Search Strategies

MEDLINE	Database: Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed						
	Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) <1946 to Present>						
	Search Strategy:						
	1 Ventricular Function, Left/ (32622)						
	2 Ventricular Dysfunction, Left/ (24705)						
	3 left ventric*.mp. (179585)						
	4 LV.mp. (41504)						
	5 1 or 2 or 3 or 4 (198982)						
	6 Echocardiography/ (78179)						
	7 speckle tracking.mp. (3722)						
	8 STE.mp. (1905)						
	9 strain.mp. (385200)						
	10 deformation.mp. (36853)						
	11 mechanic*.mp. (390628)						
	12 torsion.mp. (22257)						
	13 twist.mp. (10298)						
	14 rotation.mp. (95760)						
	15 GLS.mp. (1508)						
	16 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 (963614)						
	17 Cardiovascular Diseases/ (128863)						
	18 cardiovascular disease*.mp. (220948)						
	19 Heart Failure/ (103286)						
	20 Heart failure.mp. (176882)						
	21 HF.mp. (35998)						
	22 Mortality/ (39168)						
	23 mortality.mp. (670200)						
	24 Death/ (16230)						
	25 death.mp. (691814)						
	26 Morbidity/ (27417)						
	27 morbidity.mp. (330859)						
	28 (cardi* adj3 (event* or outcome*)).mp. (66991)						
	29 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 (1690357)						
	30 predict*.mp. (1382430)						
	31 prognos*.mp. (734497)						

	2 30 or 31 (1934125)	
	B exp Cohort Studies/ (1714	68)
	4 (cohort adj (study or studie	s)).mp. (310492)
	5 (Follow up adj (study or stu	dies)).mp. (604740)
	6 Longitudinal.mp. (250750)	
	7 (observational adj (study o	studies)).mp. (109821)
	B Epidemiologic studies/ (76 ⁻	1)
	9 (epidemiologic* adj (study	or studies)).mp. (79971)
) population based study.mp	. (24755)
	l general population.mp. (85	498)
	2 communit*.mp. (535197)	
	3 33 or 34 or 35 or 36 or 37 o	or 38 or 39 or 40 or 41 or 42 (2539317)
	5 and 16 and 29 and 32 an	d 43 (2940)
EMBASE	atabase: Embase Classic+Emb	base <1947 to 2018 February 27>
	earch Strategy:	
	heart left ventricle function/	39176)
	left ventric*.mp. (332499)	
	LV.mp. (83461)	
	1 or 2 or 3 (353062)	
	echocardiography/ (178295)	
	exp speckle tracking echoca	rdiography/ (3150)
	speckle tracking.mp. (10536)
	STE.mp. (4416)	
	strain.mp. (762166)	
) deformation.mp. (42935)	
	I mechanic*.mp. (498347)	
	2 torsion.mp. (27446)	
	3 twist.mp. (12502)	
	1 rotation.mp. (109923)	
	5 GLS.mp. (3938)	
	6 5 or 6 or 7 or 8 or 9 or 10 o	r 11 or 12 or 13 or 14 or 15 (1553350)
	7 cardiovascular disease/ (24	1943)
	3 cardiovascular disease*.m	o. (336057)
	e heart failure/ (212076)	
) Heart Failure.mp. (347509)	
	I HF.mp. (60866)	
	2 mortality/ (722163)	
	3 cardiovascular mortality/ (2)	9486)

24	all cause mortality/ (4807)
25	mortality.mp. (1271143)
26	death/ (284488)
27	death.mp. (1097060)
28	morbidity/ (309365)
29	morbidity.mp. (569914)
30	(cardi* adj3 (event* or outcome*)).mp. (110928)
31	17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30
(282	24491)
32	predict*.mp. (1798936)
33	prognos*.mp. (982782)
34	32 or 33 (2544622)
35	longitudinal study/ (109328)
36	longitudinal.mp. (297876)
37	prospective study/ (426930)
38	cohort analysis/ (346132)
39	(Cohort adj (study or studies)).mp. (217636)
40	(follow up adj (study or studies)).mp. (63815)
41	(observational adj (study or studies)).mp. (172984)
42	(epidemiologic* adj (study or studies)).mp. (100634)
43	population based study.mp. (33254)
44	general population.mp. (124629)
45	communit*.mp. (641283)
46	35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 (1963334)
47	4 and 16 and 31 and 34 and 46 (4098)

'OR and AND' are Boolean operators;

'*' indicates truncation;

'mp.' means a keyword search of title, abstract, original title, name of substance word, subject heading word and

keyword heading word.

Supplemental Table 1. Studies reporting Kaplan-Meier data as descriptive information								
Citation (Author, year)	Categories	P value	Outcomes	Participants				
Russo et al (2014)	Event-free probability in participants with any LVSD (GLS LVSD or LVEF LVSD) vs. no LVSD	<0.001, log-rank p	Composite CV end point n=58 (included ischemic stroke [n=16],	All				
	LVEF-LVSD, GLS-LVSD and no LVSD		myocardial infarction [n=10], and vascular death [n=32])					
Russo et al (2015)	Cumulative incidence in participants with GLS>-14.7% vs. GLS≤-14.7%	<0.001, p for comparison	Atrial fibrillation (AF)	All				
	Cumulative incidence in participants with:	<0.001, p for comparison	-					
	Group 1: Normal GLS/normal LAVi							
	Group 2: Abnormal GLS/normal LAVi							
	Group 4: Abnormal GLS/abnormal LAVi							
Kuznetsova et al (2016)	Cumulative incidence according to the quartiles of mid-wall strain:	<0.0001, p for trend	Composite CV end point	All				
	Low, low-medium, medium-high and high LV mid-wall strain quartile		n=96 (comprised cardiac end points, stroke, transient ischemic attack,					
	Cumulative incidence according to the groups with 0, 1, 2, 3 LV abnormalities in echocardiography including abnormal mid-	<0.0001, log-rank p)001, log-rank p of peripheral arteries)					
	wall strain, LVH and LVDD)		Composite cardiac end point					
			n=68					
			(Included coronary events, fatal and nonfatal HF, pulmonary heart disease, new-onset AF, and life- threatening arrhythmias)					
Biering- Sorensen et al (2017)	Cumulative incidence stratified by quartiles of GLS (quartile 1, 2, 3 and 4)	<0.001, Log rank p	Composite cardiac end point	All				
()			n=149					
			(comprising AMI [n=43], HF [n=78], and CV death [n=74])					
		<0.001, Log rank p	HF : n = 78	-				

		0.016, Log rank p	AMI : n = 43	
		0.15, Log rank p	CV death: n= 74	-
	Cumulative incidence stratified by quartiles of GLS (quartile 1, 2, 3 and 4)	0.12, Log rank p	Composite cardiac end point	Female
			n=77	
			(comprising AMI, HF, and CV death)	
		0.09, Log rank p	HF	-
		0.28, Log rank p	AMI	-
		0.37, Log rank p	CV death	-
	Cumulative incidence stratified by quartiles of GLS (quartile 1, 2, 3 and 4)	<0.001, Log rank p	Composite cardiac end point	Male
			n=72	
			(comprising AMI], HF, and CV death)	
		<0.001, Log rank p	HF	-
		0.030, Log rank p	AMI	-
		0.22, Log rank p	CV death	-
Brainin et al (2018)	Cumulative incidence stratified by number of walls displaying post systolic shortening (no wall 1 wall and >2 walls)	<0.001, Log rank p	Composite cardiac end point	All
			n=149 (11.5%)	
			(composite of HF [n=78], MI [n=43], and CV death [n=74])	
		<0.001, Log rank p	Deaths	-
			n=236 (18.1%)	
Modin et al (2018)	Cumulative incidence stratified by median GLS in hypertensive individuals: lower vs	P=0.016	Composite cardiac end point	Hypertensive participants
	upper nan		(Composite of either IHD or HF)	
			n=145 (65%) in hypertensive	
	Cumulative incidence stratified by median GLS in non-hypertensive individuals: lower vs upper half	P<0.001	and n=77 (35%) in non- hypertensive	Non- hypertensive participants

Maximally adjusted models of included studies

- Russo et al (2014): adjusted for age, sex, systolic blood pressure (SPB), diastolic BP, hypertension, anti-hypertensive medications, diabetes mellitus (DM), left ventricular mass index (LVMi), relative wall thickness, left atrial volume index, diastolic dysfunction, atrial fibrillation and LVEF.
- Kuznetsova et al (2016): adjusted for family clusters, sex, age, body mass index (BMI), SBP, serum cholesterol, smoking, antihypertensive treatment, DM, and a history of cardiac disease, TDI e' and LVMi.
- Cheng et al (2015): adjusted for age, sex, ethnicity, BMI, SBP, diastolic BP, anti-hypertensive treatment, total/ HDL cholesterol, DM, smoking status, left ventricular (LV) mass (LVM), LV fractional shortening, and heart rate (HR).
- Biering-Sorensen et al (2017): adjusted for age, sex, HR, hypertension, DM, previous ischemic heart disease, SBP, and pro-BNP (>150 pmol/L), LVEF (<50%), LVMi, LV dimension, deceleration time, left atrial dimension, and E/e'.

Supplement Table 2. Quality assessment of the included papers based on NEWCASTLE - OTTAWA QUALITY ASSESSMENT SCALE - COHORT STUDIES

		Russo et al 1	Cheng et al ²	Russo et al ³	Kuznetsova et al ⁴	Biering-Sorensen et al ⁵	Brainin et al ⁶	Modin et al ⁷	Shah et al ⁸
Se	Selection category								
1-	Representativeness of the cohort								
a)	Truly representative of the average person in the community st								
b)	Somewhat representative of the average person in the community (sampling described and designed to achieve	*	*	*	*	*	*	*	*
	adequately representative sample of the community) st								
c) d)	Selected group e.g. nurses, volunteers No description of the derivation of the cohort								
2-	Assessment of exposure reliability								
a)	Include assessment of inter- and intra-observer variabilities st	*	*	*	*	*	*		*
b)	Include assessment of intra-observer variability *								
C)	No description								
3-	Completeness of collection of potential								
	confounders (i.e. CVD risk factors)								
a)	Complete *	*	*	*	*	*	*	*	*
b)	Partially complete (≥ 5) *								
c)	Partially complete (< 5)								
d)	No description								
4-	Demonstration that the outcome of interest not								
	analysis)	*	*	*	*	*	*	*	*
a)	Yes 🗆								
b)	No								
Οι	Outcome category								
1-	Assessment of outcome								
a)	Independent blind assessment *	*	*	*	*	*	*	*	*
b)	Record linkage *			-	·	-	-	·	
c) d)	Self-report No description								

2-	Was follow-up long enough for outcomes to								
	occur				.1.			.1.	
a)	yes (an adequate follow up period for outcome of interest is a	*	*	*	*	*	*	*	*
	year) *								
b)	no								
3-	Adequacy of follow up of cohorts								
a)	Complete follow up - all subjects accounted for *								
b)	Subjects lost to follow up unlikely to introduce bias - small number lost - > 80% follow up, or description provided of those	*	*	*	*	*	*	*	*
	lost *								
c)	Follow up rate < 80% and no description of those lost								
d)	No statement								
Total									
Average of both reviewers		7	7	7	7	7	7	6	7

Supplement Figure 1 Global longitudinal strain as a predictor of composite cardiovascular end-point on maximally adjusted models.

Α.

Kuznetsova et al (2016) (791; 96)

Overall (I-squared = 0.0%, p = 0.341)

Weights are from random effects analysis

.69



1.25 (1.10, 1.44) 40.05

1.19 (1.09, 1.29) 100.00

1.44

Sensitivity analysis of replacing the endocardial strain with **(A)** mid-wall and **(B)** epicardial strains for Kuznetsova et al (2016) study. HRs are per unit change in strain value. The heterogeneity assessment including the I² statistics and p-value of Q test are shown.

Hazard ratio per unit change in strain value

Supplement Figure 2. Global longitudinal strain as a predictor of composite cardiac-end point on minimally adjusted models



Cheng et al (2015) adjusted for age, sex and ethnicity and Bering-Sorensen et al (2017) adjusted for age and sex. HRs are per unit change in strain value. The heterogeneity assessment including the I² statistics and p-value of Q test are shown.

Supplement Figure 3. Global longitudinal strain as a predictor of composite cardiac end-point on maximally adjusted models.

Α.



Hazard ratio per unit change in strain value

Sensitivity analysis of replacing the endocardial strain with **(A)** mid-wall and **(B)** epicardial strains for Kuznetsova et al (2016) study. HRs are per unit change in strain value. The heterogeneity assessment including the I² statistics and p-value of Q test are shown.

Supplement Figure 4. Global longitudinal strain as a predictor of (A) coronary artery disease and (heart failure) on minimally adjusted models.

A. Coronary heart disease



B. Heart failure



Cheng et al (2015) adjusted for age, sex and ethnicity and Bering-Sorensen et al (2017) adjusted for age and sex. HRs are per unit change in strain value. The heterogeneity assessment including the I² statistics and p-value of Q test are shown.

Supplement Figure 5. Global longitudinal strain as a predictor of coronary heart disease on maximally adjusted models.





B.



Sensitivity analysis of replacing the endocardial strain with **(A)** mid-wall and **(B)** epicardial strains for Kuznetsova et al (2016) study. HRs are per unit change in strain value. The heterogeneity assessment including the I² statistics and p-value of Q test are shown.

References

- Russo C, Jin Z, Elkind MS, et al. Prevalence and prognostic value of subclinical left ventricular systolic dysfunction by global longitudinal strain in a community-based cohort. *Eur J Heart Fail.* 2014;16(12):1301-1309.
- Cheng S, McCabe EL, Larson MG, et al. Distinct Aspects of Left Ventricular Mechanical Function Are Differentially Associated With Cardiovascular Outcomes and All-Cause Mortality in the Community. J Am Heart Assoc. 2015;4(10):e002071.
- 3. Russo C, Jin Z, Sera F, et al. Left Ventricular Systolic Dysfunction by Longitudinal Strain Is an Independent Predictor of Incident Atrial Fibrillation: A Community-Based Cohort Study. *Circ Cardiovasc Imaging.* 2015;8(8):e003520.
- 4. Kuznetsova T, Cauwenberghs N, Knez J, et al. Additive Prognostic Value of Left Ventricular Systolic Dysfunction in a Population-Based Cohort. *Circ Cardiovasc Imaging*. 2016;9(7).
- Biering-Sorensen T, Biering-Sorensen SR, Olsen FJ, et al. Global Longitudinal Strain by Echocardiography Predicts Long-Term Risk of Cardiovascular Morbidity and Mortality in a Low-Risk General Population: The Copenhagen City Heart Study. *Circ Cardiovasc Imaging*. 2017;10(3).
- Brainin P, Biering-Sorensen SR, Mogelvang R, Sogaard P, Jensen JS, Biering-Sorensen T. Postsystolic Shortening by Speckle Tracking Echocardiography Is an Independent Predictor of Cardiovascular Events and Mortality in the General Population. J Am Heart Assoc. 2018;7(6).
- Modin D, Biering-Sorensen SR, Mogelvang R, Landler N, Jensen JS, Biering-Sorensen T. Prognostic Value of Echocardiography in Hypertensive Versus Nonhypertensive Participants From the General Population. *Hypertension*. 2018;26:26.
- Shah AM, Claggett B, Loehr LR, et al. Heart Failure Stages Among Older Adults in the Community: The Atherosclerosis Risk in Communities Study. *Circulation*. 2017;135(3):224-240.