

**Impact of the Non-Invasive Diagnostic Algorithm on Clinical Presentation and Prognosis in
Cardiac Amyloidosis**

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Supplementary Material

Supplementary Table 1. Characteristics of study population at time of diagnosis

	Overall cohort n=887 (%)	AL n=311 (%)	ATTRm n=87 (%)	ATTRwt n=489 (%)
Gender				
<i>Males</i>	692 (78)	178 (57)	67 (77)	447 (91)
<i>Females</i>	195 (22)	133 (43)	20 (23)	42 (9)
Age at diagnosis (mean±SD)	73 ± 10	66 ± 11	69 ± 12	78 ± 6
Arterial hypertension	507 (57)	126 (41)	43 (49)	338 (69)
Diabetes mellitus	127 (14)	34 (11)	9 (10)	84 (17)
CKD	270 (30)	96 (31)	13 (15)	161 (33)
History of CAD	133 (15)	34 (11)	12 (14)	87 (18)
History of HF prior to diagnosis	555 (63)	221 (71)	33 (38)	301 (72)
History of AF prior to diagnosis	370 (42)	78 (25)	25 (29)	267 (55)
History of PMK prior to diagnosis	106 (12)	18 (6)	11 (13)	77 (16)
History of ICD prior to diagnosis	22 (3)	7 (2)	1 (1)	14 (3)
Low voltages	285 (35)	149 (53)	23 (28)	113 (26)
LBBB	61 (8)	10 (4)	6 (7)	45 (10)
NYHA at diagnosis				
<i>I-II</i>	602 (68)	166 (53)	72 (82)	364 (74)
<i>III-IV</i>	285 (32)	145 (47)	15 (17)	125 (26)
IVS (mm)	17 ± 3	15 ± 3	16 ± 3	17 ± 3
LA diameter (mm)	46 ± 7	44 ± 7	43 ± 6	47 ± 7
LVEF (%)	55 ± 10	55 ± 11	55 ± 11	54 ± 10
TAPSE (mm)	18 ± 5	18 ± 5	18 ± 5	18 ± 5
Restrictive filling pattern	265 (30)	112 (36)	18 (21)	135 (28)
Moderate-to-severe mitral regurgitation	194 (23)	65 (23)	18 (21)	111 (23)
Diagnoses by year				
<i>Before 2016</i>	199 (22)	145 (47)	15 (17)	39 (8)
<i>After 2016</i>	688 (78)	166 (53)	72 (83)	450 (92)
NAC score	-			
<i>I</i>		-	29 (69)	136 (52)
<i>II</i>			11 (26)	98 (38)
<i>III</i>			2 (5)	27 (10)
Mayo score	-			
<i>I</i>		58 (29)	-	-
<i>II</i>		66 (33)		
<i>III</i>		78 (38)		

Supplementary Table 2. TTR mutations in the ATTRv group

	n=87 (%)
Ile68Leu	39 (45)
Val122Ile	15 (17)
Val30Met	11 (13)
Phe64Leu	7 (8)
Glu89Gln	6 (7)
Tyr78Phe	2 (2)
Ala109Ser	1 (1)
Ala120Ser	1 (1)
Ala36Pro	1 (1)
Arg34Thr	1 (1)
Glu74Gln	1 (1)
Gly67Glu	1 (1)
Gly67Arg	1 (1)

Supplementary Table 3. Characteristics of patients grouped by Centre

	Bologna n=148 (%)	Firenze n=402 (%)	Genova n=45 (%)	Roma n=139 (%)	Trieste n=153 (%)
Gender					
<i>Males</i>	121 (82)	320 (80)	35 (78)	107 (77)	109 (71)
<i>Females</i>	27 (8)	82 (20)	10 (22)	32 (23)	44 (29)
Age at diagnosis (mean±SD)	74 ± 11	75 ± 10	72 ± 10	70 ± 11	71 ± 11
Arterial hypertension	111 (75)	204 (51)	22 (49)	65 (47)	105 (69)
Diabetes mellitus	19 (13)	62 (15)	5 (11)	13 (9)	28 (20)
CKD	50 (34)	131 (33)	9 (20)	15 (11)	65 (47)
History of CAD	28 (19)	60 (15)	4 (9)	17 (12)	24 (16)
History of HF prior to diagnosis	98 (66)	228 (57)	26 (58)	73 (53)	130 (85)
History of AF prior to diagnosis	70 (47)	164 (41)	11 (24)	49 (35)	76 (50)
History of PMK prior to diagnosis	24 (16)	54 (13)	1 (2)	12 (9)	15 (10)
History of ICD prior to diagnosis	3 (2)	11 (3)	0	5 (4)	3 (2)
Low voltages	32 (25)	124 (35)	17 (39)	61 (45)	51 (35)
LBBB	12 (10)	26 (8)	2 (5)	7 (5)	14 (10)
NYHA at diagnosis					
<i>I-II</i>	122 (82)	296 (74)	39 (87)	55 (40)	90 (59)
<i>III-IV</i>	26 (18)	106 (26)	6 (13)	84 (60)	63 (41)
IVS (mm)	17 ± 3	16 ± 3	16 ± 4	16 ± 3	17 ± 4
LA diameter (mm)	47 ± 6	45 ± 7	45 ± 5	46 ± 6	46 ± 9
LVEF (%)	57 ± 11	56 ± 9	51 ± 8	51 ± 9	54 ± 13
TAPSE (mm)	15 ± 3	19 ± 5	18 ± 5	17 ± 5	18 ± 7

Restrictive filling pattern	57 (59)	242 (64)	27 (64)	109 (80)	83 (65)
Moderate-to-severe mitral regurgitation	38 (27)	73 (19)	16 (36)	35 (26)	32 (22)
CA subtype					
<i>AL</i>	29 (19)	119 (30)	17 (38)	68 (49)	78 (51)
<i>ATTRv</i>	20 (14)	37 (9)	8 (18)	20 (14)	2 (1)
<i>ATTRwt</i>	99 (67)	246 (61)	20 (44)	51 (37)	73 (48)
Diagnoses by year					
<i>Before 2016</i>	16 (13)	66 (16)	0	50 (36)	64 (42)
<i>After 2016</i>	129 (87)	336 (84)	45 (100)	89 (64)	89 (58)
Follow-up time (<i>months; median [IQR]</i>)	18 [8-37]	21 [10-36]	22 [10-40]	15 [6-38]	12 [5-31]

Supplementary figure captions.

Supplementary Figure 1. Prevalence of events before and after 2016 in the overall cohort and for each CA subtype (composite outcome, *upper panel*; all-cause mortality, *lower left panel*; HF hospitalizations, *lower right panel*). Among CA patients diagnosed before 2016, 164 (82%) died – of whom 128 AL (88%), 10 ATTRv (67%), 26 ATTRwt (67%) – and 64 (46%) had an HF hospitalization – of whom 45 AL (46%), 5 ATTRv (36%), 26 ATTRwt (67%). Among those diagnosed after 2016, 235 (34%) died – of whom 90 AL (54%), 17 ATTRv (24%), 128 ATTRwt (28%) – and 131 (21%) had an HF hospitalization – of whom 30 AL (22%), 13 ATTRv (19%), 88 ATTRwt (20%).

Supplementary Figure 2. Kaplan Meier curves for all-cause mortality before (*panel A*) and after (*panel B*) PSW, and cumulative incidence (CI) for HF hospitalization before (*panel C*) and after (*panel D*) PSW, adjusted for competing risk of mortality.

Supplementary Figure 3. Forest plot showing hazard rates for the composite outcome after PSW at multivariate Cox regression analysis.

Figure 1.

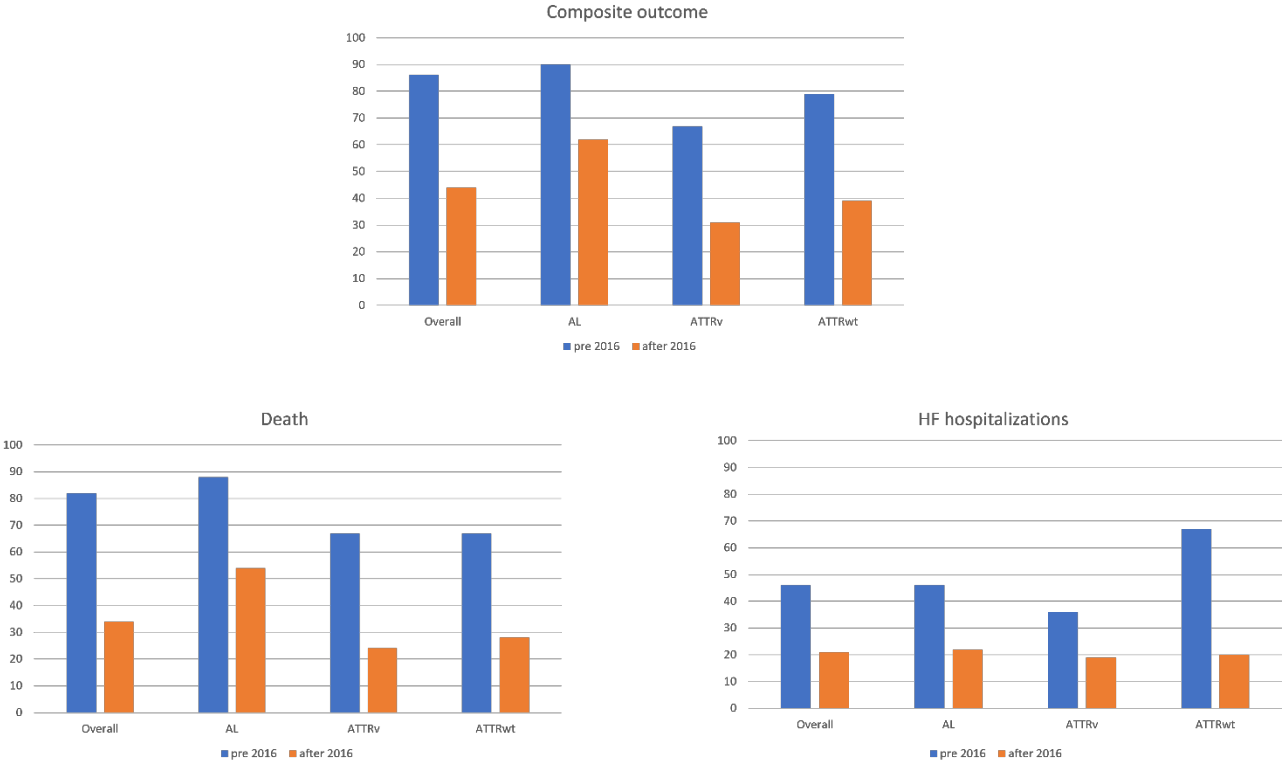
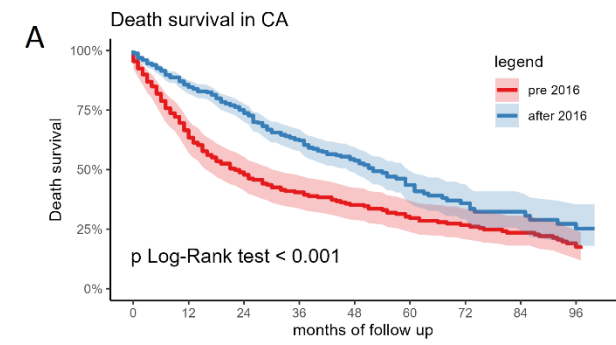
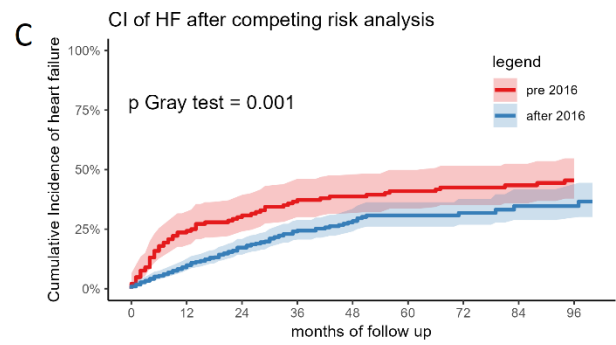
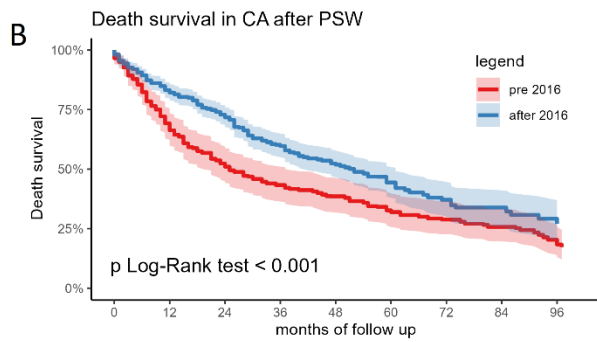


Figure 2.



pre 2016	199	129	93	77	66	53	43	35	25
after 2016	688	477	289	169	93	49	31	19	14



pre 2016	145	85	65	54	48	42	34	27	19
after 2016	637	444	260	148	82	44	29	16	12

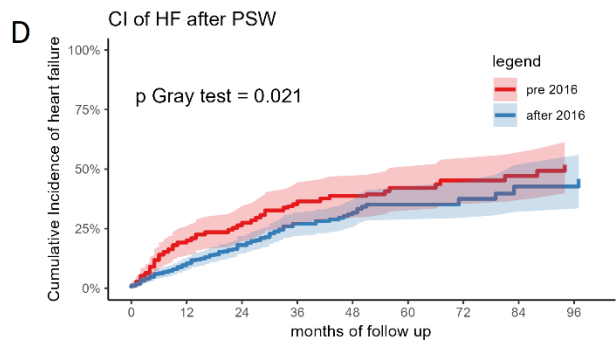


Figure 3.

