Ventricular volumes and function

Table 3i.1: Validation ex-vivo CMR cine imaging for ventricular volumes, mass and function. Values are expressed as mean difference± standard deviation (MD±SD) between CMR derived measurements and the reference standard. Coefficient of variation (CoV, value in brackets) is derived from SD of the measurements, divided by the mean value, expressed as %. SSFP: steady-state free precession. TGrE = segmented gradient echo. *Value for Cine in diastole (as per recommended approach).

Study	CMR Method of cine imaging	N	Weighing method / reference standard	LV mass (g)	RV mass(g)
Animal models					
Fieno[1]	SSFP, 1,5T, In vivo CMR (dogs)	10	water displacement	1.8±4.1*	
Lorenz[2]	SSFP, 1.5T, In vivo CMR (dogs)	10	water displacement	5.0±7.7 (7.8)	4.6±6.3(18)
Childs[3]	SSFP, 1.5T, Ex vivo CMR (dogs)	12	mould displacement	7.47±5.57 (3.49)	
				LV Volumes (mL): -1.6 ± 1.8 (3.63)	
Codella[4]	SSFP, 1.5T, In vivo CMR (dogs+pigs)	10	water displacement	1±3 (4.3)	
Gilbert[5]	SSFP, 3.0T, ex vivo CMR (sheep)	10	weight	5.76± 3.68 (3.9)	6.73 ± 4.41 (13)
Excised human hearts					
Farber[6]	SSFP, 1,5T, Ex vivo CMR (explanted hearts)	55	weight	-16±33.7(10.9)	19±31.1(22.5)
Function					
Lin[7]	TGrE, 3.0T in vivo pigs	14	conductance catheter	**Cardiac output (l/min):** -0.05 (r^2=0.85)	

Table 3i.2. Reproducibility of the measurement of LV and RV in healthy volunteers. Studies included if reporting for interstudy reproducibility. Values represent mean difference and standard deviation between two measurements (MD±SD) and coefficient of variation (CoV, derived from SD of the measurements divided by the mean value, expressed as %). LV: left ventricle. RV: right ventricle. EDV: end-diastolic volume. ESV: end-systolic volume. EF: ejection fraction

	Hudsmith[8]	**Grothues [9,10]**
N	12	20
Method	SSFP	SSFP
Field strength (T)	1.5	1.5
Interstudy reproducibility		
LV-EDV	-2.6±7.9 (5.2)	2.2±4.3 (2.9)
LV-ESV		1.5±2.8 (6.5)
LV-EF	0.5±4.9 (7.5)	-0.5±1.7 (2.4)
LV-mass	1.8±10.1 (9.4)	-1.1±4.2 (2.8)
RV-EDV	1.3±20.7 (7.4)	1.1±6.5 (4.2)
RV-ESV		-0.3±4.7 (8.1)
RV-EF	1.9±6.8 (11.4)	0.6±2.7 (4.3)
RV-mass		-0.4±4.7 (7.8)
Interobserver variability		
LV-EDV	0.8±3.9 (2.7)	
LV-ESV		
LV-EF	1.6±2.2 (3.3)	
LV-mass	5.8±5.2 (5.2)	
RV-EDV	-0.2±16.0 (9.6)	
RV-ESV		
RV-EF	-2.8±6.3 (10.7)	
RV-mass		
Intraobserver variability		
LV-EDV	8.6±8.6 (5.6)	
LV-ESV		
LV-EF	0.5±1.5 (2.3)	
LV-mass	5.4±6,2 (6.1)	

RV-EDV	-6.0±15.0 (9.0)	
RV-ESV		
RV-EF	0.1±3.2 (5.3)	
RV-mass		

Tables 3i.3: Normal values. Table A provides an overview of the studies reporting normal values for measurements of LV and RV obtained in healthy subjects (except for Kawut et al [17] including MESA population, patients without known CV disease but including CV factors). Studies using standard balanced steady-state free precession sequences (SSFP) are shown, except for MESA studies, who used a fast gradient echo sequence (FGE). Postprocessing approaches differed as to the inclusion or exclusion of papillary muscles (PMi or PMe) as a part of the blood volume. Tables B and C list the studies reporting normal ranges (mean±SD) for LV and RV, in males (M) and females (F), respectively. Following units are used: EF %; EDV, ESV, SV ml; EDVi, ESVi, SVi ml/m2; mass g; massi g/m2.

Table A	**N**	**Age**	**Measurements**	**Field strength (T)**	**Sequence**	**Postprocessing approach**	**Subgroups**		
							Age	Sex	Ethnicity
Hudsmith[8]	108	21-68 (38±12)	LV, RV, LA	1.5	SSFP	PMi	<35, ≥35	Yes	No
Petersen[11]	804	45-74 (59±7)	LV, RV, LA, RA	1.5	SSFP	PMe	45-54, 55-64, 65-74	Yes	No
Chuang[12]	685	62±9	LV	1.5	SSFP	PMe	<50, 50-59, 60-69, ≥70	Yes	No
Maceira[13]	120	20-80	LV	1.5	SSFP	PMi	20-80, 10y groups	Yes	No
Maceira[14]	120	20-80	RV	1.5	SSFP	PMi	20-80, 10y groups	Yes	No
Lorenz[2]	75	8-55 (28±9)	LV, RV	1.5	FGE	PMi	No	Yes	No
Alfakih[15]	60	20-65 (43±12)	LV, RV	1.5	SSFP, FGE	PMi	<40, ≥40	Yes	No
Natori[**Error! Bookmark not defined.**16]	800	45-84	LV	1.5	FGE	PMi	No	Yes	Yes
Kawut[17]	4123	61.5±10.1	RV	1.5	FGE	PMi	No	Yes	Yes

Table B	**Hudsmith[8]**		**Petersen[11]**		**Chuang[12]**		**Maceira[13]**		**Lorenz[2]**		**Alfakih[15]**		**Natori[16]**	
Sequence	SSFP		SSFP		SSFP		SSFP		FGE		SSFP		FGE	
	M	F	M	F	M	F	M	F	M	F	M	F	M	F
LV-EDV	160 ±29	135 ±26	163 ±35	127±24	149 ±29	112 ±21	156 ±21	128 ±21	136 ±30	96±23	170±33	135 ±19	142±34	109±23
LV-EDVi	82±13	78±12	84±16	75±13	74±14	64±10	80±9	75±9	69±11	61±10	82±15	78±19	74±15	65 ±11
LV-ESV	50±16	42±12	68±17	49±12	44±14	31±9	53±11	42 ±9.5	45±14	32±9	61±16	49±11	47±20	31±10
LV-ESVi	25±8	24±6	35±8	29±7	22±7	18±5	37±6	24±5					25±9	18±5
LV-SV	112 ±19	91±17	94±23	78±16	105 ±20	81±15	104 ±14	86±14	92±21	65±16	108±21	86 ±12	95 ±21	78 ±17
LV-SVi	56±8	54±9	49±10	46±8	52±9	46±7	53 ±6	50 ±6.2	47±8	41±8			49±10	46 ±8
LV-EF	69±6	69±6	58±6	61±5	71±6	73±6	67±5	67±5	67±5	67±5	64±5	64±5	67 ±7	72 ±17
LV-Mass	123 ±21	96±27	102±23	70±13	99±21	58±13	146 ±20	108 ±18	178 ±31	125 ±26	133 ±24	90±12	164±36	114±24
LV-Massi	63±9	55 ±12	52±10	41±7	49±9	33±6	74±9	63±8	91±11	79±8	65±10	52±7	85±15	67±11

Table C	Hudsmith[8]		Petersen[11]		Maceira[14]		Lorenz[2]		Alfakih[15]		Kawut [17]	
Sequence	**SSFP**		**SSFP**		**SSFP**		**FGE**		**SSFP**		**FGE**	
	M	F	M	F	M	F	M	F	M	F	M	F
RV-EDV	173 ±39	148 ±35	179±40	137±27	163 ±25	126 ±21	157 ±35	106 ±24	177±33	131±24	141±30	109±23
RV-EDVi	91±16	84±17	91±18	80±15	83±12	73±9	80±13	67±10	86±14	75 ±14	72 ±13	62 ±11
RV-ESV	69±22	56±18	84±25	60±17	57±15	43±13	63±20	40±14	79±16	52 ±10	45 ±14	30 ±10
RV-ESVi	36±10	32±10	43±12	35±10	29±7	25±7					23 ±7	17 ±5
RV-SV	104 ±21	90±19	97±21	77±15	106 ±17	83±13	95±22	66±16	98 ±19	78 ±17	96±21	79 ±17
RV-SVi	55±9	53±9	49±10	45±8	54±8	48±6	48±8	42±8			49 ±10	45 ±8
RV-EF	61±6	63±5	54±7	57±6	66±6	66±6	60±7	63±8	55.1 ±3.7	59.8 ±5	68 ±6	73±6
RV-Mass	38±8	35±7			66±14	48±11					23±4	19±4
RV-Massi	20±4	20 ±4			34±7	28±5					12±2	11±2

Table 3i.4: Outcomes studies against clinical endpoints for LV (Table A) and RV (Table B) function, mass or volumes.

Hazard ratios (HR) with 95% confidence intervals (95%CI) for adjusted/multivariate predictive associations with outcome endpoints. Absolute values are shown as mean±SD.

EDV: end-diastolic volume. LV M/V ratio: LV mass/volume ratio. CAD: coronary artery disease. HF: heart failure.

PAH: pulmonary artery hypertension. EF: ejection fraction. SV: systolic volume. PVR: pulmonary vascular resistance. ESV: end-systolic volume. DCM: dilated cardiomyopathy. HTx: cardiac transplantation.

Table A	**N**	**Type**	**Population**	**Follow-up (months)**	**CMR biomarker**	**Outcome-endpoint**		
Bluemke[18]	5098	Observational Prospective	Healthy volunteers	48	LV-EDV, LV-mass LV-M/V ratio	**LV Mass/Volume ratio**		
						CAD	HR 2.1 (1.1-4.1)	0.02
						Stroke	HR 4.2 (1.5-11.2)	0.0005
						LV-EDV (per 10%)		
						CAD	HR 0.9 (0.8-1)	0.09
						HF	HR 1.3 (1.2-1.5)	<0.0001
						LV mass		
						Stroke	HR 1.2 (1-1.4)	0.01
						HF	HR 1.4 (1.2-1.5)	<0.0001
Jain[19]	4965	Observational Prospective	Healthy volunteers	70	LV mass LV M/V ratio	**LV mass**		
						Stroke	HR 1.3 (1.1-1.7)	≤0.01
						HF	HR 1.8 (1.6-2.1)	≤0.001
						LV Mass/Volume ratio		
						Stroke	HR 1.3 (1.1-1.6)	≤0.01

Table B	N	Type	Population	Follow-up (months)	CMR biomarker	Outcome-endpoint		
Kawut[20]	4144	Observational Prospective	Healthy volunteers	70	RV- mass	HF/CV death	HR 2.52 (1.55-4.1)	<0.001
Van Wolferen[21]	64	Observational Prospective	PAH	32	RV-EDV RV-EF	Baseline biomarker ~ all cause-mortality		
						RVEDV	HR 1.6	<0.001
						LVEDV	HR 0.7	0.002
						SV	HR 0.76	<0.001
						Biomarker change at 1Y ~ all cause-mortality		
						RV-EDV	HR 1.05	0.036
						LV-EDV	HR 0.91	0.023
						LV-SV	HR 0.89	0.012
Van de Veerdonk[22]	110	Observational Prospective	PAH	50	RV-EF PVR	Baseline biomarker ~ all cause-mortality		
						RV-EF	HR 0.92 (0.88-0.96)	<0.001
						PVR	HR 1.001 (1.001-1.002)	0.002
						Biomarker change at 1Y ~ all cause-mortality		
						RV-EF	HR 0.93(0.88-0.99)	0.026
Swift[23]	80	Observational Prospective	PAH	32	RV-EDV RV-ESV RV-EF	Baseline biomarker ~ all cause-mortality		
						RV-ESV	HR 1.55 (1.15-2.1)	0.004
						RV-EDV	HR 1.3 (0.97-1.8)	0.078
						RV-EF	HR 0.78 (0.5-1.14)	0.187
Gulati[24]	250		DCM	82	RV-EF	RV-EF≤45% ~ adverse outcomes		

		Observational Prospective				Death/ HTx	HR 3.9 (2.16-7.04)	<0.001
						CVdeath/ HTx	HR 3.35 (1.76-6.39)	<0.001
						HF death/ admission/ HTx	HR 2.7 (1.32-5.51)	0.006

Table 3ii.1: Validation studies and comparative studies of strain imaging.

Values are shown as MD ± SD (CoV, when available) between the CMR method of study and its reference. Strain measures are expressed as %. Coefficient of correlation (R) is provided when analysed. * Only CoV available.

SPAMM: spatial modulation of magnetization. λ1 and λ2: principal strains (most positive and most negative strains). DENSE: displacement encoding with stimulated echoes. GCS: global circumferential strain. GRS: global radial strain. DMD: Duchenne muscular dystrophy. HARP: harmonic phase image analysis. FT: feature tracking. LBBB: left bundle branch block. HCM: hypertrophic cardiomyopathy. GLS: global longitudinal strain. PAH: pulmonary artery hypertension. SENC: strain-encoded MR imaging. CP: constrictive pericarditis. RCM: restrictive cardiomyopathy.

	Reference model	**Reference method**	**N**	**CMR sequence**	**Parameter**	**Correlation**		
Phantoms/animals								
Young[25]	Deformable silicone gel phantom	Analytical value		SPAMM	Axial shear strain	Homogeneous	λ1 0.122	
							λ2 0.036	
						Non-homogeneous	λ1 0.05	
							λ2 0.012	
Young[26]	Deformable silicone gel phantom	Analytical value		SPAMM DENSE	Shear strain Radial strain	SPAMM		
						Shear	1.4 ± 4.0	
						Radial	0.0 ± 4.9	
						DENSE		
						Shear	1.3 ± 2.1	
						Radial	1.2 ± 4.8	
Yeon[27]	Canine coronary artery ligation model	Sonomicrometry	19	SPAMM	Circumferential shortening	R=0.84 p<0.0001		
						Effective identification of ischaemic/remote myocardium (2±3 vs 11±10, p 0.014)		
Compared to tagging								
Young [26]	Healthy volunteers	SPAMM	19	DENSE	GCS GRS	GCS	1.2± 3.9 (CoV 20.6)	<0.05
						GRS	2.3 ± 14.0 (CoV 39.5)	NS

Hor[28]	DMD/ Healthy volunteers	HARP	230	FT	GCS	-0.36±1.67 (CoV 12.4) R=0.899, p<0.0001		
Wu[29]	Healthy volunteers/ LBBB/ HCM	HARP	30	FT	GCS	Significant differences between tagging and FT		
						$FT_{endocardial}$	−23.8 ± 9.9 vs -13.4 ± 3.3	<0.001
						$FT_{midwall}$	−16.4 ± 6.1 vs -13.4 ± 3.3	0.001
Augustine[30]	Healthy volunteers	HARP	20	FT	GCS GLS GRS	Only GCS showed reasonable agreement		
						GCS	-0.7 ± 2	
						GLS	-1 ± 7.5	
						GRS	11 ± 6	
Ohyama[31]	PAH/ healthy volunteers	HARP (GCS) SENC (GLS)	45	FT	GLS GLS RV GCS	GLS	2.8 ± 2.3 (CoV 13.3)	<0.001
							R=0.67	<0.001
						GLS RV	0.4 ± 3.2 (CoV 16.9)	0.463
							R=0.71	<0.001
						GCS	-2.8 ± 3.5 (CoV 22)	<0.001
							R=0.58	<0.001
Compared to echo								
Amaki[32]	CP/RCM	Echo	92	FT	GLS	0.7 ± 3.6 R=0.68, p<0.001		
Kempny[33]*	Tetralogy of Fallot	Echo	53	FT	GLS GCS GRS GLS RV	GLS	CoV 15.8	
						GCS	CoV 17.0	
						GRS	CoV 69	
						GLS RV	CoV 16.6	
Padiyath[34]	Tetralogy of Fallot	Echo	20	FT	GLS GCS GRS	GLS	-1.38 ± 4.59 (CoV 26.8)	
						GCS	0.77 ± 3.39 (CoV 15.5)	
						GRS	-10.88 ± 22.23 (CoV 70.0)	

					GLS RV	GLS RV	0.05 ± 4.34 (CoV 28.8)
Onishi[35]	Evaluation of LV function	Echo	72	FT	Radial dysynchrony	-0.3 ± 41.8 R=0.93, p<0.0001 Best agreement in patients with marked dysynchrony	

Table 3ii.2. Reproducibility values reported for main strain measurements.

Variability is reported as MD±SD(CoV) (CoV: derived from SD of the measurements divided by the mean value, expressed as %). When not available, we report MD±SD (Kutty and Padiyath), or intraclass correlation (ICC) (Castillo, Rosen and Yoneyama). *All values reported for healthy volunteers except Padiyath, who included Tetralogy of Fallot patients. FT: feature tracking. HARP: harmonic phase image analysis. SPAMM: spatial modulation of magnetization. C-SPAMM: complementary spatial modulation of magnetization. GCS: global circumferential strain. GLS: global longitudinal strain. GRS: global radial strain.

	Augustine [30]	**Kempny [33]**	**Morton [36]**	**Kutty [37]**	**Padiyath [34]***	**Castillo [38]**	**Rosen [39]**	**Yoneyama [40]**	**Swoboda [41]**
Sequence	FT	FT	FT	FT	FT	Tagging (HARP)	Tagging (HARP)	Tagging (SPAMM)	Tagging (C-SPAMM)
N	12	25	16	15	10	24	24	30	12
Interstudy									
GCS			1.0±3.5 (20.3)						(3.7-5.5)
GLS			-1.1±5.4 (26.4)						
GRS			-3.2±5.7 (27.2)						(13.8-23.4)
LV torsion									(9.8-12.2)
Interobserver									
GCS	4.9	8.5		-0.01±1.7 (7.1)	-0.19±1.25 (5.8)	0.84	0.81		(3.5-6.2)
GLS	10.9	9.6		-0.32±1.1 (5.5)	-2.23±3.2 (17.9)				
GRS	32.3	21.4		-1.57±5.5 (11.0)	-3.21±8.5 (32.3)	0.71			(11.8-21.8)
LV torsion								0.94	(3.5-7.2)
Intraobserver									
GCS	2.8	6.7			-0.19	0.89	0.84		(1.5-4.3)
GLS	12.3	10.8			-2.23				

GRS	22.9	21.4			-3.21	0.77			(10.6-14.8)
LV torsion								0.91	(1.2-4.4)

Table 3ii.3: Normal values reported by different studies for main strain measurements.

Venkatesh provided normality values for strain according to segment, age, sex and ethnicity. Augustine for sex and segments, and Moore [42] and Del-Canto for each myocardial segment. GCS, GLS and GRS are expressed as %, SRe s^{-1} and LV torsion º or º/cm.

SPAMM: spatial modulation of magnetization. HARP: harmonic phase image analysis. FT: feature tracking. GCS: global circumferential strain. GLS: global longitudinal strain. GRS: global radial strain. SR_E: early diastolic strain rate. MESA: multi-ethnic study of atherosclerosis, includes volunteers without previous history of cardiovascular disease.

	Edvardsen [43]	**Donekal [44]**	**Yoneyama [40]**	**Venkatesh [45]**	**Del-Canto [46]**	**Nelson [47]**	**Augustine [30]**	**Kempny [33]**	**Kutty [37]**	**Padiyath [34]**	**Morton [36]**
Sequence	Tagging (SPAMM)	Tagging (SPAMM)	Tagging (SPAMM)	Tagging (SPAMM)	Tagging (SPAMM)	Tagging (HARP)	FT	FT	FT	FT	FT
N	188	1116	1478	129	39	15	145	25	20	20	16
Population	MESA	MESA	MESA	MESA low-risk	Low Risk	Healthy volunteers	Healthy volunteers	Healthy volunteers	Healthy volunteers	Healthy volunteers	Healthy volunteers
GCS	-17.1±5	-15.5±3.2		-18±2.2	-20.3±3	−21.9±0.5	−21 ± 0.03	-22.0±3.9	-24.6±2.4	-24.6±2.5	-17.4±4.6
GLS							−19 ± 0.03	-21.3±3.3	-20.0±5.1	-19.9±5.1	-20±5.2
GRS				25.8±8.4	12.1±4.4		25 ± 0.06	28.0 ± 11.3	50 ± 12.4	50.9±12.4	20.8±6.6
SR_E	2.2±1.1	1.04±0.4									
Torsion		8.7±2.04º	3.9±1.3º/cm F: 4.2±1.3 M: 3.5±1.1	3.61±1.15 º/cm			15.52 ± 7.55 º				

Table 3ii.4 Outcome studies for RWMA and strain parameters

Hazard ratios (HR) with 95% confidence intervals (95%CI) for adjusted/multivariate predictive associations with outcome endpoints. Chi-square test ($\chi 2$) was used to assess the predictive value of biomarkers.

HARP: harmonic phase image analysis. MESA: multi-ethnic study of atherosclerosis. SRI: strain relaxation index. HF: heart failure. AF: atrial fibrillation. SPAMM: spatial modulation of magnetization. DSMR: dobutamine stress MR. WMA: wall motion abnormality. CAD: coronary artery disease. LGE: late gadolinium enhancement. RWMI: regional wall motion index. MI: myocardial infarction. CR: contractile reserve. SENC: strain-encoded MR imaging. FT: feature tracking. DCM: dilated cardiomyopathy. GLS: global longitudinal strain.

	N	**Sequence**	**Population**	**Follow-up (months)**	**CMR biomarker**	**Outcome-endpoint**		
Ambale-Venkatesh [48]	1544	Tagging (HARP)	Healthy population (MESA)	96	SRI	HF	HR 2.25 (1.3-3.89)	0.039
						HF/AF	HR 1.88 (1.29-2.74)	0.099
Kuijpers [49]	211	Tagging (SPAMM) DSMR	Chest pain	17.3	WMA with tagging	Improved detection of WMA with tagging (27% vs 32%, p 0.002). Survival (17 months) if CMR – 98.2%.		
Kelle [50]	177	DSMR	CAD and scar in LGE	20.3	RWMI	Infarct size was the only predictor of events (death+MI), HR 1.303 (1.026–1.655), p 0.03		
						In high-risk patients (LGE in >6 segments), CR+ was the only predictor of events		
						CR-	χ^2=0.7	
						CR+	χ^2=4.0	<0.001
Korosoglou [51]	320	SENC DSMR	CAD	28	WMA SENC	WMA and SENC improved the prediction of cardiac death+MI compared with clinical info		
						Clinical	χ^2=13.0	
						Rest WMA	χ^2=26.1	<0.001
						Stress WMA	$\chi 2$=39.3	<0.001
						SENC	$\chi 2$=50.7	<0.001
Buss [52]	210	FT	DCM	63.6	GLS	GLS >-12.5% was associated with CV events		

						GLS	HR 1.27 (1.06-1.52)	<0.02

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