

# ADDITIONAL FILE 1

**Table S1. CMR scans details on each site.**

	Scanner	Vendor	Model	Coil	Gradient Strength (mT/m)	Slew rate (T/m/s)	Normal global native T1 values (mean $\pm$ SD, ms)
<b>1.5T</b>	1	Siemens	Avanto	Body	SQ45; Q33	SQ200; Q125	980 $\pm$ 35
	2	Siemens	Aera	Body	XJ33; XQ45	XJ125; XQ200	1006 $\pm$ 28
	3	Siemens	Avanto	Body	SQ 45; Q33	SQ200; Q125	965 $\pm$ 35
	4	Siemens	Avanto	Body	SQ45; Q33	SQ200; Q125	950 $\pm$ 30
	5	Siemens	Avanto	Heart	SQ 45; Q33	SQ200; Q125	1150 $\pm$ 30
	6	Siemens	Avanto	Body	SQ45; Q33	SQ200; Q125	945 $\pm$ 35
	7	Siemens	Avanto	Body	SQ45; Q33	SQ200; Q125	956 $\pm$ 28
	8	Siemens	Avanto	Body	SQ45; Q33	SQ200; Q125	964 $\pm$ 25
	9	Siemens	Symphony Tim	Body	30	125	949 $\pm$ 32
	10	Siemens	Aera	Body	XJ33; XQ45	XJ125; XQ200	1004 $\pm$ 26
	11	Siemens	Avanto	Body	SQ45; Q33	SQ200; Q125	949 $\pm$ 25
	12	Siemens	Avanto	Body	SQ45; Q33	SQ200; Q125	995 $\pm$ 27
	13	Siemens	Avanto	Body	SQ45; Q33	SQ200; Q125	965 $\pm$ 35
<b>3T</b>	1	Siemens	Verio	Heart	45	200	1177 $\pm$ 37
	2	Siemens	Skyra	Body	45	200	1220 $\pm$ 35

**Table S2. Typical CMR protocol details**

Sequences	Type of sequence	Parameters
Cine	Balanced steady-state free precession sequence	slice thickness, 7 mm; field of view, $320 \times 320 \text{ mm}^2$ ; temporal resolution, 28.9 ms; TE/TR, 1.6/3.6 ms; flip angle, $35^\circ$ ; image resolution, $256 \times 144\text{--}222$
Late gadolinium enhancement	gradient echo inversion-recuperation sequence	TR/TE, 650/1.56 ms; slice thickness, 6 mm; number of slabs, 14; flip angle, $10^\circ$ ; field of view, $350 \times 400 \text{ mm}^2$ ; matrix size, $152 \times 134$ ; and inversion time, 270–325 ms
T1 mapping pre contrast	5 (3) 3 Modified Look-Locker Imaging	<ul style="list-style-type: none"> <li>At 1.5T: slice thickness, 6 mm; field of view, <math>360 \times 360 \text{ mm}^2</math>; TE/TR, 1.13/2.26 ms; flip angle, <math>35^\circ</math>; matrix resolution, <math>256 \times 144\text{--}222</math></li> <li>At 3T: slice thickness, 6 mm; field of view, <math>360 \text{ mm}^2</math>; TE/TR, 251.03/1.07 ms; flip angle, <math>35^\circ</math></li> </ul>
T1 mapping post contrast	4 (1) 3 (1) 2 Modified Look-Locker Imaging	

**Table S3. Comparisons between patients without MACE and patients with the two subgroups of MACE.**

	<b>All patients (n=225)</b>	<b>No HF- or Arrhythmia- related events "No MACE" (n=167)</b>	<b>HF- or Arrhythmia- related events "MACE" (n=58)</b>	<b>p-value<sup>†</sup></b>
<b>Demographics</b>				
Age, years	57.5±14.5	58.3±13.7	55.5±16.6	0.348
Male, %	146 (64.9)	100 (61.7)	46 (79.3)	<b>0.015</b>
<b>Clinical and biological indices</b>				
Heart rate, beats/min ( <i>nmiss</i> =49)	73±16	72±16	76±17	0.052
Systolic blood pressure, mmHg ( <i>nmiss</i> =43)	123±23	124±22	118±24	<b>0.013</b>
Diastolic blood pressure, mmHg ( <i>nmiss</i> =43)	74±14	74±13	73±17	0.164
NYHA functional class ( <i>nmiss</i> =43)				
≤ II	147 (80.8)	115 (86.5)	32 (62.3)	<b>0.002</b>
>II	35 (19.2)	18 (13.5)	17 (34.7)	<b>0.002</b>
eGFR, ml/mn ( <i>nmiss</i> =32)	89±40	87±37	95±45	0.261
Hematocrit, % ( <i>nmiss</i> =34)	41.9±4.5	41.5±4.4	42.9±4.5	0.110
<b>Cardiovascular risk factors</b>				
Body mass index, kg/m <sup>2</sup> ( <i>nmiss</i> =31)	26.7±5.2	26.8±5.2	26.4±5.3	0.607
Hypertension ( <i>nmiss</i> =28)	66 (33.5)	52 (35.9)	14 (26.9)	0.305
Diabetes mellitus ( <i>nmiss</i> =28)	29 (14.7)	19 (13.10)	10 (19.2)	0.361
Atrial fibrillation ( <i>nmiss</i> =28)	13 (6.6)	6 (4.1)	7 (13.5)	<b>0.044</b>
Dyslipidemia ( <i>nmiss</i> =28)	52 (26.4)	40 (27.6)	12 (23.1)	0.586
Smoking, current or previous ( <i>nmiss</i> =28)	76 (38.6)	55 (37.9)	21 (40.4)	0.868
Alcohol excess ( <i>nmiss</i> =30)	14 (7.2)	10 (7.0)	4 (7.7)	1.000
Family history of cardiomyopathy or SD ( <i>nmiss</i> =29)	32 (16.3)	24 (16.7)	8 (15.4)	1.000

<b>Medication</b>				
RAS inhibitors ( <i>nmiss</i> =25)	186 (93.0)	140 (95.2)	46 (86.8)	0.056
Diuretics ( <i>nmiss</i> =26)	151 (75.9)	107 (73.3)	44 (83.0)	0.191
Beta blocker ( <i>nmiss</i> =26)	183 (92.0)	136 (93.2)	47 (88.7)	0.376
<b>CMR parameters</b>				
LVEF, % ( <i>nmiss</i> =3)	29.3±9.7	30.7±9.7	25.4±8.6	<b>&lt;0.001</b>
LVEDV, ml/m <sup>2</sup> ( <i>nmiss</i> =7)	145±48	141±47	157±48	<b>0.013</b>
LV mass, g/m <sup>2</sup> ( <i>nmiss</i> =10)	90.5±24.4	90.3±25.2	90.9±22.1	0.382
LGE presence, % ( <i>nmiss</i> =7)	113 (51.8)	76 (47.2)	37 (64.9)	<b>0.030</b>
Native T1 Zscore ( <i>nmiss</i> =8)	3.0±2.3	2.7±2.2	3.8±2.3	<b>0.001</b>
ECV, % ( <i>nmiss</i> =12)	29.3±4.1	28.7±3.8	31.1±4.3	<b>0.001</b>
Global strain ( <i>nmiss</i> =29)	-8.8±2.9	-9.1±2.9	-7.9±2.8	<b>0.004</b>

† Fisher's exact test for qualitative variables and Wilcoxon's test for quantitative variables. Reference group in "No MACE " (*n*=167). Values are mean ± standard deviation (SD), *n* (%). *p*≤0.05 (versus patients without MACEs)

HF= heart-failure, MACE= major adverse cardiovascular event, NYHA=New York Heart Association, e GFR=estimated glomerular filtration rate, SD=sudden death, RAS=renin-angiotensin-aldosterone system, CMR = cardiac magnetic resonance, LVEF= left ventricular ejection fraction, LVEDV= left ventricular end-diastolic volume, LV= left ventricular, LGE= late gadolinium enhancement, ECV= extracellular volume fraction, *nmiss*= number of missing values.

**Table S4. Causes of heart failure (HF)-related (n=42) and arrhythmia-relates events (n=16) in MACE (n=58)**

Patients with MACE (n=58)	Type of event	Cause
1	HF-related event	Hospitalization for acute HF
2	HF-related event	Hospitalization for acute HF
3	HF-related event	Hospitalization for acute HF
4	Arrhythmia-related event	Sudden death
5	HF-related event	Hospitalization for acute HF
6	HF-related event	Hospitalization for acute HF
7	Arrhythmia-related event	Sustained VT
8	HF-related event	Hospitalization for acute HF
9	HF-related event	Hospitalization for acute HF
10	HF-related event	Hospitalization for acute HF
11	Arrhythmia-related event	Sustained VT
12	Arrhythmia-related event	Appropriate ICD shock
13	Arrhythmia-related event	Sustained VT
14	Arrhythmia-related event	Appropriate ICD shock
15	HF-related event	Hospitalization for acute HF
16	Arrhythmia-related event	Sustained VT
17	HF-related event	Hospitalization for acute HF
18	HF-related event	Hospitalization for acute HF
19	HF-related event	Hospitalization for acute HF
20	HF-related event	Heart transplant
21	HF-related event	Heart transplant
22	HF-related event	Hospitalization for acute HF
23	HF-related event	Death due to cardiogenic shock
24	Arrhythmia-related event	Sustained VT

25	HF-related event	Hospitalization for acute HF
26	Arrhythmia-related event	Appropriate ICD shock
27	HF-related event	Hospitalization for acute HF
28	HF-related event	Hospitalization for acute HF
29	HF-related event	Death due to cardiogenic shock
30	HF-related event	Hospitalization for acute HF
31	Arrhythmia-related event	Sudden death
32	HF-related event	Death due to refractory acute pulmonary edema
33	HF-related event	Heart transplant
34	HF-related event	Heart transplant
35	Arrhythmia-related event	Sustained VT
36	HF-related event	Hospitalization for acute HF
37	HF-related event	Heart transplant
38	HF-related event	Hospitalization for acute HF
39	HF-related event	Hospitalization for acute HF
40	HF-related event	Hospitalization for acute HF
41	HF-related event	Hospitalization for acute HF
42	HF-related event	Death due to refractory acute pulmonary edema
43	HF-related event	Death due to refractory acute pulmonary edema
44	HF-related event	Heart transplant
45	HF-related event	Hospitalization for acute HF
46	HF-related event	Hospitalization for acute HF
47	Arrhythmia-related event	Appropriate ICD shock
48	HF-related event	Death due to cardiogenic shock
49	Arrhythmia-related event	Appropriate ICD shock
50	HF-related event	Hospitalization for acute HF
51	Arrhythmia-related event	Sudden death

52	HF-related event	Hospitalization for acute HF
53	HF-related event	Hospitalization for acute HF
54	HF-related event	Hospitalization for acute HF
55	Arrhythmia-related event	Sustained VT
56	HF-related event	Hospitalization for acute HF
57	HF-related event	Heart transplant
58	Arrhythmia-related event	Sustained VT

*HF= Heart failure; ICD= implantable cardioverter-defibrillator; MACE= major adverse cardiovascular event; VT= ventricular tachycardia*

**Table S5. CMR parameters - univariate analysis in the prediction of MACE.**

	MACE (n=58)		
	OR	95% CI <sup>†</sup>	P-value AUC <sup>‡</sup>
HR	1.02	1.00-1.04	0.089 59.5%
LVEF	0.94	0.91-0.97	<b>&lt;0.001</b> 66.7%
LVEF > optimal cutoff <sup>††</sup>	0.30	0.16-0.57	<b>&lt;0.001</b> 64.5%
LVEDV	1.01	1.00-1.01	<b>0.038</b> 61.1%
LV mass	1.00	0.99-1.01	0.539 87.9%
LGE presence	2.07	1.11-3.97	<b>0.023</b> 58.9%
Native T1 Zscore	1.25	1.08-1.44	<b>0.003</b> 65.4%
Native T1 Zscore > optimal cutoff <sup>†††</sup>	3.54	1.86-6.76	<b>&lt;0.001</b> 64.3%
ECV global	1.16	1.07-1.26	<b>&lt;0.001</b> 65.8%
Base ECV	1.10	1.02-1.18	<b>0.009</b> 61.0%
Mid-ECV	1.12	1.04-1.20	<b>0.002</b> 63.4%
Apex ECV	1.09	1.01-1.16	<b>0.024</b> 58.8%
ECV > optimal cutoff <sup>†††</sup>	2.55	1.36-4.79	<b>0.004</b> 61.4%
ECV maximum	1.09	1.04-1.15	<b>0.001</b> 62.5%
ECV ratio	3.32	1.09-10.13	<b>0.035</b> 57.9%

<sup>†</sup> Odds ratios with 95% confidence intervals (univariate logistic regression)

<sup>‡</sup> Area under the ROC curve

<sup>††</sup> The Youden index was used to depict optimal cutoff values from the ROC curves (27.8 for MACE, 27.8 for heart failure and 34.0 for arrhythmia)

<sup>†††</sup> The Youden index was used to depict optimal cutoff values from the ROC curves (4.0 for MACE, 3.8 for heart failure and 4.2 for arrhythmia)

<sup>††††</sup> The Youden index was used to depict optimal cutoff values from the ROC curves (30.1 for MACE, 32.1 for heart failure and 30.5 for arrhythmia)

HF= heart failure, CMR= cardiovascular magnetic resonance, HR= heart rate, LVEF= left ventricular ejection fraction, LVEDV= left ventricular end-diastolic volume, LV= left ventricular, NYHA= New York Heart Association, LGE= late gadolinium enhancement, ECV= extracellular volume fraction.



**Table S6. Multivariate analysis of MACE prediction – Stepwise Cox proportional hazards**

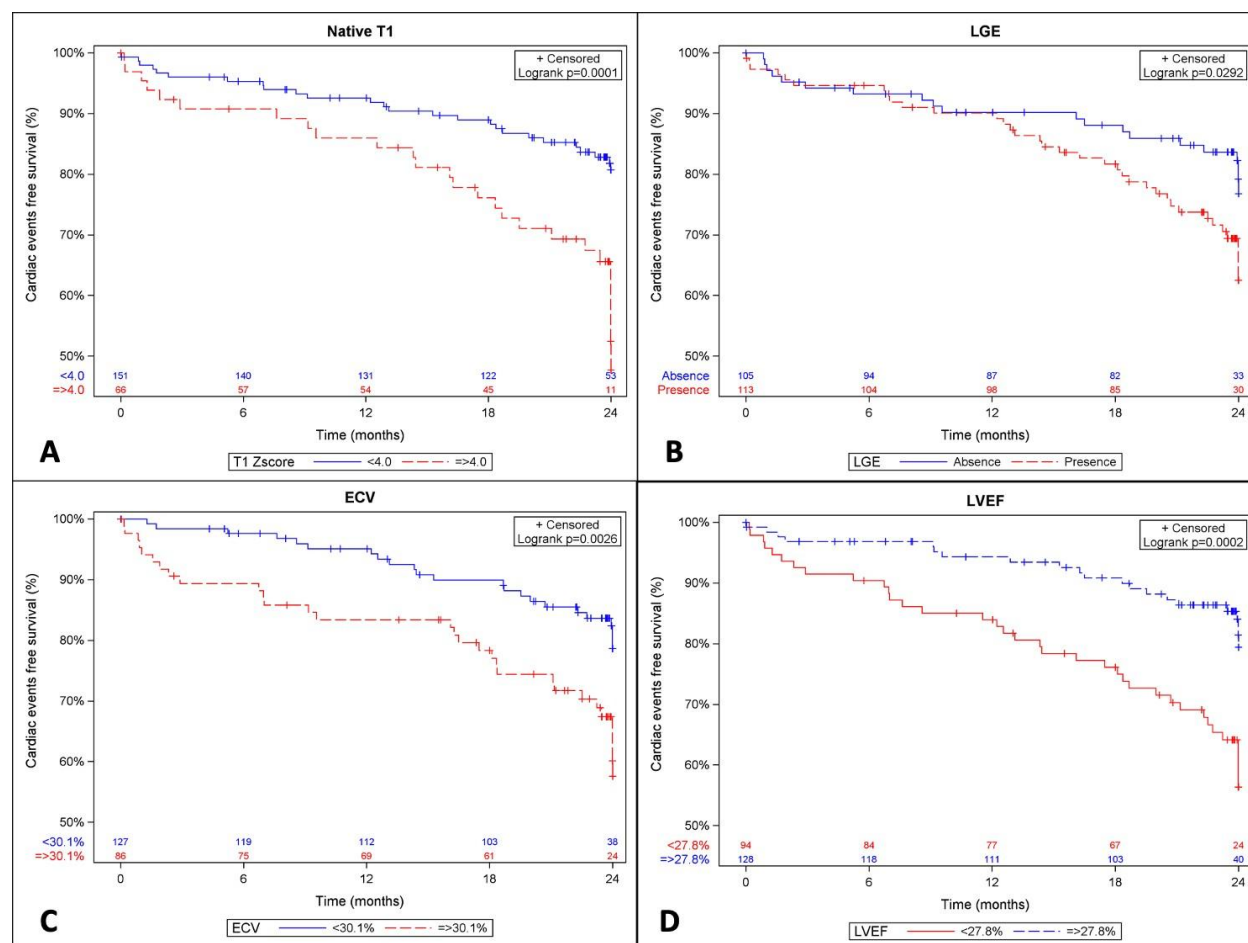
<b>Outcome : MACE (n=225)</b>				
<b>Variable</b>	<b>Adjusted hazard-ratio</b>	<b>95% CI</b>		<b>p</b>
<b>Men (ref. Women)</b>	2.35	1.23	4.50	<b>0.010</b>
<b>NYHA2&gt;II (ref. ≤II)</b>	2.59	1.43	4.71	<b>0.002</b>
<b>LVEF&gt;27.8<sup>†</sup></b>	0.50	0.28	0.88	<b>0.016</b>
<b>ECV&gt;32.1<sup>†</sup></b>	1.96	1.16	3.30	<b>0.012</b>

<sup>†</sup> For each outcome, the Youden index was used to depict optimal cutoff values from the ROC curves (see table 2)

HF= heart failure, LVEF= left ventricular ejection fraction, LVEDV= left ventricular end-diastolic volume, LV= left ventricular, NYHA= New York Heart Association, LGE= late gadolinium enhancement, ECV= extracellular volume fraction.

\*p≤0.05 is considered significant.

**Figure S1. Cumulative 2-year MACE-free survival rate depending on cardiac magnetic resonance imaging parameters.**



(A) Native T1 Z-score: <4.0 vs.  $\geq 4.0$ ; based on the optimal cutoff determined by the Youden index

(B) Late gadolinium enhancement (LGE): present vs. absent

(C) Extracellular volume (ECV): <30.1% vs.  $\geq 30.1\%$ ; based on the optimal cutoff determined by the Youden index

(D) Left ventricular ejection fraction (LVEF): <27.8% vs.  $\geq 27.8\%$ ; based on the optimal cutoff determined by the Youden index