

SUPPLEMENTAL MATERIAL

Table S1. List of participating centers.

	Affiliation
Trieste, Italy	Center for Diagnosis and Treatment of Cardiomyopathies, Cardiovascular Department, Azienda Sanitaria Universitaria Giuliano-Isontina (ASUGI), University of Trieste, Trieste, Italy
Florence, Italy	Cardiomyopathy Unit, Careggi University Hospital, University of Florence, Florence, Italy
Rome, Italy	Division of Cardiology, Department of Clinical and Molecular Medicine, Sapienza University of Rome, Rome, Italy
Rome, Italy	Department of Clinical, Internal, Anesthesiologist and Cardiovascular Sciences, La Sapienza University, Rome, Italy
Rome, Italy	Department of Cardiovascular Sciences, Fondazione Policlinico Universitario A. Gemelli IRCCS
Bologna, Italy	Cardiology Unit, St. Orsola Hospital, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy
Padova, Italy	Department of Cardiac, Thoracic and Vascular Sciences and Public Health, University of Padova, Padova, Italy
Genoa, Italy	Department of Internal Medicine, University of Genoa, Genoa, Italy
Messina, Italy	Department of Cardiology, University of Messina, Messina, Italy

Table S2. Median (IQR 25-75) values of the ECG/echo indexes according to each etiology.

ECG/echo index	CA (N 416)	HCM (N 594)	AFD (N 171)	Overall p value	CA vs HCM p value	CA vs AFD p value	HCM vs AFD p value
Sokolow/CSA	0.90 (0.57-1.25)	1.84 (1.35-2.47)	1.88 (1.14-2.67)	<0.001	<0.001	<0.001	0.708
Sokolow/LVMI	0.09 (0.05-0.13)	0.19 (0.14-0.27)	0.20 (0.13-0.28)	<0.001	<0.001	<0.001	0.653
Sokolow/Max LVWT	0.88 (0.56-1.25)	1.48 (1.07-2.00)	1.74 (1.19-2.38)	<0.001	<0.001	<0.001	0.002
Rahman index	31 (7.5%)	8 (1.3%)	4 (2.3%)	<0.001*	<0.001*	<0.001*	0.317*
Total QRS/LVMI	0.63 (0.50-0.81)	1.28 (0.98-1.66)	1.32 (1.02-1.69)	<0.001	<0.001	<0.001	0.504
Total QRS/Max LVWT	6.21 (5.06-7.73)	9.81 (7.57-12.30)	11.47 (9.13-14.38)	<0.001	<0.001	<0.001	<0.001

*Fisher's exact test

Legend. AFD: Anderson Fabry Disease; CA: Cardiac Amyloidosis; CSA: cross-sectional area of the LV wall; HCM: Hypertrophic Cardiomyopathy; IQR=Interquartile Range LVMI: left ventricular mass index; max LVWT: maximum left ventricular wall thickness

Table S3. Baseline characteristics of ATTR and AL population.

	ATTR (n=309)	AL (n=107)	P value
Age (years)	79 (73-83)	67 (59-76)	<0.001
Sex, female (n, %)	28 (9%)	36 (34%)	<0.001
BMI (kg/m ²)	25 (23-28)	24 (22-26)	0.001
History of AF (n, %)	155 (50%)	36 (34%)	<0.001
CKD (n, %)	118 (50%)	57 (72%)	<0.001
IVS (mm)	18 (16-20)	16 (14-18)	<0.001
PW (mm)	16 (14-18)	13 (13-16)	<0.001
LVEDD (mm)	45 (41-49)	44 (40-48)	0.054
LVMI (g/m ²)	173 (145-216)	147 (120-171)	<0.001
SR (n, %)	208 (67%)	89 (83%)	0.002
HR (bpm)	72 (64-79)	78 (69-90)	<0.001
AVB 1st degree (n, %)	95 (30%)	20 (18%)	0.014
Ventricular pacing (n, %)	22 (7%)	3 (2%)	0.106
BBB (n, %)			
Left	46 (15%)	5 (4%)	0.003
Right	56 (18%)	13 (11%)	
Pseudonecrosis (n, %)			
Anterior	72 (24%)	44 (41%)	0.016
Inferior	22 (7%)	4 (4%)	
Sokolow index (mm)	16 (11-22)	14 (8-18)	0.006
Low QRS voltages (n, %)	91 (29%)	60 (56%)	<0.001
Total QRS score (mV)	11 (9-14)	10 (8-13)	0.005

Legend. AF: atrial fibrillation; AL; Amyloid Light Chain; ATTR: Transthyretin; AVB: atrioventricular block; BBB: bundle branch block; BMI: body mass index; CKD: chronic kidney disease; HR: heart rate; IVS: interventricular septum; LV: Left ventricle; LVEDD: LV end diastolic diameter; LVMI: LV mass index; PW: posterior wall; RV: right ventricle; SR: sinus rhythm. Continuous variables are reported as median (interquartile range).

Table S4. New cut-offs to discriminate CA vs HCM and AFD.

Low Voltages+ MaxLVWT $\geq 1,7$ cm			Total QRS/Max LVWT < 8,3		
Statistic	Value	95% CI	Statistic	Value	95% CI
<i>Sensitivity</i>	19.07%	15.55% to 23.00%	<i>Sensitivity</i>	78.27%	74.17% to 81.99%
<i>Specificity</i>	98.68%	97.14% to 99.51%	<i>Specificity</i>	77.70%	73.59% to 81.46%
<i>PLR</i>	14.40	6.36 to 32.60	<i>PLR</i>	3.51	2.94 to 4.20
<i>NLR</i>	0.82	0.78 to 0.86	<i>NLR</i>	0.28	0.23 to 0.34
<i>PPV</i>	93.48%	86.36% to 97.01%	<i>PPV</i>	77.75%	74.51% to 80.69%
<i>NPV</i>	55.05%	53.91% to 56.19%	<i>NPV</i>	78.22%	74.96% to 81.16%
<i>Accuracy</i>	58.96%	55.67% to 62.19%	<i>Accuracy</i>	77.99%	75.14% to 80.65%

Legend. LVWT = Left Ventricular Wall Thickness; NLR=Negative Likelihood Ratio; NPV=Negative Predictive Value; PLR=Positive Likelihood Ratio; PPV=Positive Predictive Value.

Table S5. Baseline characteristics of CA vs HCM+AFD population.

	CA (n=416)	HCM+AFD (N=765)	P value
Age (years)	77 (69-82)	58 (47-67)	<0.001
Sex, female (n, %)	64 (15%)	296 (39%)	<0.001
BMI (kg/m ²)	24.7 (22.6-27.4)	25.7 (23.4-28.7)	<0.001
History of AF (n, %)	191 (46%)	161 (21%)	<0.001
CKD (n, %)	175 (55%)	57 (7%)	<0.001
Echocardiographic data			
IVS (mm)	17 (15-19)	17 (15-20)	0.41
PW (mm)	15 (13-17)	11 (10-13)	<0.001
LVEDD (mm)	45 (41-49)	45 (41-48)	0.61
LVMI (g/m ²)	165 (139-204)	140 (116.6-174.5)	<0.001
Electrocardiographic data			
SR (n, %)	297 (71%)	690 (90%)	<0.001
HR (bpm)	73 (65-81)	64 (56-72)	<0.001
AVB 1st degree (n, %)	116 (28%)	80 (10%)	<0.001
Ventricular pacing (n, %)	25 (6%)	14 (2%)	<0.001
BBB (n, %)			
Left	51 (12%)	95 (12%)	<0.001
Right	69 (17%)	52 (7%)	
Pseudonecrosis (n, %)			<0.001
Anterior	116 (29%)	67 (9%)	
Inferior	26 (7%)	31 (4%)	

Sokolow index (mm)	15 (9-21)	28 (20-37)	<0.001
Low QRS voltages (n, %)	151 (36%)	25 (3%)	<0.001
Total QRS score (mV)	10.8 (8.7-13.5)	18.3 (14.7-23.2)	<0.001

Continuous variables are reported as median (interquartile range).

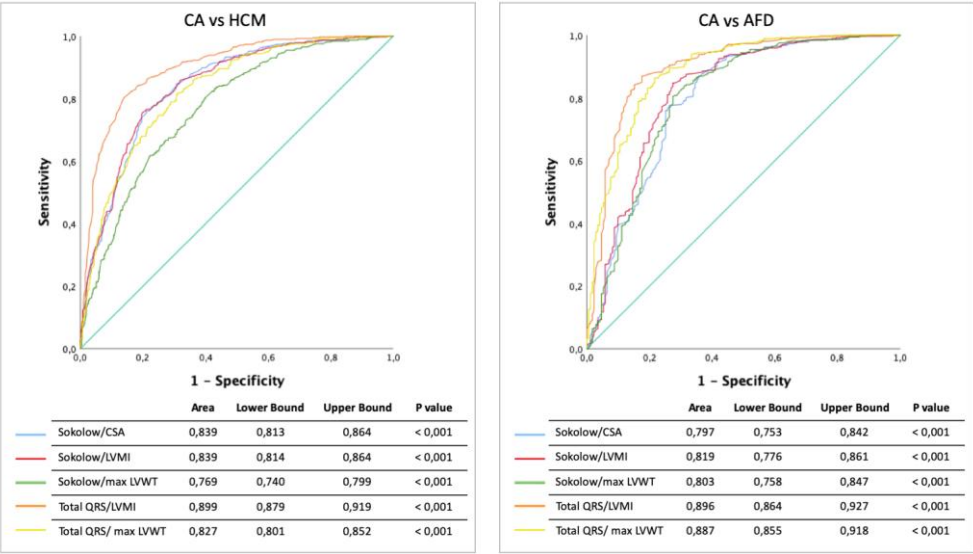
Legend. AF: atrial fibrillation; AFD: Anderson-Fabry Disease; AVB: atrioventricular block; BBB: bundle branch block; BMI: body mass index; CA: Cardiac Amyloidosis; CKD: chronic kidney disease; HCM: Hypertrophic Cardiomyopathy; HR: heart rate; IVS: interventricular septum; LVEDD: LV end diastolic diameter; LVMI: LV mass index; PW: posterior wall; SR: sinus rhythm.

Table S6. Pairwise AUC comparison among different criteria using DeLong test (referring to Figure 2, left panel).

Comparison among criteria	DeLong p-value
Sokolow/CSA vs Sokolow/LVMI	0.57
Sokolow/CSA vs Sokolow/Max LVWT	0.001
Sokolow/CSA vs Total QRS/LVMI	0.063
Sokolow/CSA vs Total QRS/Max LVWT	0.396
Sokolow/LVMI vs Sokolow/Max LVWT	0.014
Sokolow/LVMI vs Total QRS/LVMI	0.019
Sokolow/LVMI vs Total QRS/Max LVWT	0.246
Sokolow/Max LVWT vs Total QRS/LVMI	<0.0001
Sokolow/Max LVWT vs Total QRS/Max LVWT	0.001
Total QRS/LVMI vs Total QRS/Max LVWT	0.135

Legend. CSA: cross-sectional area of the LV wall. LVMI: left ventricular mass index; max LVWT: maximum left ventricular wall thickness.

Figure S1. ROC curve with AUC for each index to differentiate CA vs HCM and CA vs AFD, in the overall population



Legend. CA=Cardiac Amyloidosis; CSA: cross-sectional area of the LV wall HCM=Hypertrophic Cardiomyopathy; LVMI: left ventricular mass index; max LVWT: maximum left ventricular wall thickness