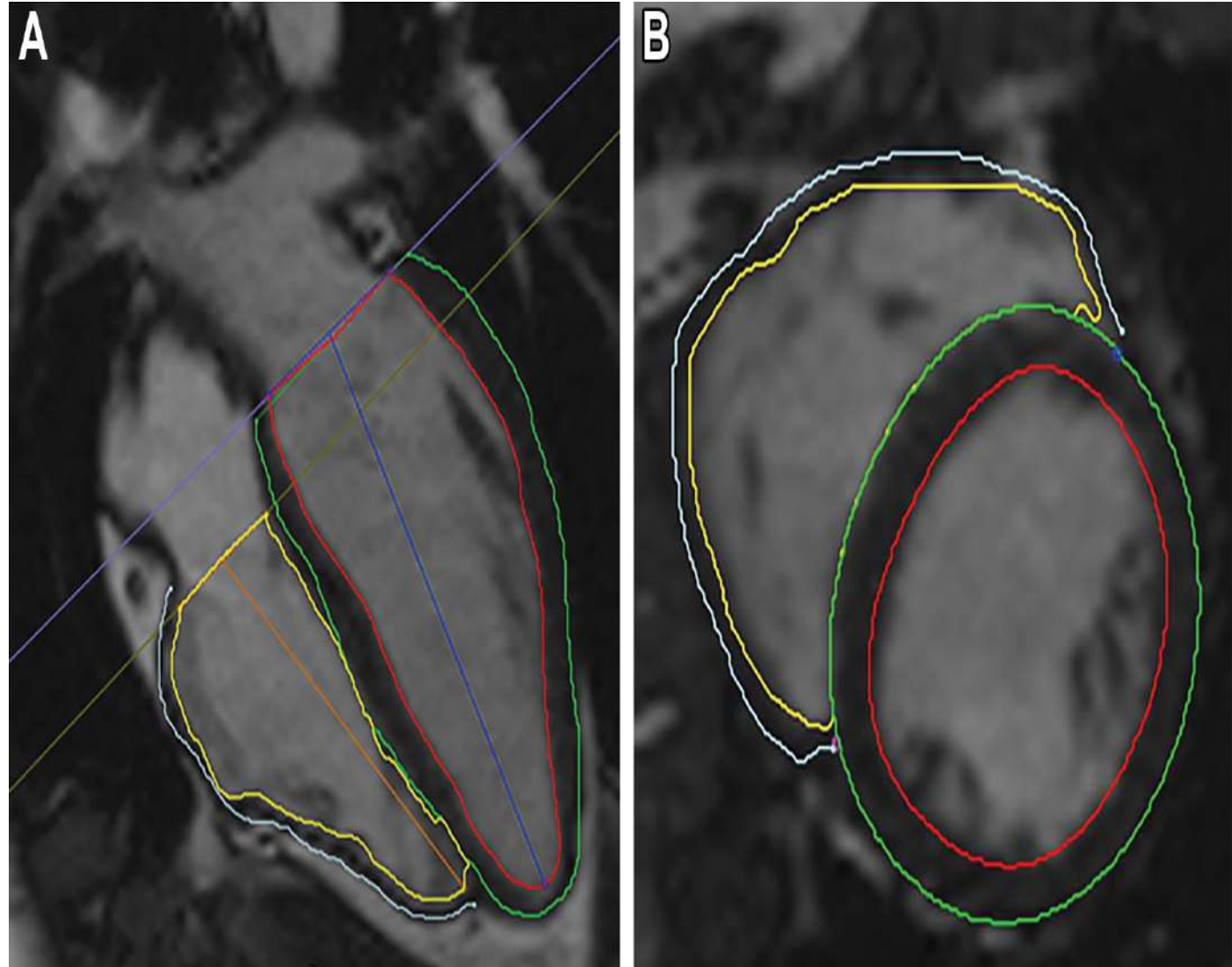
Sequence	Advantages	Disadvantages
Tagging	Well validated Better reproducibility True tissue marker Good tag tracking Visual assessment of RWMA 2D and 3D acquisitions	Additional acquisition sequence Dedicated postprocessing software needed Time-consuming postprocessing Low spatial resolution Low temporal resolution Diastolic tag fading in SPAMM Through-plane motion of tags Tag deposition delay, underestimation of strain
FT	No separate acquisition Automated rapid postprocessing Easier analysis Multiple vendors available Reproducibility of planes Can be estimated from 2D and 3D data	Limited by pixel size Lower spatial and temporal resolution No physical speckles and/or tissue markers (reliant on contours) Relies on accuracy of segmentation Motion artifacts in through-plane in 2D No standardization Less useful for regional strain
SENC	Quick examination with single-shot acquisition in one heartbeat Allows real-time strain measurements for stress CMR High spatial resolution Postprocessing is quick	Additional acquisition sequence Low temporal resolution Measures only through-plane strain (only LS and CS) Cannot measure radial strain Low SNR (STEAM acquisition) Tag fading in diastole Mainly a research sequence
DENSE	Short acquisition time High spatial resolution Good endocardial border definition Three strain directions from 2D or 3D acquisitions	Additional acquisition sequence and analysis software Limited clinical experience Low SNR (STEAM acquisition) Low temporal resolution
Tissue (phase velocity) mapping	Widely available sequence High spatial resolution Quick postprocessing	Additional acquisition sequence Long acquisition time Lower temporal resolution than tagging

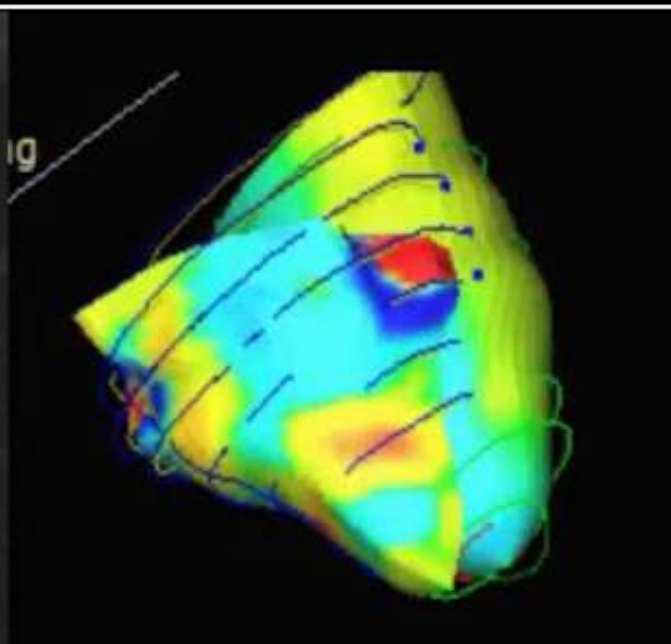
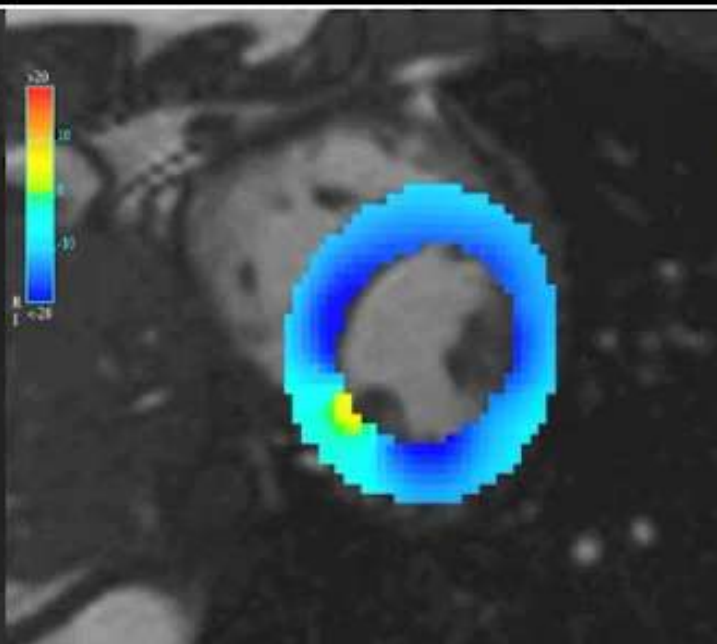
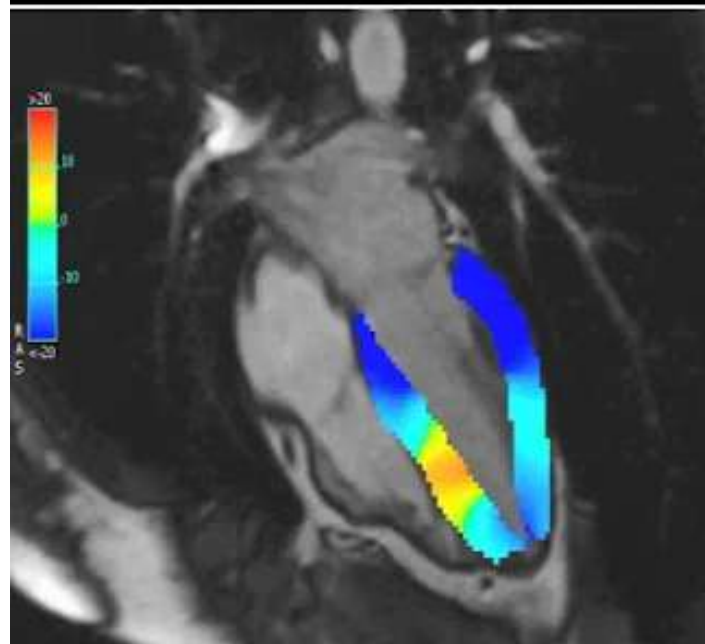
Note.—CS = circumferential strain, LS = longitudinal strain, RWMA = regional wall motion abnormalities, SNR = signal-to-noise ratio, SPAMM = spatial modulation of magnetization, STEAM = STimulated Echo Acquisition Mode, 2D = two dimensional.



## Feature Tracking

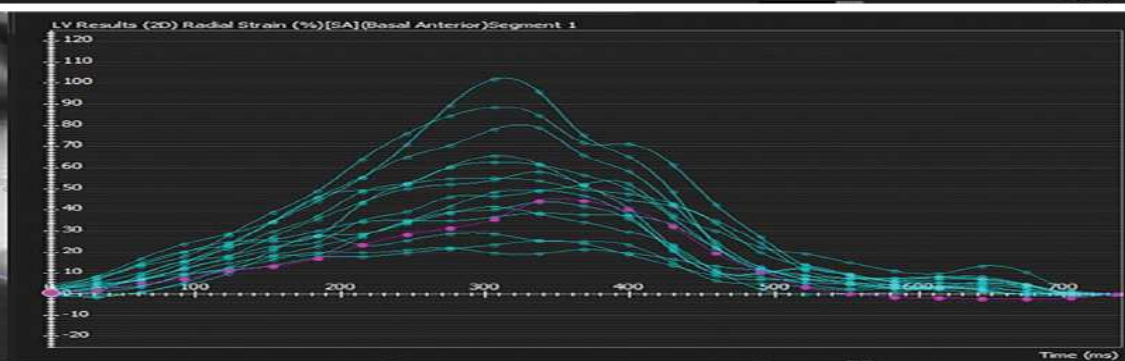
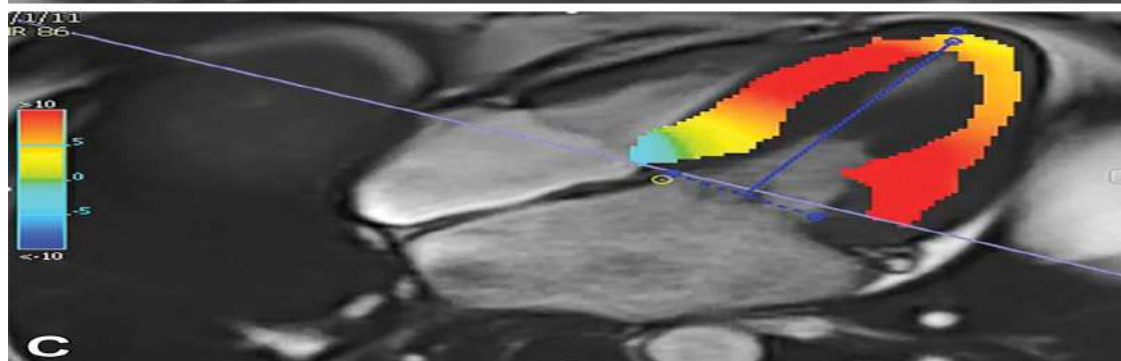
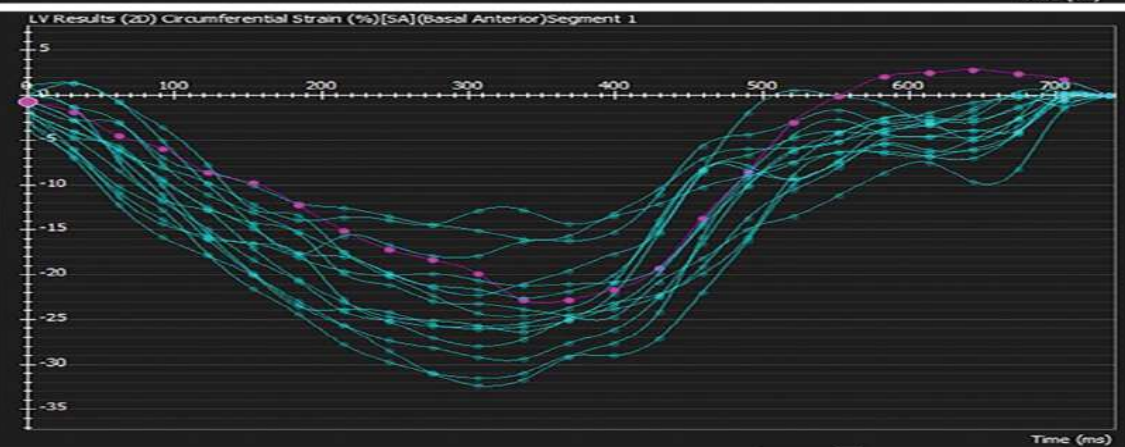
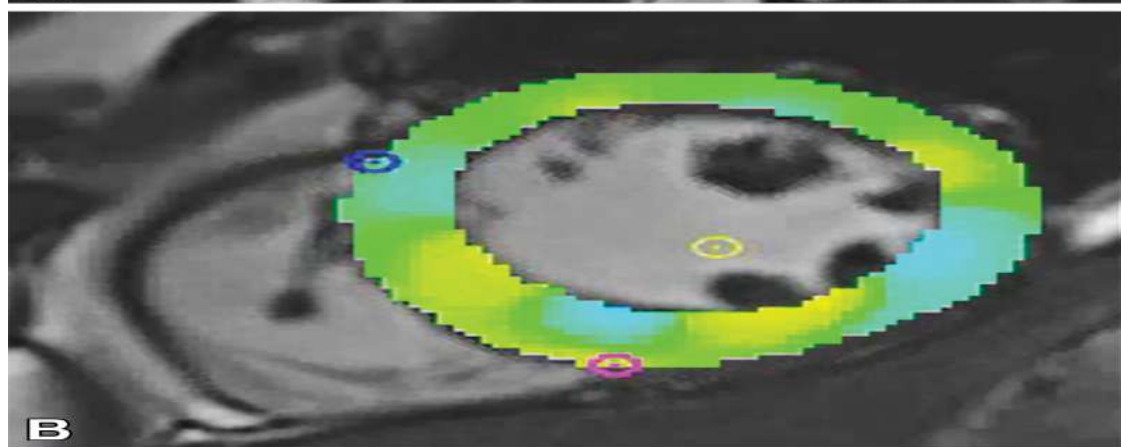
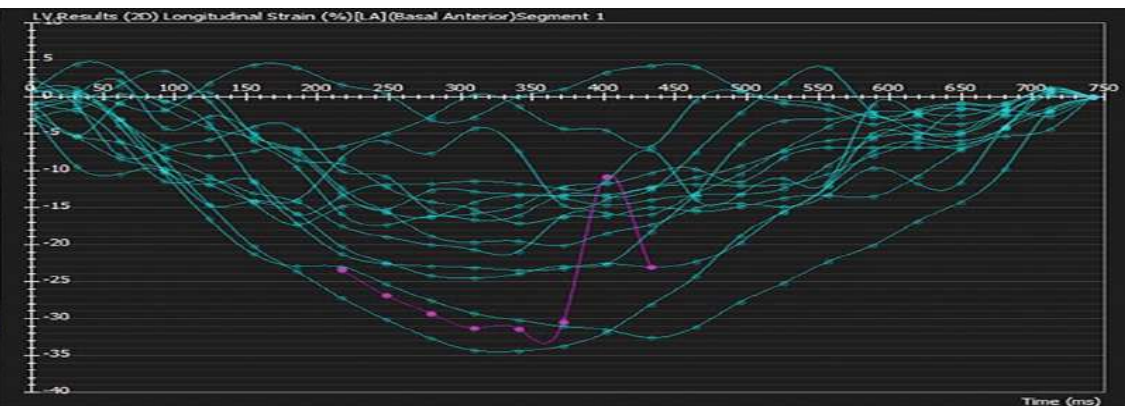
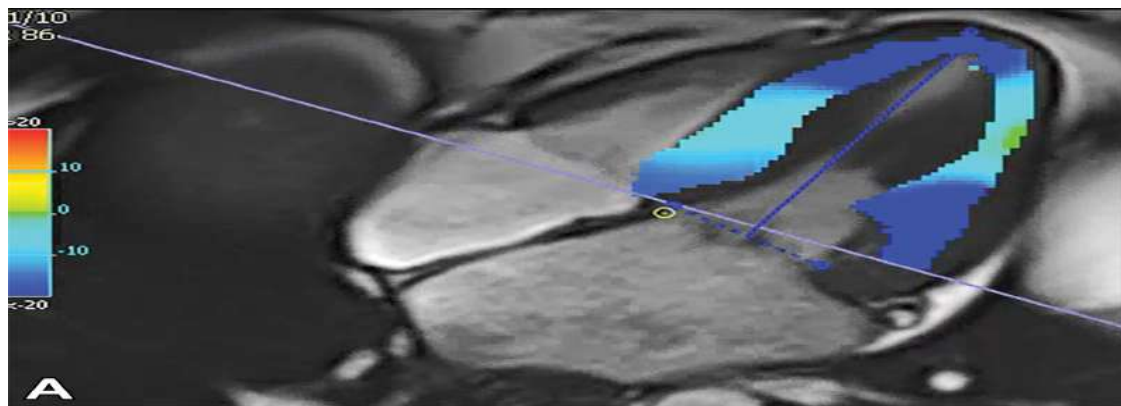
- The most recent CMR strain technique based on postprocessing of routinely acquired SSFP cine images.
- CMR FT is based on optical flow principles, in which a small window is identified on one image and a similar window of comparable size is detected on the subsequent frame using maximum likelihood methods. Subsequently, the distance between these two identified regions is determined, which equates to the local tissue displacement.





# Strain Measurements

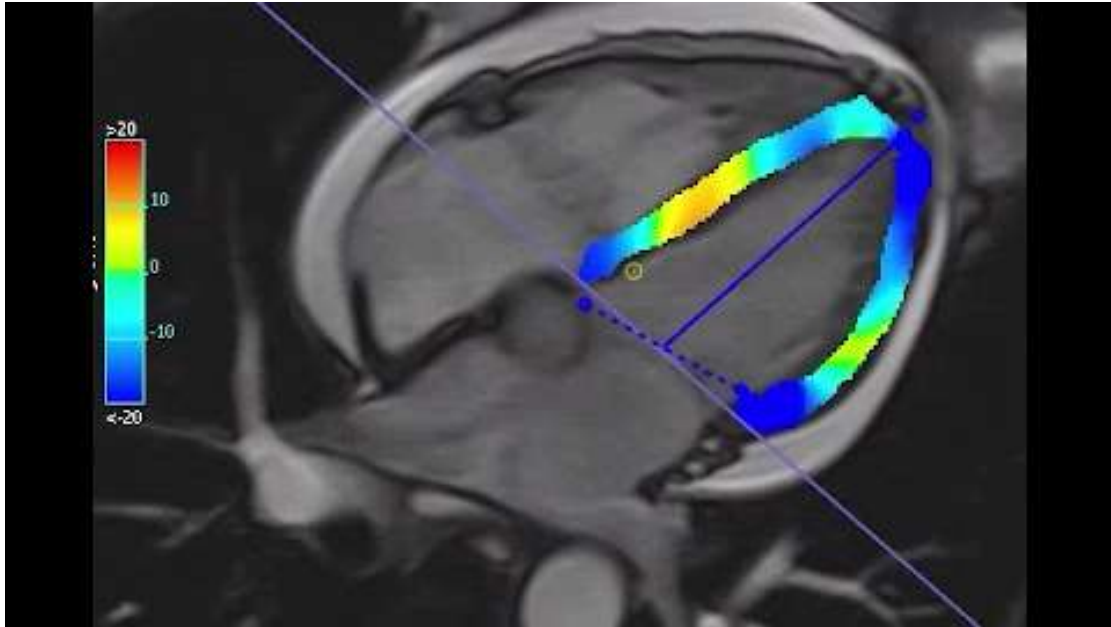
- Strain, expressed without a unit, or as a percentage, is measured in longitudinal, circumferential and radial directions.
  
- Several strain metrics are available.
  - Strain rate (rate of change of strain) (1/sec)
    - A better marker of actual contractility owing to lesser dependence on load and chamber size than strain.
    - It can be registered as peak systolic, early diastolic and late diastolic strain rates (useful for evaluation of cardiomyopathies and HFpEF).
  
  - Time to peak strain (in seconds)
    - The time from the beginning of the cardiac cycle to the maximal positive or negative strain, normalized to the RR interval duration (useful in LV dyssynchrony).
  
  - Torsion
    - A sensitive marker for both systolic and diastolic dysfunction and is useful for cardiomyopathies.
    - It can be expressed by either as twist angle (degrees), circumferential longitudinal shear angle (degree), torsion (degree/centimeter), or torsion rate (degree/ (centimeter x second)).
  
  - Displacement (in mm)
  - Velocity (in mm/sec)



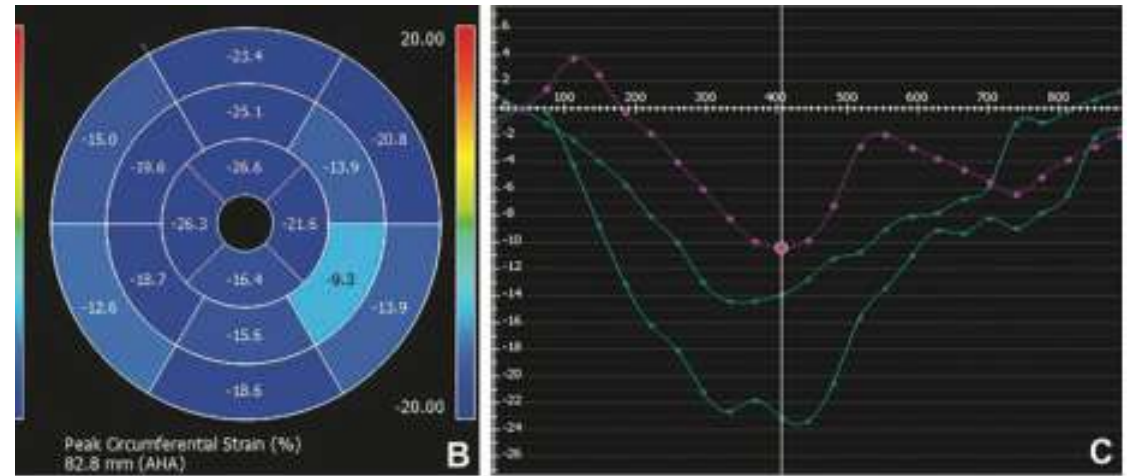
# Clinical Applications

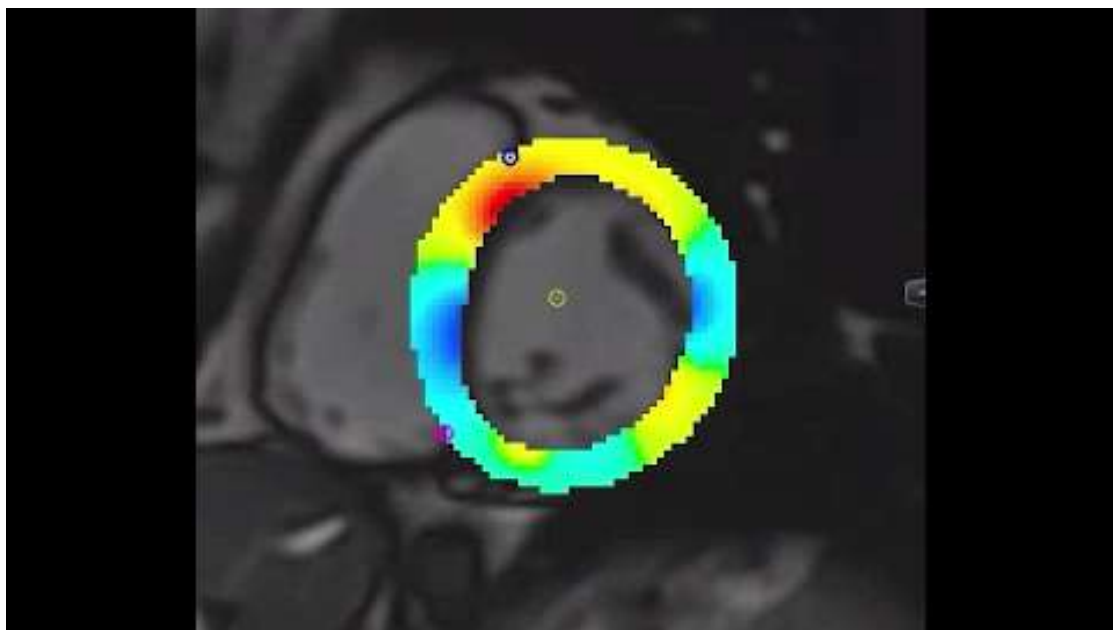
**Table 3: Clinical Applications and Indications for MRI Myocardial Strain**

Clinical Application	Specific Indications for MRI Myocardial Strain
Early diagnosis	Cardiotoxicity of anticancer therapeutics Ischemic heart disease Nonischemic cardiomyopathy (hypertension, HFpEF) Repaired congenital heart diseases Pulmonary hypertension
Prognosis and risk stratification	Ischemic heart disease; also identifies segments that will recover function Nonischemic cardiomyopathy Congenital heart disease Pulmonary hypertension Valvular heart disease: early identification of patients for surgeries
Therapeutic decision making	LV dyssynchrony: identifies responders for cardiac resynchronization therapy Ischemic heart disease: identifies segments that will recover function Valvular heart disease: identifies asymptomatic patients who may benefit from surgery
Family screening	Hypertrophic cardiomyopathy, muscular dystrophies

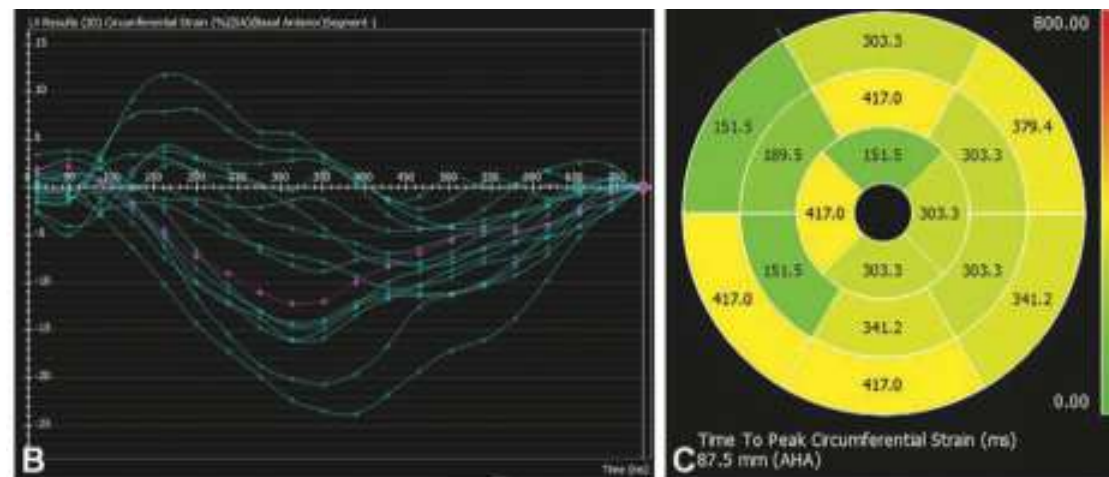


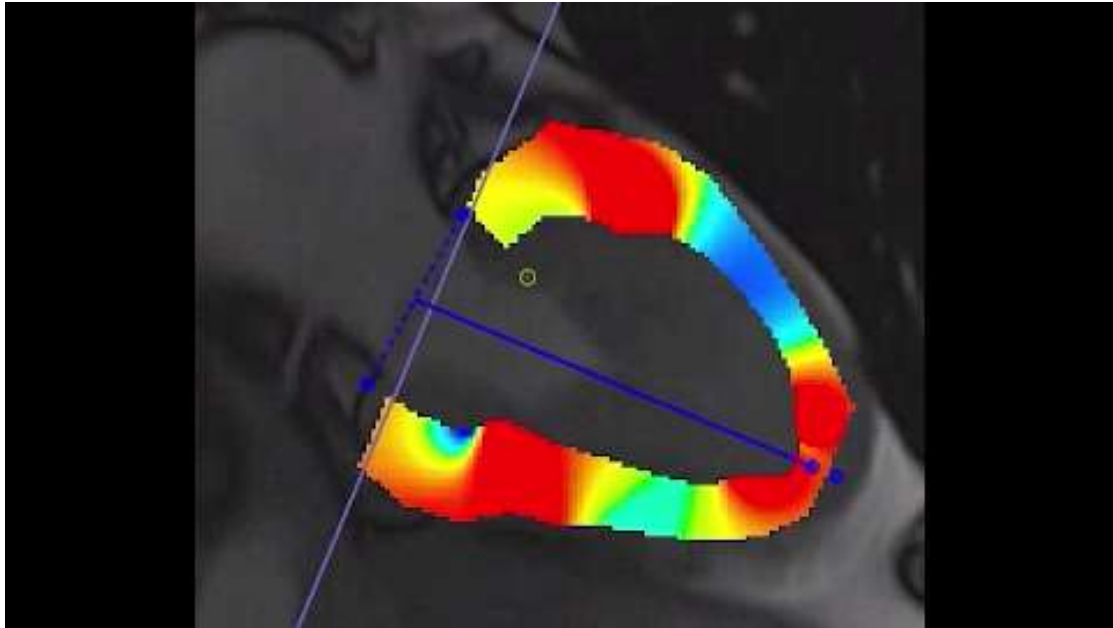
Chemotherapy cardiotoxicity.



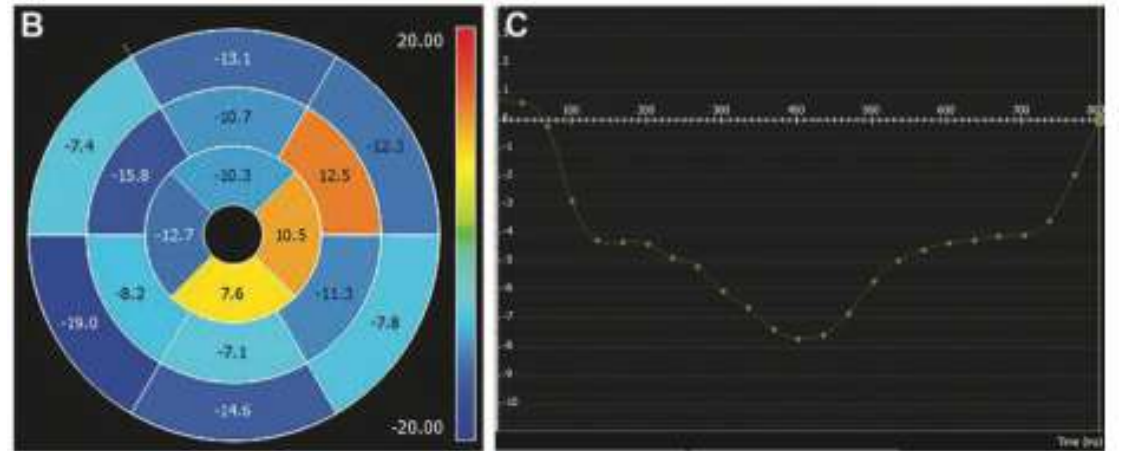


LV dyssynchrony.





Cardiac amyloidosis.





# Conclusion



CMR myocardial strain imaging is now increasingly available and performed, primarily owing to the development of FT technique.



Myocardial strain is clinically useful in the early diagnosis of myocardial dysfunction, risk stratification and prognostication of several disease. It may be useful in identifying patients with LV dyssynchrony who will benefit from cardiac resynchronization therapy.

# Journal Club

## 19.2.2024

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Registrar: DR SAIFUL AMRI BIN MAT RASID  
Radiologist: DR ZUL KHAIRUL AZWADI ISMAIL



## Early Diastolic Longitudinal Strain Rate at MRI and Outcomes in Heart Failure with Preserved Ejection Fraction

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\* J.H. and W.Y. contributed equally to this work.

Conflicts of interest are listed at the end of this article.

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**Background:** Assessment of subclinical myocardial dysfunction by using feature tracking has shown promise in prognosis evaluation of heart failure with preserved ejection fraction (HFpEF). Global early diastolic longitudinal strain rate (eGLSR) can identify earlier diastolic dysfunction; however, limited data are available on its prognostic value in HFpEF.

**Purpose:** To evaluate the association between left ventricular (LV) eGLSR and primary composite outcomes (all-cause death or heart failure hospitalization) in patients with HFpEF.

**Materials and Methods:** In this retrospective study, consecutive patients with HFpEF (included from January 2010 to March 2013) underwent cardiovascular MRI. The correlation between eGLSR and variables was assessed by using linear regression. The association between eGLSR (obtained with use of feature tracking) and outcomes was analyzed by using Cox proportional regression.

**Results:** A total of 186 patients with HFpEF (mean age  $\pm$  standard deviation, 59 years  $\pm$  12; 77 women) were included. The eGLSR was weakly correlated with LV end-diastole volume index (Pearson correlation coefficient [r] = -0.35;  $P < .001$ ), heart rate ( $r = 0.35$ ;  $P < .001$ ), and LV ejection fraction ( $r = 0.30$ ;  $P < .001$ ) and moderately correlated with LV end-systole volume index ( $r = -0.41$ ;  $P < .001$ ). At a median follow-up of 9.2 years (interquartile range, 8.7–10.0 years), 72 patients experienced primary composite outcomes. Impaired eGLSR, defined as an eGLSR of less than 0.57 per second, was associated with a greater rate of heart failure hospitalization or all-cause death (hazard ratio, 2.0 [95% CI: 1.1, 3.7];  $P = .02$ ) after adjusting for multiple clinical and imaging-based variables.

**Conclusion:** Left ventricular global early diastolic longitudinal strain rate obtained from cardiovascular MRI feature tracking was independently associated with adverse outcomes in patients with heart failure with preserved ejection fraction.

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Online supplemental material is available for this article.

An earlier incorrect version appeared online. This article was corrected on October 22, 2021.

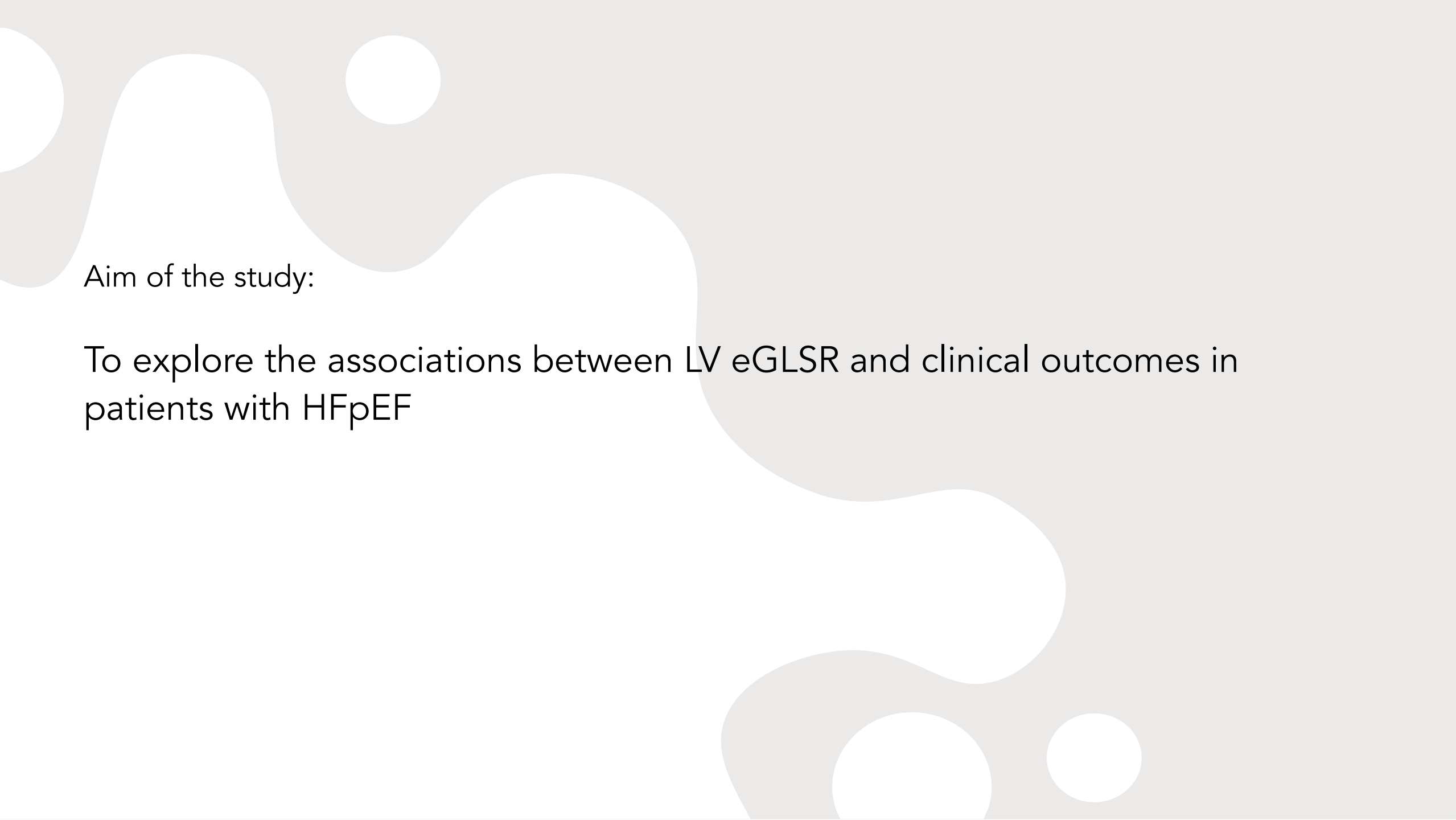
Heart failure with preserved ejection fraction (HFpEF) has been increasingly recognized as a threat to global health, with an increase in adverse outcomes, including mortality, hospitalization, and a decreased quality of life (1). Abnormal left ventricular (LV) diastolic performance is an important pathophysiologic mechanism underlying HFpEF due to elevated LV filling pressure and wall stiffness (2,3), usually evaluated noninvasively with echocardiography with use of spectral and tissue Doppler of the LV mitral valve apparatus. However, assessment may be limited by sampled segmental abnormality and error (4).

Speckle-tracking echocardiography and feature-tracking cardiovascular MRI (CMR) strain imaging (longitudinal, circumferential, and radial) have allowed for

quantitative assessment of myocardial deformation, and both have been shown to be associated with prognosis of patients with HFpEF (5–7). Previous work has indicated strong reproducibility and diagnostic value of LV global early diastolic longitudinal strain rate (eGLSR) from CMR feature tracking in quantifying cardiac dysfunction (8,9); however, there are limited data regarding the prognostic value of eGLSR in patients with HFpEF. We hypothesized that LV eGLSR may be independently associated with all-cause death or heart failure hospitalization in HFpEF and could provide incremental prognostic information beyond clinical and conventional imaging parameters. The aim of this study was, therefore, to explore the association between the LV eGLSR and clinical outcomes in patients with HFpEF.

# INTRODUCTION

- Heart failure with preserved ejection fraction (HFpEF) has been increasingly recognized as a threat to global health, with an increase in adverse outcomes, including mortality, hospitalization, and a decreased quality of life
- Abnormal left ventricular (LV) diastolic performance is an important pathophysiologic mechanism underlying HFpEF due to elevated LV filling pressure and wall stiffness
  - evaluated noninvasively with echocardiography with use of spectral and tissue Doppler of the LV mitral valve apparatus (may be limited by sampled segmental abnormality and error)
- Speckle-tracking echocardiography and feature-tracking cardiovascular MRI (CMR) strain imaging (longitudinal, circumferential, and radial) have allowed for quantitative assessment of myocardial deformation and both have been shown to be associated with prognosis of patients with HFpEF



Aim of the study:

To explore the associations between LV eGLSR and clinical outcomes in patients with HFpEF

# Material and Methods



# Material and Methods

-Retrospective study

- Patients with HFpEF who underwent CMR and echocardiography at Fuwai Hospital, Beijing, China, were consecutively included from

January 2010 to March 2013.

## Inclusion criteria:

- (a) symptoms of heart failure greater than New York Heart Association class II
- (b) brain natriuretic peptide level greater than 35 pg/mL or *N*-terminal pro-brain natriuretic peptide level greater than 125 pg/mL at the time of diagnosis
- (c) LV ejection fraction of 50% or more
- (d) at least one of
  - (i) underlying LV structural abnormalities (left atrial maximum volume index >34 mL/m<sup>2</sup> in sinus rhythm or LV end-diastole mass index  $\geq$ 115 g/m<sup>2</sup> for men and >95 g/m<sup>2</sup> for women, measured with echocardiography)
- or
  - (ii) LV diastolic dysfunction (early and/or late peak diastolic mitral inflow velocity [E/A] <1 or early peak mitral inflow velocity and/or mean mitral annular peak early diastolic velocity [E/E'] >13)
- (e) an echocardiographic and natriuretic peptide score of 5 or more calculated by using the Heart Failure Association pretest assessment, echocardiography and natriuretic peptide, functional testing, final etiology—or HFA-PEFF—

-suggested by the Heart Failure Association of the European Society of Cardiology

## Exclusion criteria

- Primary cardiomyopathy (hypertrophic, dilated, and restrictive)
- Primary severe valvular heart disease
- Acute coronary syndrome
- Restrictive pericardial disease
- Severe arrhythmia
- Severe renal dysfunction (glomerular filtration rate <30 mL/min/1.73 m<sup>2</sup>).

# CMR Protocol and Analysis

- MRI examination at 1.5 T (Magnetom Avanto, Siemens Healthineers) with an eight-channel cardiac coil
- Cardiac short-axis and two, three, and four chamber view cine images were acquired using a standard breath-held steady-state free precession cine sequence.
- Typical imaging parameters were as follows:
  - section thickness, 8 mm; gap, 2 mm
  - repetition time, 3.0–3.4 msec; echo time, 1.5–1.7 msec
  - matrix size, 192 to 224 × 224 to 224 × 256
  - field of view, 320 × 320 to 380 × 380 mm<sup>2</sup>
  - temporal resolution, 30–55 msec, depending on heart rate.
- LV mass and LV end-diastole and end-systole volume were measured using Argus software (version VA60C, Siemens Healthineers) and normalized using body surface area calculated with the Mosteller equation .
- Feature-tracking analysis was performed using the QStrain package (Medis Medical Imaging Systems). The endocardial and epicardial contours were automatically detected with manual correction in end-systole and end-diastole (Papillary muscles were excluded from the endocardial contour) -Three-directional myocardial strain and strain rate were derived:
  - global longitudinal (GLS), radial, and circumferential strains
  - global systolic longitudinal (sGLSR), radial, and circumferential strain rates
  - eGLSR, radial, and circumferential strain rates.



# Statistical analysis

# Statistical analysis

- Variables are presented as means  $\pm$  standard deviations, medians with interquartile ranges.
- Data analysis was done using SPSS
- Sample size estimation was performed by using the Power Analysis and Sample Size software, or PASS (version 15.0.5, NCSS).
  - A total of 186 patients included in the study ( $>95\%$  power)
- Patients were stratified according to the eGLSR median because established eGLSR cutoff values are lacking.

Type of test	Intention
2 sample independent T test, Wilcoxon rank sum test	To assess the difference between the 2 groups.
Kaplan-Meier Analysis	To calculate time-event rates
Log rank test	To test differences among the survival curves
Univariable Cox regression	To identify variables associated with outcomes
Sensitivity analysis	

# Results

**Table 1: Baseline Characteristics Stratified according to eGLSR Median of 0.57 per Second from Feature Tracking**

Variable	All Patients (n = 186)	eGLSR < Median (n = 90)	eGLSR ≥ Median (n = 96)	P Value
<b>Demographics</b>				
Sex				.03*
F	77 (41)	30 (33)	47 (49)	
M	109 (59)	60 (67)	49 (51)	
Age (y) <sup>‡</sup>	59 ± 12	58 ± 12	60 ± 12	.15
Height (cm) <sup>‡</sup>	166.9 ± 8.7	168.1 ± 7.4	165.9 ± 9.7	.09
Weight (kg) <sup>‡</sup>	73.2 ± 13.0	74.3 ± 12.1	72.0 ± 13.8	.22
Body mass index (kg/m <sup>2</sup> ) <sup>‡</sup>	26.2 ± 3.7	26.3 ± 3.9	26.0 ± 3.5	.60
Body surface area (m <sup>2</sup> ) <sup>‡</sup>	1.81 ± 0.20	1.83 ± 0.17	1.79 ± 0.22	.19
Smoking	76/180 (42)	44/87 (51)	32/93 (34)	.03*
<b>Comorbidities</b>				
Hypertension	186 (100)	90 (100)	96 (100)	>.99
Atrial fibrillation	49 (26)	17 (19)	32 (33)	.03*
Coronary artery disease	40 (22)	26 (29)	14 (15)	.02*
Known myocardial infarction	28 (15)	20 (22)	8 (8)	.008*
Diabetes	46 (25)	27 (30)	19 (20)	.11
Hyperlipidemia	105 (56)	56 (62)	49 (51)	.12
<b>Clinical variables</b>				
Hematocrit (%) <sup>‡</sup>	41.9 ± 6.3	42.0 ± 6.9	41.7 ± 5.7	.70
GFR (mL/min/1.73 m <sup>2</sup> ) <sup>‡</sup>	90.3 ± 35.0	90.2 ± 32.1	90.5 ± 37.7	.95
Systolic blood pressure (mm Hg) <sup>‡</sup>	171 ± 25	170 ± 24	172 ± 27	.49
NT-proBNP (pg/mL) <sup>‡</sup>	279.7 (213.8–515.0)	279.7 (217.3–574.3)	282.8 (207.3–472.1)	.26
<b>Medication use</b>				
ACE inhibitor	136 (73)	73 (81)	63 (66)	.01*
β-blocker	143 (77)	72 (80)	71 (74)	.33
Aspirin	140 (75)	75 (83)	65 (68)	.01*
Diuretic	94 (51)	52 (58)	42 (44)	.06
Calcium channel blocker	104 (56)	49 (54)	55 (57)	.70
Amiodarone	19 (10)	7 (8)	12 (13)	.29
Statin	123 (66)	65 (72)	58 (60)	.09
Follow-up time (y) <sup>‡</sup>	9.2 (8.7–10.0)	9.3 (8.7–10.1)	9.2 (8.6–9.8)	.37
<b>Primary outcomes</b>				
All-cause mortality	72 (39)	45 (50)	27 (28)	.002*
Heart failure hospitalization	18 (10)	10 (11)	8 (8)	.52
Heart failure hospitalization	54 (29)	35 (39)	19 (20)	.004*

Note.—Unless otherwise specified, data are numbers of patients, with percentages in parentheses. A global early diastolic longitudinal strain rate (eGLSR) of 0.57 per second or greater indicates better diastolic function. ACE = angiotensin-converting enzyme inhibitor, GFR = glomerular filtration rate, NT-proBNP = N-terminal pro-brain natriuretic peptide.

\* Statistically significant difference.

<sup>‡</sup> Data are means ± standard deviations.

<sup>‡</sup> Data are medians, with interquartile ranges in parentheses.

# Table 2

**Table 2: Echocardiography and Cardiovascular MRI Data of Patients with HFpEF**

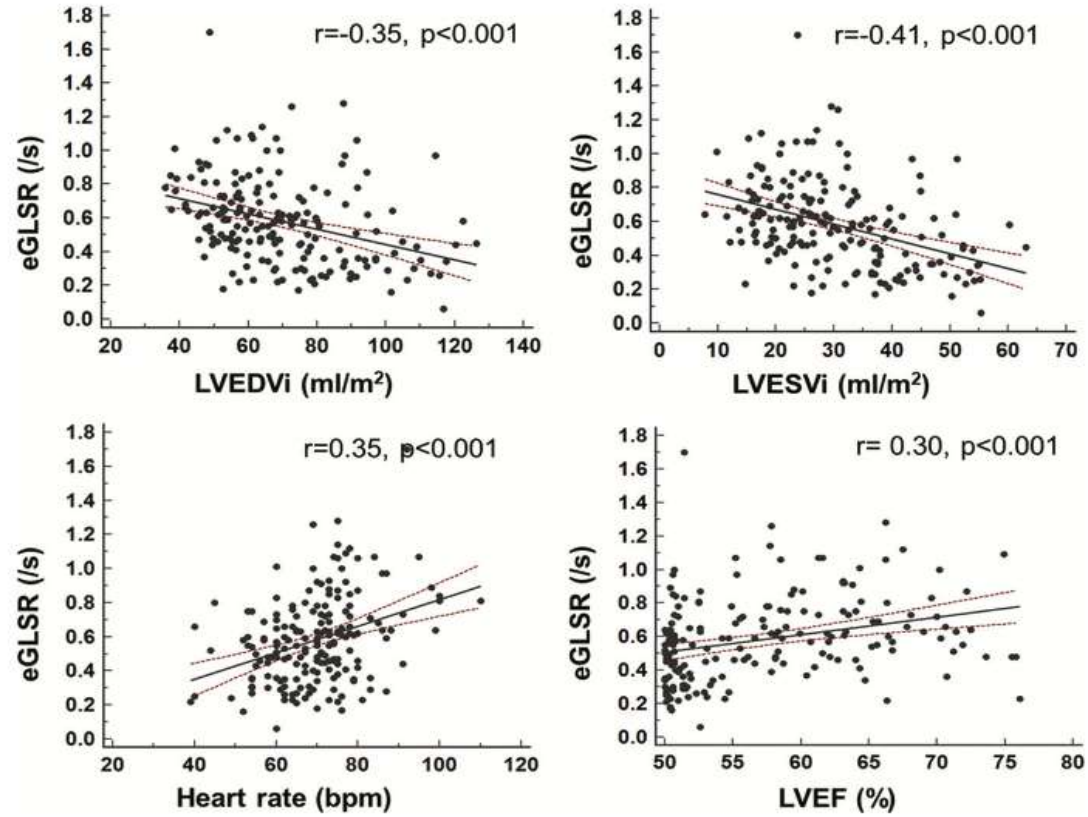
Variable	All Patients (n = 186)	eGLSR < Median (n = 90)	eGLSR ≥ Median (n = 96)	P Value
<b>Echocardiography parameters</b>				
E/A <1 or E'/A' <1*	68 (37)	41 (46)	27 (28)	.01†
LA anteroposterior diameter (mm)	38.6 ± 5.7	38.9 ± 5.3	38.3 ± 6.1	.42
<b>CMR parameters</b>				
Heart rate (beats/min)	70 ± 11	66 ± 10	73 ± 12	<.001†
LVEF (%)‡	55 (51-63)	52 (50-58)	59 (52-64)	<.001†
Cardiac index (mL/m <sup>2</sup> )	2.65 ± 0.72	2.68 ± 0.74	2.62 ± 0.71	.63
LAVi (mL/m <sup>2</sup> )	52 ± 22	52 ± 22	45 ± 16	.007‡
LVEDVi (mL/m <sup>2</sup> )	69 ± 20	76 ± 20	63 ± 17	<.001†
LVESVi (mL/m <sup>2</sup> )	30 ± 11	35 ± 12	26 ± 10	<.001†
LVMi (g/m <sup>2</sup> )	52 ± 22	57 ± 22	47 ± 20	.002‡
Presence of LGE*	49 (26)	34 (38)	15 (16)	<.001†
GLS (%)	-15.2 ± 5.3	-12.5 ± 4.2	-17.8 ± 4.8	<.001†
GCS (%)	-17.4 ± 6.2	-15.7 ± 6.2	-19.1 ± 5.7	<.001†
GRS (%)	59.2 ± 31.7	51.0 ± 26.1	67.1 ± 34.5	<.001†
sGLSR (per second)	-0.79 ± 0.29	-0.62 ± 0.19	-0.94 ± 0.27	<.001†
eGLSR (per second)	0.58 ± 0.25	0.38 ± 0.11	0.77 ± 0.20	<.001†
sGCSR (per second)	-0.88 ± 0.33	-0.78 ± 0.32	-0.98 ± 0.31	<.001†
eGCSR (per second)	0.72 ± 0.31	0.58 ± 0.25	0.85 ± 0.31	<.001†
sGRSR (per second)	1.68 ± 0.77	1.21 ± 0.67	1.91 ± 0.78	<.001†
eGRSR (per second)	-1.43 ± 0.75	-1.21 ± 0.56	-1.65 ± 0.84	<.001†

Note.—Unless otherwise specified, data are means ± standard deviations. The median global early diastolic longitudinal strain rate (eGLSR) was 0.57 per second. CMR = cardiovascular MRI, E/A = early/late peak diastolic mitral inflow velocity, E'/A' = mean mitral annular peak early/late diastolic velocity, eGCSR = global early diastolic circumferential strain rate, eGRSR = global early diastolic radial strain rate, GCS = global circumferential strain, GLS = global longitudinal strain, GRS = global radial strain, LA = left atrial, LAVi = LA maximum volume index, LGE = late gadolinium enhancement, LVEDVi = left ventricular end-diastole volume index, LVEF = left ventricular ejection fraction, LVESVi = left ventricular end-systole volume index, LVMi = left ventricular end-diastole mass index, sGCSR = global systolic circumferential strain rate, sGLSR = global systolic longitudinal strain rate, sGRSR = global systolic radial strain rate.

\* Data are numbers of patients, with percentages in parentheses.

† Statistically significant difference.

‡ Data are medians, with approximate interquartile ranges in parentheses.



**Figure 4:** Linear graphs show correlations between global early diastolic longitudinal strain rate (eGLSR) and imaging or structural variables. LVEDVi = left ventricular end-diastole volume index, LVEF = left ventricular ejection fraction, LVESVi = left ventricular end-systole volume index.

# Table 3

**Table 3: Univariable and Multivariable Cox Proportional Regression with Strain as a Dichotomous Variable**

Variable	Univariable Analysis		Multivariable Analysis	
	Unadjusted Hazard Ratio	P Value	Adjusted Hazard Ratio	P Value
Female sex	0.9 (0.6, 1.5)	.80		
Age (per year)	1.01 (0.99, 1.03)	.59		
Body mass index (kg/m <sup>2</sup> )	0.95 (0.89, 1.02)	.16		
Heart rate (beats/min)	0.99 (0.97, 1.01)	.54		
Coronary artery disease	1.5 (0.9, 2.5)	.15		
Known myocardial infarction	1.9 (1.1, 3.4)	.02*	1.3 (0.6, 2.8)	.52
Diabetes	0.9 (0.5, 1.6)	.81		
Atrial fibrillation	1.3 (0.8, 2.2)	.31		
Hematocrit (%)	0.99 (0.95, 1.03)	.73		
Glomerular filtration rate (mL/min/1.73 m <sup>2</sup> )	0.99 (0.99, 1.00)	.05	0.99 (0.98, 1.00)	.04*
NT-proBNP (pg/mL, log transformed)	1.02 (0.38, 2.71)	.97		
E/A <1 or E'/A' <1	1.03 (0.64, 1.66)	.90		
Left ventricular ejection fraction (%)	1.00 (0.97, 1.03)	.84		
LAVi (mL/m <sup>2</sup> )	1.01 (0.99, 1.02)	.43		
LVMi (g/m <sup>2</sup> )	1.01 (0.99, 1.02)	.37		
LVEDVi (mL/m <sup>2</sup> )	1.01 (1.00, 1.01)	.29		
LVESVi (mL/m <sup>2</sup> )	1.01 (0.99, 1.03)	.43		
Presence of late gadolinium enhancement	1.8 (1.1, 2.9)	.02*	1.3 (0.7, 2.7)	.44
GLS > -15.2%	1.7 (1.1, 2.7)	.03*	1.3 (0.6, 2.5)	.52
GCS > -17.1%	1.1 (0.7, 1.8)	.61		
GRS < 53.0%	1.04 (0.66, 1.66)	.86		
sGLSR > -0.76/sec	1.6 (1.01, 2.59)	.04*	0.8 (0.4, 1.6)	.48
eGLSR < 0.57/sec	2.1 (1.3, 3.3)	.003*	2.0 (1.1, 3.7)	.02*
sGCSR > -0.85/sec	1.3 (0.8, 2.1)	.22		
eGCSR < 0.69/sec	1.2 (0.8, 1.9)	.42		

Note.—Data in parentheses are 95% CIs. Strain parameters are described as dichotomous variables according to their respective median values. Multivariable analysis ( $n = 184$ ; 70 events, due to two patients with missing glomerular filtration rate data) was based on covariates from univariable Cox analysis, with  $P < .10$ . E/A = early/late peak diastolic mitral inflow velocity, E'/A' = mean mitral annular peak early/late diastolic velocity, eGCSR = global early diastolic circumferential strain rate, eGLSR = global early diastolic longitudinal strain rate, eGRSR = global early diastolic radial strain rate, GCS = global circumferential strain, GLS = global longitudinal strain, GRS = global radial strain, LAVi = left atrial maximum volume index, LVEDVi = left ventricular end-diastole volume index, LVESVi = left ventricular end-systole volume index, LVMi = left ventricular end-diastole mass index, NT-proBNP = *N*-terminal pro-brain natriuretic peptide, sGCSR = global systolic circumferential strain rate, sGLSR = global systolic longitudinal strain rate, sGRSR = global systolic radial strain rate.

\* Statistically significant difference.

# Table 4

**Table 4: Univariable and Multivariable Cox Regression for Primary Outcomes in Patients with Heart Rate of 90 Beats per Minute or Lower**

Variable	Univariable Analysis		Multivariable Analysis	
	Unadjusted Hazard Ratio	P Value	Adjusted Hazard Ratio	P Value
Female sex	0.97 (0.60, 1.56)	.89		
Age (per year)	1.00 (0.98, 1.02)	.84		
Body mass index (kg/m <sup>2</sup> )	0.96 (0.89, 1.02)	.19		
Coronary artery disease	1.4 (0.8, 2.4)	.23		
Known myocardial infarction	1.9 (1.1, 3.4)	.02*	1.3 (0.6, 2.8)	.52
Diabetes	0.9 (0.5, 1.6)	.80		
Atrial fibrillation	1.3 (0.7, 2.1)	.41		
Hematocrit (%)	0.99 (0.95, 1.03)	.63		
Glomerular filtration rate (mL/min/1.73 m <sup>2</sup> )	0.99 (0.99, 1.00)	.07	0.99 (0.98, 1.00)	.04*
NT-proBNP (pg/mL, log transformed)	1.1 (0.4, 2.8)	.92		
E/A <1 or E'/A' <1	1.0 (0.6, 1.6)	>.99		
Left ventricular ejection fraction (%)	1.00 (0.97, 1.03)	.94		
LAVi (mL/m <sup>2</sup> )	1.01 (0.99, 1.02)	.33		
LVMi (g/m <sup>2</sup> )	1.01 (0.99, 1.02)	.28		
LVEDVi (mL/m <sup>2</sup> )	1.01 (1.00, 1.02)	.25		
LVESVi (mL/m <sup>2</sup> )	1.01 (0.99, 1.03)	.42		
Presence of late gadolinium enhancement	1.8 (1.1, 3.0)	.02*	1.4 (0.7, 2.7)	.41
GLS > -15.2%	1.7 (1.0, 2.7)	.04*	1.3 (0.6, 2.6)	.55
GCS > -17.1%	1.3 (0.8, 2.0)	.34		
GRS < 53.0%	1.1 (0.7, 1.8)	.67		
sGLSR > -0.76/sec	1.5 (0.9, 2.5)	.08*	0.8 (0.4, 1.6)	.45
eGLSR < 0.57/sec	2.0 (1.2, 3.3)	.005*	1.9 (1.1, 3.6)	.03*
sGCSR > -0.85/sec	1.4 (0.9, 2.3)	.15		
eGCSR < 0.69/sec	1.3 (0.8, 2.1)	.25		

Note.—Data in parentheses are 95% CIs. Strain parameters are described as dichotomous variables according to their respective median values. Multivariable analysis ( $n = 176$ ; 68 events, due to one patient with missing glomerular filtration rate data) was based on covariates from univariable Cox analysis, with  $P < .10$ . E/A = early/late peak diastolic mitral inflow velocity, E'/A' = mean mitral annular peak early/late diastolic velocity, eGCSR = global early diastolic circumferential strain rate, cGLSR = global early diastolic longitudinal strain rate, eGRSR = global early diastolic radial strain rate, GCS = global circumferential strain, GLS = global longitudinal strain, GRS = global radial strain, LAVi = left atrial maximum volume index, LVEDVi = left ventricular end-diastole volume index, LVESVi = left ventricular end-systole volume index, LVMi = left ventricular end-diastole mass index, NT-proBNP = N-terminal pro-brain natriuretic peptide, sGCSR = global systolic circumferential strain rate, sGLSR = global systolic longitudinal strain rate, sGRSR = global systolic radial strain rate.

\* Statistically significant difference.



# Discussion

## 2 key findings in this study

- Global early diastolic longitudinal strain rate (eGLSR) measured with feature tracking was a strong risk factor independently associated with all-cause death and heart failure hospitalization of patients with heart failure with preserved ejection fraction (HFpEF) (hazard ratio, 2.0;  $P = .02$ )
- Patients with HFpEF with lower eGLSR (ie, poorer diastolic function) had more abnormal geometry and more impaired cardiac function assessed with echocardiographic and cardiovascular MRI indexes (all  $P < .001$ ).

# Summary

- Diastolic dysfunction can be reflected by feasible and sensitive left ventricular global early diastolic longitudinal strain rate (eGLSR) using cardiovascular MRI in heart failure with preserved ejection fraction (HFpEF)
- eGLSR is independently associated with all-cause death and heart failure hospitalization.