Early rhythm control therapy in patients with atrial fibrillation and heart failure.

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SUPPLEMENTAL MATERIAL

Early rhythm control in patients with heart failure

Supplemental Tables

Supplemental Table I. Characteristics of EAST-AFNET4 heart failure patients as defined per left ventricular ejection fraction subgroup

	Early rhythm control. reduced (N=57)	Usual care. reduced (N=75)	Early rhythm control. mid-range (N=110)	Usual care. mid-range (N=101)	Early rhythm control. preserved (N=224)	Usual care. preserved (N=218)	Total (N=785)
Sex							
Male	43 (75.4%)	61 (81.3%)	82 (74.5%)	77 (76.2%)	111 (49.6%)	115 (52.8%)	489 (62.3%)
Female	14 (24.6%)	14 (18.7%)	28 (25.5%)	24 (23.8%)	113 (50.4%)	103 (47.2%)	296 (37.7%)
Age							
means and standard deviation	68.5 (10.1)	70.1 (8.8)	69.3 (9.2)	71.5 (7.8)	69.9 (9.0)	70.0 (9.6)	70.0 (9.1)
Median (Q1, Q3)	70.0 (62.0, 77.0)	71.0 (64.5, 77.0)	70.5 (64.0, 75.8)	73.0 (67.0, 77.0)	71.0 (64.0, 76.2)	71.0 (64.0, 76.0)	71.0 (65.0, 76.0)
range	42.0 - 89.0	41.0 - 85.0	42.0 - 87.0	51.0 - 89.0	39.0 - 90.0	34.0 - 91.0	34.0 - 91.0
Body Mass Index (calculated) [kg/m²]							
missing variables	0	0	0	0	1	1	2
means and standard deviation	29.9 (6.9)	28.8 (5.0)	29.6 (5.8)	29.8 (5.7)	30.0 (6.1)	30.6 (5.6)	30.0 (5.8)
Median (Q1, Q3)	27.9 (25.4, 32.7)	28.1 (25.6, 31.2)	28.7 (25.9, 32.3)	29.2 (26.1, 32.2)	29.5 (26.3, 32.8)	29.8 (26.8, 34.2)	29.4 (26.2, 33.1)
range	18.6 - 58.2	18.4 - 40.9	19.0 - 52.2	18.8 - 53.3	16.6 - 52.6	18.1 - 48.4	16.6 - 58.2
LVEF at baseline							
means and standard deviation	31.2 (5.5)	31.1 (5.5)	44.3 (2.9)	44.3 (2.8)	60.8 (6.3)	60.8 (6.2)	51.4 (12.7)
Median (Q1, Q3)	31.0 (30.0, 35.0)	31.0 (30.0, 35.0)	45.0 (42.0, 46.0)	45.0 (42.0, 46.0)	60.0 (55.0, 65.0)	60.0 (57.2, 65.0)	52.0 (43.0, 62.0)
range	13.0 - 39.0	18.0 - 39.0	40.0 - 49.1	40.0 - 49.0	50.0 - 82.0	50.0 - 85.0	13.0 - 85.0
Cardiomyopathy							
No	24 (42.1%)	46 (61.3%)	77 (70.0%)	82 (81.2%)	206 (92.0%)	201 (92.2%)	636 (81.0%)
Tachycardiomyopathy	9 (15.8%)	7 (9.3%)	10 (9.1%)	3 (3.0%)	6 (2.7%)	2 (0.9%)	37 (4.7%)
Hypertrophic cardiomyopathy	0 (0.0%)	1 (1.3%)	3 (2.7%)	1 (1.0%)	1 (0.4%)	1 (0.5%)	7 (0.9%)
Dilatative cardiomyopathy	11 (19.3%)	14 (18.7%)	11 (10.0%)	9 (8.9%)	2 (0.9%)	6 (2.8%)	53 (6.8%)
Other cardiomyopathy	10 (17.5%)	4 (5.3%)	4 (3.6%)	4 (4.0%)	8 (3.6%)	6 (2.8%)	36 (4.6%)
Unknown	3 (5.3%)	3 (4.0%)	5 (4.5%)	2 (2.0%)	1 (0.4%)	2 (0.9%)	16 (2.0%)
AF type							
First episode	21 (36.8%)	37 (49.3%)	45 (40.9%)	45 (44.6%)	69 (30.8%)	61 (28.0%)	278 (35.4%)
Paroxysmal	12 (21.1%)	10 (13.3%)	29 (26.4%)	23 (22.8%)	89 (39.7%)	88 (40.4%)	251 (32.0%)
Persistent or long-standing persistent	24 (42.1%)	28 (37.3%)	36 (32.7%)	33 (32.7%)	66 (29.5%)	69 (31.7%)	256 (32.6%)
Duration of AF history at baseline (days)							
means and standard deviation	68.4 (87.7)	90.7 (158.3)	78.2 (105.6)	84.4 (237.5)	72.0 (94.1)	72.8 (149.5)	76.2 (142.8)
Median (Q1, Q3)	34.0 (5.0, 108.0)	29.0 (3.5, 131.5)	24.0 (7.0, 113.2)	23.0 (5.0, 97.0)	34.0 (6.0, 102.5)	25.0 (6.0, 81.2)	28.0 (6.0, 102.0)
range	0.0 - 346.0	0.0 - 1148.0	0.0 - 404.0	0.0 - 2310.0	0.0 - 639.0	0.0 - 1737.0	0.0 - 2310.0
CHA2DS2-Vasc Score							
means and standard deviation	3.7 (1.3)	3.9 (1.3)	3.8 (1.3)	4.1 (1.6)	4.2 (1.5)	4.0 (1.4)	4.0 (1.4)
Median (Q1, Q3)	4.0 (3.0, 5.0)	4.0 (3.0, 5.0)	4.0 (3.0, 5.0)	4.0 (3.0, 5.0)	4.0 (3.0, 5.0)	4.0 (3.0, 5.0)	4.0 (3.0, 5.0)
range	2.0 - 7.0	1.0 - 8.0	1.0 - 7.0	2.0 - 9.0	2.0 - 8.0	2.0 - 9.0	1.0 - 9.0
Overall symptom score (EHRA)							

missing variables	3	3	6	1	26	18	57
EHRA I (asymptomatic)	20 (37.0%)	21 (29.2%)	31 (29.8%)	31 (31.0%)	29 (14.6%)	34 (17.0%)	166 (22.8%)
EHRA II	16 (29.6%)	41 (56.9%)	52 (50.0%)	50 (50.0%)	113 (57.1%)	118 (59.0%)	390 (53.6%)
EHRA III	17 (31.5%)	10 (13.9%)	21 (20.2%)	19 (19.0%)	55 (27.8%)	45 (22.5%)	167 (22.9%)
EHRA IV	1 (1.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	3 (1.5%)	5 (0.7%)
Systolic blood pressure [mmHg]							
missing variables	1	0	0	1	1	0	3
means and standard deviation	128.6 (20.8)	130.0 (18.4)	133.1 (21.4)	134.9 (18.0)	137.4 (18.1)	138.6 (19.4)	135.4 (19.4)
Median (Q1, Q3)	130.0 (113.8, 145.0)	130.0 (115.5, 145.0)	130.0 (120.0, 143.5)	135.0 (121.5, 144.2)	137.0 (126.5, 147.0)	136.5 (126.0, 150.0)	133.5 (120.0, 148.0)
range	90.0 - 180.0	90.0 - 176.0	85.0 - 199.0	92.0 - 200.0	100.0 - 185.0	97.0 - 198.0	85.0 - 200.0
Diastolic blood pressure [mmHg]							
missing variables	1	0	0	1	1	0	3
means and standard deviation	77.9 (15.9)	81.9 (13.0)	81.6 (14.0)	81.6 (12.2)	82.1 (12.4)	81.8 (12.4)	81.6 (12.9)
Median (Q1, Q3)	80.0 (63.8, 90.0)	80.0 (75.0, 90.0)	80.0 (70.0, 90.0)	81.0 (75.0, 90.0)	80.0 (73.0, 90.0)	80.0 (70.2, 90.0)	80.0 (71.0, 90.0)
range	45.0 - 113.0	53.0 - 109.0	50.0 - 120.0	50.0 - 110.0	51.0 - 115.0	55.0 - 120.0	45.0 - 120.0
Heart failure (NYHA classification)							
No heart failure	9 (15.8%)	16 (21.3%)	30 (27.3%)	38 (37.6%)	0 (0.0%)	0 (0.0%)	93 (11.8%)
I	9 (15.8%)	15 (20.0%)	25 (22.7%)	18 (17.8%)	0 (0.0%)	0 (0.0%)	67 (8.5%)
II	28 (49.1%)	31 (41.3%)	47 (42.7%)	40 (39.6%)	178 (79.5%)	183 (83.9%)	507 (64.6%)
III	11 (19.3%)	13 (17.3%)	8 (7.3%)	5 (5.0%)	46 (20.5%)	35 (16.1%)	118 (15.0%)
MOCA total score							
missing variables	5	4	7	3	3	7	29
means and standard deviation	25.9 (3.9)	25.2 (3.4)	24.6 (4.1)	24.9 (3.9)	25.3 (3.7)	25.4 (4.0)	25.2 (3.9)
Median (Q1, Q3)	26.0 (24.0, 29.0)	26.0 (23.0, 28.0)	26.0 (22.0, 28.0)	25.0 (23.0, 28.0)	26.0 (23.0, 28.0)	26.0 (24.0, 28.5)	26.0 (23.0, 28.0)
range	14.0 - 30.0	15.0 - 30.0	7.0 - 30.0	13.0 - 30.0	12.0 - 30.0	7.0 - 30.0	7.0 - 30.0
At least mild cognitive impairment (MoCA < 26)							
missing variables	5	4	7	3	3	7	29
No	35 (67.3%)	36 (50.7%)	53 (51.5%)	46 (46.9%)	115 (52.0%)	117 (55.5%)	402 (53.2%)
Yes	17 (32.7%)	35 (49.3%)	50 (48.5%)	52 (53.1%)	106 (48.0%)	94 (44.5%)	354 (46.8%)
Previous pharmacological or electrical cardioversion							
missing variables	4	0	3	1	2	0	10
No	31 (58.5%)	42 (56.0%)	63 (58.9%)	63 (63.0%)	119 (53.6%)	124 (56.9%)	442 (57.0%)
Yes	22 (41.5%)	33 (44.0%)	44 (41.1%)	37 (37.0%)	103 (46.4%)	94 (43.1%)	333 (43.0%)
Catheter ablation							
No Ablation	44 (77.2%)	63 (84.0%)	84 (76.4%)	91 (90.1%)	176 (78.6%)	189 (86.7%)	647 (82.4%)
Ablation	13 (22.8%)	12 (16.0%)	26 (23.6%)	10 (9.9%)	48 (21.4%)	29 (13.3%)	138 (17.6%)
Surgical treatment of AF							
No	57 (100.0%)	75 (100.0%)	110 (100.0%)	101 (100.0%)	224 (100.0%)	217 (99.5%)	784 (99.9%)
Yes	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	1 (0.1%)
Prior stroke or transient ischemic attack							
No	54 (94.7%)	63 (84.0%)	99 (90.0%)	85 (84.2%)	196 (87.5%)	200 (91.7%)	697 (88.8%)
Yes	3 (5.3%)	12 (16.0%)	11 (10.0%)	16 (15.8%)	28 (12.5%)	18 (8.3%)	88 (11.2%)
Arterial hypertension							
No	12 (21.1%)	17 (22.7%)	13 (11.8%)	21 (20.8%)	18 (8.0%)	18 (8.3%)	99 (12.6%)
Yes	45 (78.9%)	58 (77.3%)	97 (88.2%)	80 (79.2%)	206 (92.0%)	200 (91.7%)	686 (87.4%)
Severe coronary artery disease (previous myocardial infarction, CABG or PCI)							

No	41 (71.9%)	57 (76.0%)	84 (76.4%)	74 (73.3%)	179 (79.9%)	174 (79.8%)	609 (77.6%)
Yes	16 (28.1%)	18 (24.0%)	26 (23.6%)	27 (26.7%)	45 (20.1%)	44 (20.2%)	176 (22.4%)
Stable heart failure (NYHA stage II or LVEF < 50%)							
No	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Yes	57 (100.0%)	75 (100.0%)	110 (100.0%)	101 (100.0%)	224 (100.0%)	218 (100.0%)	785 (100.0%)
Left ventricular hypertrophy on echocardiography (> 15mm wall thickness)							
No	55 (96.5%)	71 (94.7%)	107 (97.3%)	95 (94.1%)	217 (96.9%)	214 (98.2%)	759 (96.7%)
Yes	2 (3.5%)	4 (5.3%)	3 (2.7%)	6 (5.9%)	7 (3.1%)	4 (1.8%)	26 (3.3%)
Chronic kidney disease (MDRD stage III or IV)							
No	49 (86.0%)	58 (77.3%)	97 (88.2%)	82 (81.2%)	183 (81.7%)	187 (85.8%)	656 (83.6%)
Yes	8 (14.0%)	17 (22.7%)	13 (11.8%)	19 (18.8%)	41 (18.3%)	31 (14.2%)	129 (16.4%)
Peripheral artery disease							
No	54 (94.7%)	72 (96.0%)	104 (94.5%)	96 (95.0%)	214 (95.5%)	210 (96.3%)	750 (95.5%)
Yes	3 (5.3%)	3 (4.0%)	6 (5.5%)	5 (5.0%)	10 (4.5%)	8 (3.7%)	35 (4.5%)
History of valve replacement							
No	57 (100.0%)	73 (97.3%)	110 (100.0%)	100 (99.0%)	220 (98.2%)	215 (98.6%)	775 (98.7%)
Yes	0 (0.0%)	2 (2.7%)	0 (0.0%)	1 (1.0%)	4 (1.8%)	3 (1.4%)	10 (1.3%)
Signs of valvular disease							
No	24 (42.1%)	32 (42.7%)	55 (50.0%)	40 (39.6%)	129 (57.6%)	102 (46.8%)	382 (48.7%)
Yes	33 (57.9%)	43 (57.3%)	55 (50.0%)	61 (60.4%)	95 (42.4%)	116 (53.2%)	403 (51.3%)
Heart rhythm							
Atrial fibrillation or atrial flutter	42 (73.7%)	59 (78.7%)	68 (61.8%)	63 (62.4%)	105 (46.9%)	109 (50.0%)	446 (56.8%)
Sinus rhythm and pacing	15 (26.3%)	16 (21.3%)	42 (38.2%)	38 (37.6%)	119 (53.1%)	109 (50.0%)	339 (43.2%)
Heart rate in sinus rhythm							
missing variables	43	61	69	64	105	111	453
means and standard deviation	61.8 (12.5)	73.4 (24.6)	63.9 (13.2)	68.8 (10.9)	66.6 (12.6)	65.6 (11.6)	66.3 (13.0)
Median (Q1, Q3)	61.5 (52.8, 70.2)	66.5 (59.8, 75.0)	63.0 (56.0, 71.0)	69.0 (60.0, 77.0)	65.0 (57.0, 75.0)	65.0 (59.0, 72.0)	65.0 (57.0, 74.0)
range	42.0 - 83.0	46.0 - 134.0	45.0 - 112.0	50.0 - 97.0	44.0 - 100.0	41.0 - 108.0	41.0 - 134.0
Diastolic LA diameter (maximal diameter) [mm]							
missing variables	6	7	15	14	51	60	153
means and standard deviation	49.2 (8.7)	49.5 (11.1)	44.2 (7.8)	45.2 (7.5)	45.0 (7.5)	44.8 (8.5)	45.7 (8.5)
Median (Q1, Q3)	48.0 (43.5, 54.5)	48.0 (41.0, 54.8)	44.0 (40.0, 49.0)	45.0 (40.0, 49.5)	44.0 (40.0, 48.0)	43.0 (40.0, 48.0)	44.0 (40.0, 50.0)
range	34.0 - 70.0	32.0 - 85.0	26.0 - 73.0	28.0 - 65.0	28.0 - 74.0	31.0 - 82.0	26.0 - 85.0
Hb value [g/l]							
missing variables	0	1	1	2	0	1	5
means and standard deviation	143.9 (15.6)	145.6 (14.1)	141.6 (16.2)	144.4 (15.5)	138.6 (15.1)	141.0 (14.6)	141.5 (15.2)
Median (Q1, Q3)	146.0 (136.0, 154.0)	147.5 (137.2, 155.5)	143.0 (133.0, 154.0)	147.0 (134.0, 154.6)	139.0 (128.9, 148.1)	141.0 (130.0, 152.0)	142.0 (131.0, 152.0)
range	109.0 - 180.0	112.0 - 175.0	82.0 - 184.0	100.0 - 177.0	93.0 - 174.0	97.0 - 174.0	82.0 - 184.0
GFR (MDRD formula)							
missing variables	0	1	2	1	2	2	8
means and standard deviation	73.5 (15.7)	69.8 (23.4)	77.1 (19.0)	75.5 (21.8)	73.7 (22.5)	74.0 (19.9)	74.1 (20.9)
Median (Q1, Q3)	75.7 (63.0, 83.4)	70.5 (54.5, 82.8)	76.2 (65.5, 88.2)	74.7 (63.1, 91.3)	71.6 (59.1, 87.4)	73.6 (60.8, 86.4)	73.7 (60.5, 87.1)
range	41.0 - 117.6	23.6 - 144.8	32.9 - 166.3	32.6 - 156.0	22.8 - 153.9	21.7 - 134.7	21.7 - 166.3
Chronic obstructive lung disease							
missing variables	0	0	0	0	1	3	4
No	53 (93.0%)	68 (90.7%)	99 (90.0%)	88 (87.1%)	198 (88.8%)	184 (85.6%)	690 (88.3%)
Yes	4 (7.0%)	7 (9.3%)	11 (10.0%)	13 (12.9%)	25 (11.2%)	31 (14.4%)	91 (11.7%)

Malignant diseases							
missing variables	2	0	0	0	0	0	2
No	51 (92.7%)	73 (97.3%)	102 (92.7%)	95 (94.1%)	209 (93.3%)	204 (93.6%)	734 (93.7%)
Yes, currently under therapy or with currently active disease manifestation	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	2 (0.9%)	3 (0.4%)
Yes, not under current therapy and without active disease manifestation	4 (7.3%)	2 (2.7%)	8 (7.3%)	5 (5.0%)	15 (6.7%)	12 (5.5%)	46 (5.9%)
Thyroid dysfunction (hypothyroidism or hyperthyroidism)							
No	51 (89.5%)	72 (96.0%)	100 (90.9%)	96 (95.0%)	200 (89.3%)	202 (92.7%)	721 (91.8%)
Yes	6 (10.5%)	3 (4.0%)	10 (9.1%)	5 (5.0%)	24 (10.7%)	16 (7.3%)	64 (8.2%)
Diabetes mellitus							
No	38 (66.7%)	53 (70.7%)	80 (72.7%)	71 (70.3%)	160 (71.4%)	169 (77.5%)	571 (72.7%)
Yes	19 (33.3%)	22 (29.3%)	30 (27.3%)	30 (29.7%)	64 (28.6%)	49 (22.5%)	214 (27.3%)
Heart rate [beats/minute]							
missing variables	42	59	67	61	103	107	439
means and standard deviation	62.3 (12.2)	72.3 (23.2)	65.8 (18.1)	67.5 (11.7)	66.7 (12.8)	66.0 (11.9)	66.5 (13.7)
Median (Q1, Q3)	63.0 (53.5, 70.5)	66.5 (59.8, 75.0)	63.0 (56.0, 71.5)	67.5 (59.5, 77.0)	65.0 (57.0, 75.0)	65.0 (59.0, 72.0)	65.0 (57.0, 74.0)
range	42.0 - 83.0	46.0 - 134.0	45.0 - 147.0	42.0 - 97.0	44.0 - 100.0	41.0 - 108.0	41.0 - 147.0
Digoxin or Digitoxin at discharge							
No	55 (96.5%)	65 (86.7%)	102 (92.7%)	87 (86.1%)	212 (94.6%)	204 (93.6%)	725 (92.4%)
Yes	2 (3.5%)	10 (13.3%)	8 (7.3%)	14 (13.9%)	12 (5.4%)	14 (6.4%)	60 (7.6%)
Beta Blockers at discharge							
No	6 (10.5%)	7 (9.3%)	22 (20.0%)	9 (8.9%)	33 (14.7%)	26 (11.9%)	103 (13.1%)
Yes	51 (89.5%)	68 (90.7%)	88 (80.0%)	92 (91.1%)	191 (85.3%)	192 (88.1%)	682 (86.9%)
Ca channel antagonists at discharge							
No	43 (75.4%)	60 (80.0%)	74 (67.3%)	77 (76.2%)	153 (68.3%)	141 (64.7%)	548 (69.8%)
Yes	14 (24.6%)	15 (20.0%)	36 (32.7%)	24 (23.8%)	71 (31.7%)	77 (35.3%)	237 (30.2%)
ACE inhibitors or Angiotensin II receptor blocker at discharge							
No	9 (15.8%)	11 (14.7%)	27 (24.5%)	29 (28.7%)	63 (28.1%)	53 (24.3%)	192 (24.5%)
Yes	48 (84.2%)	64 (85.3%)	83 (75.5%)	72 (71.3%)	161 (71.9%)	165 (75.7%)	593 (75.5%)
Oral anticoagulation (NOAC & VKA) at discharge							
No	2 (3.5%)	5 (6.7%)	9 (8.2%)	8 (7.9%)	18 (8.0%)	30 (13.8%)	72 (9.2%)
Yes	55 (96.5%)	70 (93.3%)	101 (91.8%)	93 (92.1%)	206 (92.0%)	188 (86.2%)	713 (90.8%)
Mineralocorticoid receptor antagonist at discharge							
No	36 (63.2%)	55 (73.3%)	96 (87.3%)	92 (91.1%)	205 (91.5%)	202 (92.7%)	686 (87.4%)
Yes	21 (36.8%)	20 (26.7%)	14 (12.7%)	9 (8.9%)	19 (8.5%)	16 (7.3%)	99 (12.6%)
Insulin at discharge							
No	52 (91.2%)	68 (90.7%)	106 (96.4%)	95 (94.1%)	213 (95.1%)	208 (95.4%)	742 (94.5%)
Yes	5 (8.8%)	7 (9.3%)	4 (3.6%)	6 (5.9%)	11 (4.9%)	10 (4.6%)	43 (5.5%)
Oral antidiabetics at discharge							
No	47 (82.5%)	59 (78.7%)	92 (83.6%)	81 (80.2%)	185 (82.6%)	191 (87.6%)	655 (83.4%)
Yes	10 (17.5%)	16 (21.3%)	18 (16.4%)	20 (19.8%)	39 (17.4%)	27 (12.4%)	130 (16.6%)
Diuretics at discharge							
No	20 (35.1%)	31 (41.3%)	56 (50.9%)	55 (54.5%)	120 (53.6%)	107 (49.1%)	389 (49.6%)
Yes	37 (64.9%)	44 (58.7%)	54 (49.1%)	46 (45.5%)	104 (46.4%)	111 (50.9%)	396 (50.4%)
Antianginal drugs at discharge							
No	56 (98.2%)	75 (100.0%)	109 (99.1%)	98 (97.0%)	221 (98.7%)	217 (99.5%)	776 (98.9%)
Yes	1 (1.8%)	0 (0.0%)	1 (0.9%)	3 (3.0%)	3 (1.3%)	1 (0.5%)	9 (1.1%)

Statin at discharge							
No	34 (59.6%)	39 (52.0%)	55 (50.0%)	59 (58.4%)	112 (50.0%)	126 (57.8%)	425 (54.1%)
Yes	23 (40.4%)	36 (48.0%)	55 (50.0%)	42 (41.6%)	112 (50.0%)	92 (42.2%)	360 (45.9%)
Inhibitor of platelet aggregation at discharge							
No	42 (73.7%)	62 (82.7%)	87 (79.1%)	76 (75.2%)	190 (84.8%)	189 (86.7%)	646 (82.3%)
Yes	15 (26.3%)	13 (17.3%)	23 (20.9%)	25 (24.8%)	34 (15.2%)	29 (13.3%)	139 (17.7%)

LVEF Left ventricular ejection fraction; AF atrial fibrillation; LA left atrium; CABG Coronary artery bypass graft; PCI Percutaneous coronary intervention; CHA2DS2-Vasc score conducted with Congestive Heart failure; EHRA score European Heart Rhythm Association score for assessment of atrial fibrillation symptoms; NYHA class New York Heart Association classification of symptoms in heart failure patients. EQ-5D score European Quality of Life 5 Dimensions score; SF-12 Short Form Health survey 12-items; MoCA score Montreal Cognitive Assessment Score. NOAC Novel oral anticoagulants; VKA Vitamin K antagonists. MDRD Modification of Diet in Renal Disease.

EAST-AFNET4 indicates Early Treatment for Atrial Fibrillation for Stroke Prevention Trial.

Supplemental Table II. EAST-AFNET4 heart failure patients with and without ischemic cardiomyopathy (ICM) by randomized groups. There was no interaction between etiology of heart failure and the randomized intervention.

Outcome	Subgroup	Early rhythm control	Usual care	Treatment effect	p-value	p-value interaction (between treatment and ischemic cardiomyopathy indicator)
First primary outcome	ICM No	62/319 (19.4)	86/322 (26.7)	0.73 (0.52 to 1.02)	0.06	0.89
	ICM Yes	32/1330 (2.4)	44/1328 (3.3)	0.76 (0.48 to 1.21)	0.24	
Second primary outcome - nights spent in hospital/yr	ICM No	8.26±30.71	7.37±25.82	1.28 (0.98 to 1.68)	0.08	0.99
	ICM Yes	8.71±14.13	7.78±15.73	1.27 (0.77 to 2.09)	0.35	
Change in left ventricular ejection fraction	ICM No	6.06±12.07	4.79±11.53	1.08 (-0.50 to 2.66)	0.18	0.43
	ICM Yes	3.75±9.76	2.91±11.36	-0.33 (-3.42 to 2.77)	0.84	

EAST-AFNET4 indicates Early Treatment for Atrial Fibrillation for Stroke Prevention Trial.

Supplemental Table III. Outcomes of EAST-AFNET4 heart failure patients according to a "CABANA-like" composite endpoint including death, disabling stroke, serious bleeding, or cardiac arrest by randomized groups.

	Early rhythm control	Usual care	Treatment effect	p-value	Interaction p-value between treatment group and HF
CABANA events/person-yr (incidence/100 person-yr)	51/1831 (2.8)	71/1894 (3.7)	0.74 (0.51 to 1.06)	0.10	0.32

EAST-AFNET4 indicates Early Treatment for Atrial Fibrillation for Stroke Prevention Trial. CABANA indicates Catheter Ablation Versus Antiarrhythmic Drug Therapy for Atrial Fibrillation.

Supplemental Table IV. Background therapy of EAST-AFNET4 heart failure patients by randomized groups at discharge from baseline visit: initial rhythm control therapy

	Early rhythm control (N=396)	Usual care (N=402)	Total (N=798)
Initial rhythm control			
None	27 (6.8%)	379 (94.3%)	406 (50.9%)
Other antiarrhythmic drug	21 (5.3%)	1 (0.2%)	22 (2.8%)
Propafenone	21 (5.3%)	0 (0.0%)	21 (2.6%)
Flecainide	133 (33.6%)	6 (1.5%)	139 (17.4%)
Amiodarone	123 (31.1%)	15 (3.7%)	138 (17.3%)
Dronedarone	40 (10.1%)	1 (0.2%)	41 (5.1%)
AF ablation	31 (7.8%)	0 (0.0%)	31 (3.9%)

AF Atrial fibrillation.

Supplemental Table V. Clinical characteristics of EAST-AFNET4 heart failure patients with and without catheter ablation.

	Ablation (N=140)	No Ablation (N=658)	Total (N=798)
Randomgroup			
Usual care	52 (37.1%)	350 (53.2%)	402 (50.4%)
Early rhythm control	88 (62.9%)	308 (46.8%)	396 (49.6%)
LVEF at baseline categories			
missing variables	2	11	13
reduced	25 (18.1%)	107 (16.5%)	132 (16.8%)
mid-range	36(26.1%)	175 (27.0%)	211 (26.9%)
preserved	77 (55.8%)	365 (56.4%)	442 (56.3%)
Gender			
Male	84 (60.0%)	414 (62.9%)	498 (62.4%)
Female	56 (40.0%)	244 (37.1%)	300 (37.6%)
Age			
means and standard deviation	66.5 (7.9)	70.7 (9.3)	69.9 (9.2)
Median (Q1, Q3)	68.0 (61.0, 72.2)	72.0 (65.0, 77.0)	71.0 (64.0, 76.0)
range	49.0 - 81.0	34.0 - 91.0	34.0 - 91.0
Body Mass Index (calculated) [kg/m²]			
missing variables	0	3	3
means and standard deviation	29.9 (5.3)	30.0 (6.0)	30.0 (5.9)
Median (Q1, Q3)	29.6 (26.1, 32.8)	29.3 (26.2, 33.3)	29.4 (26.2, 33.2)
range	19.9 - 46.6	16.6 - 58.2	16.6 - 58.2
LVEF at baseline			
missing variables	2	11	13
means and standard deviation	50.7 (13.0)	51.5 (12.7)	51.4 (12.7)
Median (Q1, Q3)	50.0 (41.5, 60.0)	53.0 (43.0, 62.0)	52.0 (43.0, 62.0)
range	20.0 - 79.0	13.0 - 85.0	13.0 - 85.0
Cardiomyopathy			
missing variables	0	2	2
No	110 (78.6%)	537 (81.9%)	647 (81.3%)
Tachycardiomyopathy	10 (7.1%)	27 (4.1%)	37 (4.6%)
Hypertrophic cardiomyopathy	1 (0.7%)	6 (0.9%)	7 (0.9%)
Dilatative cardiomyopathy	9 (6.4%)	44 (6.7%)	53 (6.7%)
Other cardiomyopathy	7 (5.0%)	29 (4.4%)	36 (4.5%)
Unknown	3 (2.1%)	13 (2.0%)	16 (2.0%)
Atrial fibrillation type			
missing variables	0	2	2
First episode	40 (28.6%)	242 (36.9%)	282 (35.4%)
Paroxysmal	27 (19.3%)	225 (34.3%)	252 (31.7%)
Persistent or long-standing persistent	73 (52.1%)	189 (28.8%)	262 (32.9%)
Duration of AF history at baseline (days)			
missing variables	0	1	1
means and standard deviation	99.4 (174.1)	71.6 (134.4)	76.5 (142.5)
Median (Q1, Q3)	36.0 (6.0, 139.5)	25.0 (5.0, 93.0)	27.0 (5.0, 102.0)
range	0.0 - 1737.0	0.0 - 2310.0	0.0 - 2310.0
CHA2DS2-Vasc Score			
means and standard deviation	3.7 (1.3)	4.1 (1.4)	4.0 (1.4)
Median (Q1, Q3)	3.0 (3.0, 5.0)	4.0 (3.0, 5.0)	4.0 (3.0, 5.0)

range	2.0 - 8.0	1.0 - 9.0	1.0 - 9.0
Overall symptom score (EHRA)			
missing variables	9	51	60
EHRA I (asymptomatic)	29 (22.1%)	140 (23.1%)	169 (22.9%)
EHRA II	62 (47.3%)	334 (55.0%)	396 (53.7%)
EHRA III	40 (30.5%)	128 (21.1%)	168 (22.8%)
EHRA IV	0 (0.0%)	5 (0.8%)	5 (0.7%)
Heart failure (NYHA classification)			
missing variables	0	2	2
No heart failure	17 (12.1%)	77 (11.7%)	94 (11.8%)
I	10 (7.1%)	58 (8.8%)	68 (8.5%)
II	91 (65.0%)	423 (64.5%)	514 (64.6%)
III	22 (15.7%)	98 (14.9%)	120 (15.1%)
Prior stroke or transient ischemic attack			
No	125 (89.3%)	584 (88.8%)	709 (88.8%)
Yes	15 (10.7%)	74 (11.2%)	89 (11.2%)
Arterial hypertension			
No	13 (9.3%)	89 (13.5%)	102 (12.8%)
Yes	127 (90.7%)	569 (86.5%)	696 (87.2%)
Severe coronary artery disease (previous myocardial infarction, CABG or PCI)			
No	112 (80.0%)	507 (77.1%)	619 (77.6%)
Yes	28 (20.0%)	151 (22.9%)	179 (22.4%)
Diastolic Left atrial diameter (maximal diameter) [mm]			
missing variables	25	138	163
means and standard deviation	46.9 (8.1)	45.4 (8.6)	45.7 (8.5)
Median (Q1, Q3)	46.0 (40.0, 51.5)	44.0 (40.0, 49.0)	44.0 (40.0, 50.0)
range	32.0 - 73.0	26.0 - 85.0	26.0 - 85.0
Diabetes			
missing variables	0	2	2
No diabetes or imp. glucose tolerance	104 (74.3%)	477 (72.7%)	581 (73.0%)
Yes (managed by diet, oral antidiabetics, and/or insulin or no therapy)	36 (25.7%)	179 (27.3%)	215 (27.0%)

LVEF Left ventricular ejection fraction. CABG Coronary artery bypass graft; PCI Percutaneous coronary intervention; CHA2DS2-Vasc score conducted with Congestive Heart failure; EHRA score European Heart Rhythm Association score for assessment of atrial fibrillation symptoms; NYHA class New York Heart Association classification of symptoms in heart failure patients. EAST-AFNET4 indicates Early Treatment for Atrial Fibrillation for Stroke Prevention Trial.

Supplement Table VI. Further safety outcomes of EAST-AFNET4 heart failure patients by randomized groups.

	Early rhythm control (N=396)	Usual care (N=402)	Total (N=798)
Safety outcome type			
1 - TIA	6 (0.6%)	5 (0.4%)	11 (0.5%)
2 - Ischemic stroke (including transient events with matching lesion on cerebral imaging)	7 (0.7%)	14 (1.2%)	21 (1.0%)
3 - Haemorrhagic stroke	1 (0.1%)	4 (0.4%)	5 (0.2%)
6 - STEMI, anterior	1 (0.1%)	1 (0.1%)	2 (0.1%)
7 - STEMI, posterior	3 (0.3%)	0 (0.0%)	3 (0.1%)
9 - NSTEMI	8 (0.8%)	15 (1.3%)	23 (1.0%)
10 - Unstable AP	5 (0.5%)	5 (0.4%)	10 (0.5%)
11 - Stable AP or atypical chest pain	21 (2.0%)	19 (1.7%)	40 (1.8%)
12 - Worsening of heart failure, decompensated	118 (11.1%)	153 (13.6%)	271 (12.4%)
13 - Worsening of heart failure, not decompensated	5 (0.5%)	9 (0.8%)	14 (0.6%)
14 - Torsade de Pointes tachycardia	1 (0.1%)	0 (0.0%)	1 (0.0%)
15 - Ventricular tachycardia	3 (0.3%)	2 (0.2%)	5 (0.2%)
16 - Ventricular fibrillation	3 (0.3%)	2 (0.2%)	5 (0.2%)
17 - Drug-induced bradycardia	12 (1.1%)	9 (0.8%)	21 (1.0%)
18 - AV nodal block	1 (0.1%)	1 (0.1%)	2 (0.1%)
19 - Ablation-induced or drug-induced atrial flutter / atrial tachycardia	5 (0.5%)	0 (0.0%)	5 (0.2%)
20 - Syncope	11 (1.0%)	20 (1.8%)	31 (1.4%)
21 - Bleeding caused by catheter intervention or antithrombotic therapy	12 (1.1%)	24 (2.1%)	36 (1.6%)
23 - Pericardial tamponade	1 (0.1%)	1 (0.1%)	2 (0.1%)
25 - Drug toxicity of AF-related drug therapy	6 (0.6%)	2 (0.2%)	8 (0.4%)
26 - Non-fatal cardiac arrest	4 (0.4%)	2 (0.2%)	6 (0.3%)
28 - Any type of cardiovascular surgery	22 (2.1%)	18 (1.6%)	40 (1.8%)
29 - Implantation of a pacemaker, ICD, CRT or any other cardiac device	39 (3.7%)	40 (3.5%)	79 (3.6%)
30 - Percutaneous coronary (e.g. PCI), cerebrovascular or peripheral procedure	23 (2.2%)	40 (3.5%)	63 (2.9%)
31 - Blood pressure related (hypotension, hypertension; except syncope)	16 (1.5%)	23 (2.0%)	39 (1.8%)
32 - Cardiovascular infection (e.g. endocarditis, pericarditis, infectious myocarditis)	3 (0.3%)	2 (0.2%)	5 (0.2%)
33 - Major bleeding	32 (3.0%)	43 (3.8%)	75 (3.4%)
34 - Pulmonary embolism or deep vein thrombosis	7 (0.7%)	2 (0.2%)	9 (0.4%)
35 - Hospitalisation for AF	166 (15.6%)	144 (12.8%)	310 (14.1%)
36 - Other cardiovascular event	35 (3.3%)	39 (3.5%)	74 (3.4%)
37 - Other event	468 (44.0%)	456 (40.4%)	924 (42.1%)
38 - Death as primary event (sudden death)	19 (1.8%)	34 (3.0%)	53 (2.4%)

TIA transient ischemic attack; STEMI ST-elevation myocardial infarction; NSTEMI Non-ST-elevation myocardial infarction; AP angina pectoris; AV-nodal block Atrio-ventricular nodal block; AF atrial fibrillation; ICD implantable cardioverter and defibrillator; CRT cardiac resynchronization therapy; PCI percutaneous coronary intervention.

Supplemental Table VII. Change in left ventricular ejection fraction at 24 months in EAST-AFNET4 heart failure patients by randomized groups.

Outcome	Early rhythm control	Usual care	Effect	p-value
LVEF change from reduced to mid-range/preserved	24/384 (6.25)	26/378 (6.88)	0.84 (0.48 to 1.48)	0.55
LVEF change from reduced to preserved	24/378 (6.35)	29/366 (7.92)	0.73 (0.41 to 1.30)	0.29

LVEF Left ventricular ejection fraction

Supplemental Table VIII. Sensitivity analysis for first primary outcome by left ventricular function subgroup using only complete cases (n=785).

Outcome	Subgroup LVEF	Early rhythm control	Usual care	Treatment effect	p-value
First primary outcome events events/person-yr (incidence/100 person-yr)	reduced	21/229 (9.2)	35/258 (13.6)	0.64 (0.36 to 1.12)	0.12
	mid-range	23/476 (4.8)	28/419 (6.7)	0.77 (0.44 to 1.34)	0.35
	preserved	50/934 (5.4)	63/939 (6.7)	0.81 (0.56 to 1.18)	0.28

LVEF Left ventricular ejection fraction.

Supplemental Table IX. Change in EHRA score of EAST-AFNET4 heart failure patients by randomized groups.

	Early rhythm control - FU 24 months	Usual Care - FU 24 months
EHRA Improved	164/291 (56.4)	169/312 (54.2)
EHRA Unchanged	100/291 (34.4)	114/312 (36.5)
EHRA Worsened	27/291 (9.3)	29/312 (9.3)
p-value mixed ordered logistic regression		0.38

Supplemental Table X. Change in EHRA score of EAST-AFNET4 heart failure patients as per LVEF subgroup.

LVEF category	EHRA change 24 months	Early rhythm control	Usual care
reduced	Improved	19/43 (44.19)	29/52 (55.77)
	Unchanged	16/43 (37.21)	18/52 (34.62)
	Worsened	8/43 (18.60)	5/52 (9.62)
mid-range	Improved	52/90 (57.78)	47/80 (58.75)
	Unchanged	31/90 (34.44)	24/80 (30.00)
	Worsened	7/90 (7.78)	9/80 (11.25)
preserved	Improved	92/156 (58.97)	90/175 (51.43)
	Unchanged	53/156 (33.97)	71/175 (40.57)
	Worsened	11/156 (7.05)	14/175 (8.00)

LVEF Left ventricular ejection fraction. EHRA score European Heart Rhythm Association score for assessment of atrial fibrillation symptoms; EAST-AFNET4 indicates Early Treatment for Atrial Fibrillation for Stroke Prevention Trial.

Supplemental Table XI. Background therapy of EAST-AFNET4 heart failure patients by randomized groups at discharge from baseline visit: anticoagulation therapy.

		Early rhythm control (N=396)	Usual care (N=402)	Total (N=798)
Baseline				
	Neither of both	29 (7.4%)	43 (10.7%)	72 (9.0%)
	Combination of both	0 (0.0%)	2 (0.5%)	2 (0.3%)
	Vitamin K Antagonist	122 (31.0%)	126 (31.3%)	248 (31.2%)
	NOAC	243 (61.7%)	231 (57.5%)	474 (59.5%)
12 months				
	Neither of both	39 (11.4%)	37 (10.6%)	76 (11.0%)
	Combination of both	0 (0.0%)	1 (0.3%)	1 (0.1%)
	Vitamin K Antagonist	97 (28.4%)	109 (31.3%)	206 (29.9%)
	NOAC	206 (60.2%)	201 (57.8%)	407 (59.0%)
24 months				
	Neither of both	36 (11.1%)	38 (11.5%)	74 (11.3%)
	Combination of both	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Vitamin K Antagonist	90 (27.7%)	90 (27.2%)	180 (27.4%)
	NOAC	199 (61.2%)	203 (61.3%)	402 (61.3%)

NOAC Novel oral anticoagulants. EAST-AFNET4 indicates Early Treatment for Atrial Fibrillation for Stroke Prevention Trial.

Supplemental Table XII. Background therapy of EAST-AFNET4 heart failure patients by randomized groups at discharge from baseline visit: antihypertensive therapy and heart failure therapy.

		Early rhythm control (N=396)	Usual care (N=402)	Total (N=798)
Baseline				
	None	97 (24.6%)	91 (22.6%)	188 (23.6%)
	Combinations	56 (14.2%)	45 (11.2%)	101 (12.7%)
	Mineralocorticoid receptor antagonists (Spironolactone or Eplerenone)	4 (1.0%)	5 (1.2%)	9 (1.1%)
	Sacubitril, Valsartan, and ACE inhibitors	136 (34.5%)	165 (41.0%)	301 (37.8%)
	Angiotensin II receptor blocker	101 (25.6%)	96 (23.9%)	197 (24.7%)
12 months				
	None	95 (27.8%)	83 (23.9%)	178 (25.8%)
	Combinations	44 (12.9%)	37 (10.6%)	81 (11.7%)
	Mineralocorticoid receptor antagonists (Spironolactone or Eplerenone)	12 (3.5%)	5 (1.4%)	17 (2.5%)
	Sacubitril, Valsartan, and ACE inhibitors	101 (29.5%)	133 (38.2%)	234 (33.9%)
	Angiotensin II receptor blocker	90 (26.3%)	90 (25.9%)	180 (26.1%)
24 months				
	None	89 (27.4%)	77 (23.3%)	166 (25.3%)
	Combinations	44 (13.5%)	36 (10.9%)	80 (12.2%)
	Mineralocorticoid receptor antagonists (Spironolactone or Eplerenone)	10 (3.1%)	7 (2.1%)	17 (2.6%)
	Sacubitril, Valsartan, and ACE inhibitors	91 (28.0%)	123 (37.2%)	214 (32.6%)
	Angiotensin II receptor blocker	91 (28.0%)	88 (26.6%)	179 (27.3%)

EAST-AFNET4 indicates Early Treatment for Atrial Fibrillation for Stroke Prevention Trial.

Supplemental Table XIII. Background therapy of EAST-AFNET4 heart failure patients by randomized groups at discharge from baseline visit: rate control therapy.

		Early rhythm control (N=396)	Usual care (N=402)	Total (N=798)
Baseline				
	None	57 (14.5%)	36 (9.0%)	93 (11.7%)
	Combinations	23 (5.8%)	40 (10.0%)	63 (7.9%)
	Digoxin or Digitoxin	2 (0.5%)	1 (0.2%)	3 (0.4%)
	Verapamil or Diltiazem	3 (0.8%)	4 (1.0%)	7 (0.9%)
	Beta Blocker	309 (78.4%)	321 (79.9%)	630 (79.1%)
12 months				
	None	88 (25.7%)	44 (12.6%)	132 (19.1%)
	Combinations	9 (2.6%)	32 (9.2%)	41 (5.9%)
	Digoxin or Digitoxin	5 (1.5%)	2 (0.6%)	7 (1.0%)
	Verapamil or Diltiazem	5 (1.5%)	3 (0.9%)	8 (1.2%)
	Beta Blocker	235 (68.7%)	267 (76.7%)	502 (72.8%)
24 months				
	None	97 (29.8%)	47 (14.2%)	144 (22.0%)
	Combinations	12 (3.7%)	31 (9.4%)	43 (6.6%)
	Digoxin or Digitoxin	0 (0.0%)	2 (0.6%)	2 (0.3%)
	Verapamil or Diltiazem	2 (0.6%)	3 (0.9%)	5 (0.8%)
	Beta Blocker	214 (65.8%)	248 (74.9%)	462 (70.4%)

ACE Angiotensin Converting Enzyme. AF atrial fibrillation. EAST-AFNET4 indicates Early Treatment for Atrial Fibrillation for Stroke Prevention Trial.

Supplemental Table XIV. Impact of digitoxin at baseline in EAST-AFNET4 heart failure patients.

Outcome	Digitoxin	No Digitoxin	Effect	p-value
First primary outcome	15/285 (5.3)	209/3014 (6.9)	0.75 (0.43 to 1.30)	0.31
Second primary outcome	6.72±25.50	8.01±25.97	0.75(0.47 to 1.19)	0.22
Change in left ventricular ejection fraction	5.30±11.65	5.12±11.09	-1.24 (-3.85 to 1.38)	0.36

EAST-AFNET4 indicates Early Treatment for Atrial Fibrillation for Stroke Prevention Trial.

Supplemental Table XV. Impact of digitoxin at baseline in EAST-AFNET4 heart failure patients as per LVEF subgroup.

Outcome	Subgroup	Digitoxin	No Digitoxin	Effect	p-value	p-value interaction (between digitoxin indicator and LVEF category)
First primary outcome	reduced	4/51 (7.8)	52/436 (11.9)	0.66 (0.22 to 1.91)	0.4377	0.95
	mid-range	5/112 (4.4)	46/782 (5.9)	0.82 (0.31 to 2.14)	0.6858	
	preserved	6/107 (5.6)	107/1765 (6.1)	0.78 (0.33 to 1.84)	0.5741	
Second primary outcome - nights spent in hospital/yr	reduced	23.77±30.81	23.94±36.80	1.49 (0.54 to 4.13)	0.4384	0.08
	mid-range	8.12±10.21	20.11±30.18	0.38 (0.18 to 0.80)	0.0111	
	preserved	17.79±10.21	19.61±29.12	0.76 (0.39 to 1.49)	0.4214	
Change in left ventricular ejection fraction	reduced	17.31±14.18	17.78±11.81	-0.72 (-7.20 to 5.75)	0.8265	0.67
	mid-range	6.61±8.36	9.29±9.89	-2.73 (-7.01 to 1.55)	0.2117	
	preserved	-0.54±7.28	-0.27±8.42	-0.11 (-4.00 to 3.79)	0.9576	

LVEF Left ventricular ejection fraction. EAST-AFNET4 indicates Early Treatment for Atrial Fibrillation for Stroke Prevention Trial.

Supplemental Table XVI. Change in NYHA class at 24 months in EAST-AFNET4 heart failure patients by randomized groups.

LVEF category	NYHA change 24 months	Early rhythm control	Usual care
reduced	Improved	18/46 (39.13)	27/54 (50.00)
	Unchanged	21/46 (45.65)	20/54 (37.04)
	Worsened	7/46 (15.22)	7/54 (12.96)
mid-range	Improved	45/96 (46.88)	25/80 (31.25)
	Unchanged	34/96 (35.42)	40/80 (50.00)
	Worsened	17/96 (17.71)	15/80 (18.75)
preserved	Improved	110/181 (60.77)	94/191 (49.21)
	Unchanged	61/181 (33.70)	81/191 (42.41)
	Worsened	10/181 (5.52)	16/191 (8.38)

LVEF Left ventricular ejection fraction. NYHA class New York Heart Association classification of symptoms in heart failure patients. EAST-AFNET4 indicates Early Treatment for Atrial Fibrillation for Stroke Prevention Trial.

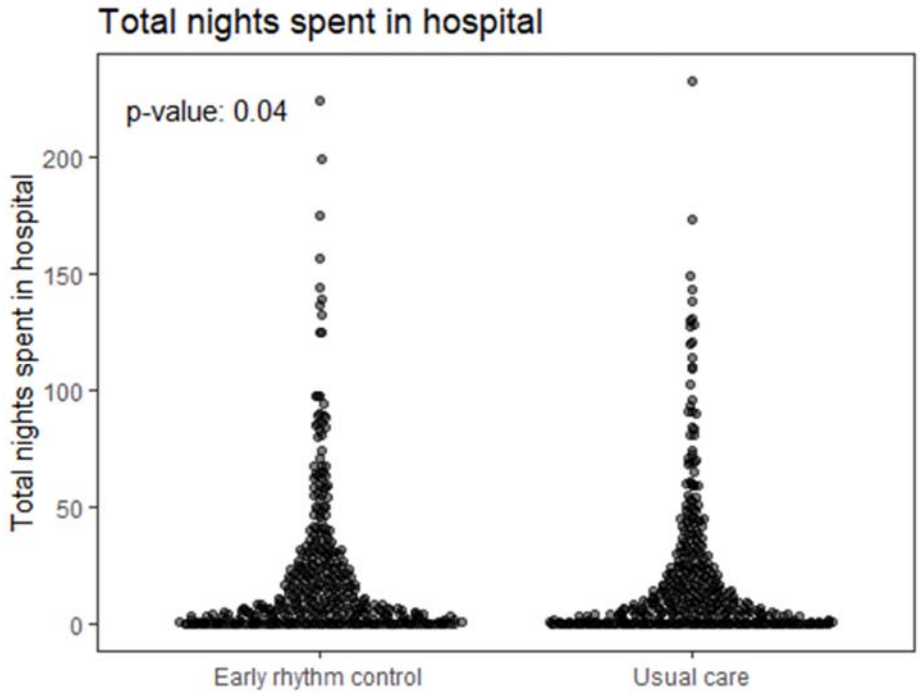
Supplemental Table XVII. Complete case analysis of EAST-AFNET4 heart failure patients for secondary outcomes where imputation was necessary.

Outcome	Early rhythm control	Usual care	Treatment effect	p-value
Change in left ventricular ejection fraction; Number of observations: 597	5.6±11.7	4.4±11.5	0.84 (-0.57 to 2.25)	0.24
Change in EQ-5D score; Number of observations: 486	3.2±17.1	1.8±18.3	2.16 (-0.54 to 4.86)	0.12
Change in SF-12 Mental Score; Number of observations: 492	1.2±11.0	3.0±10.6	-0.60 (-2.15 to 0.95)	0.44
Change in SF-12 Physical Score; Number of observations: 493	1.2±8.1	0.8±9.0	0.39 (-0.97 to 1.76)	0.57
Change in MoCA score; Number of observations: 547	0.2±3.1	0.3±3.2	-0.03 (-0.49 to 0.43)	0.91
Sinus rhythm — no. of patients with feature/total no. (%)	246/313 (78.59)	175/320 (54.69)	3.17 (2.21 to 4.54)	<0.001
Asymptomatic — no. of patients with feature/total no. (%)	99/325 (30.46)	117/331 (35.35)	1.36 (0.93 to 1.99)	0.11
NYHA Improved	173/325 (53.2)	150/331 (45.3)		0.06
NYHA Unchanged	117/325 (36.0)	142/331 (42.9)		
NYHA Worsened	35/325 (10.8)	39/331 (11.8)		

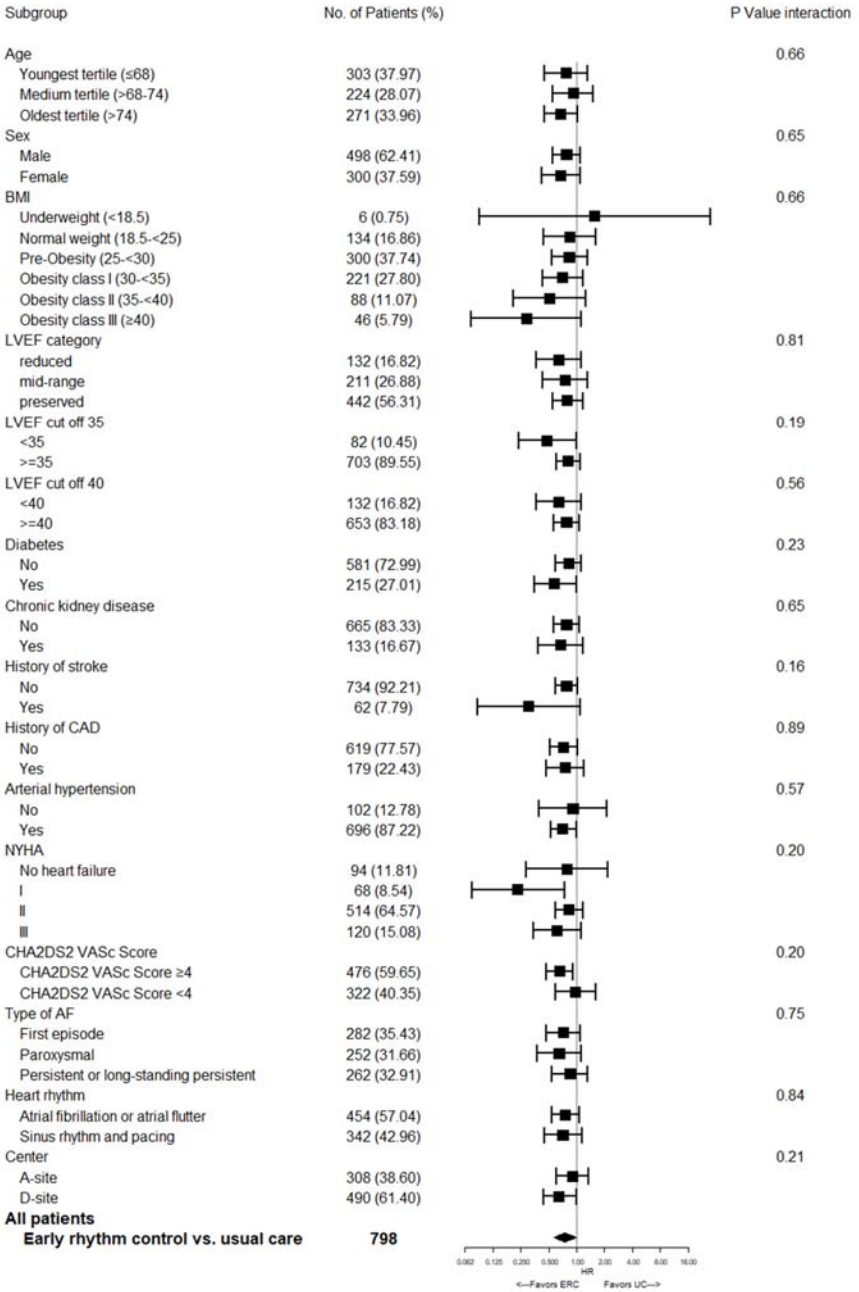
EQ-5D score European Quality of Life 5 Dimensions score; SF-12 Short Form Health survey 12-items; MoCA score Montreal Cognitive Assessment Score. NYHA class New York Heart Association classification of symptoms in heart failure patients. EAST-AFNET4 indicates Early Treatment for Atrial Fibrillation for Stroke Prevention Trial.

Supplemental Figures

Supplemental Figure I. Nights spent in hospital of EAST-AFNET4 heart failure patients by randomized groups.

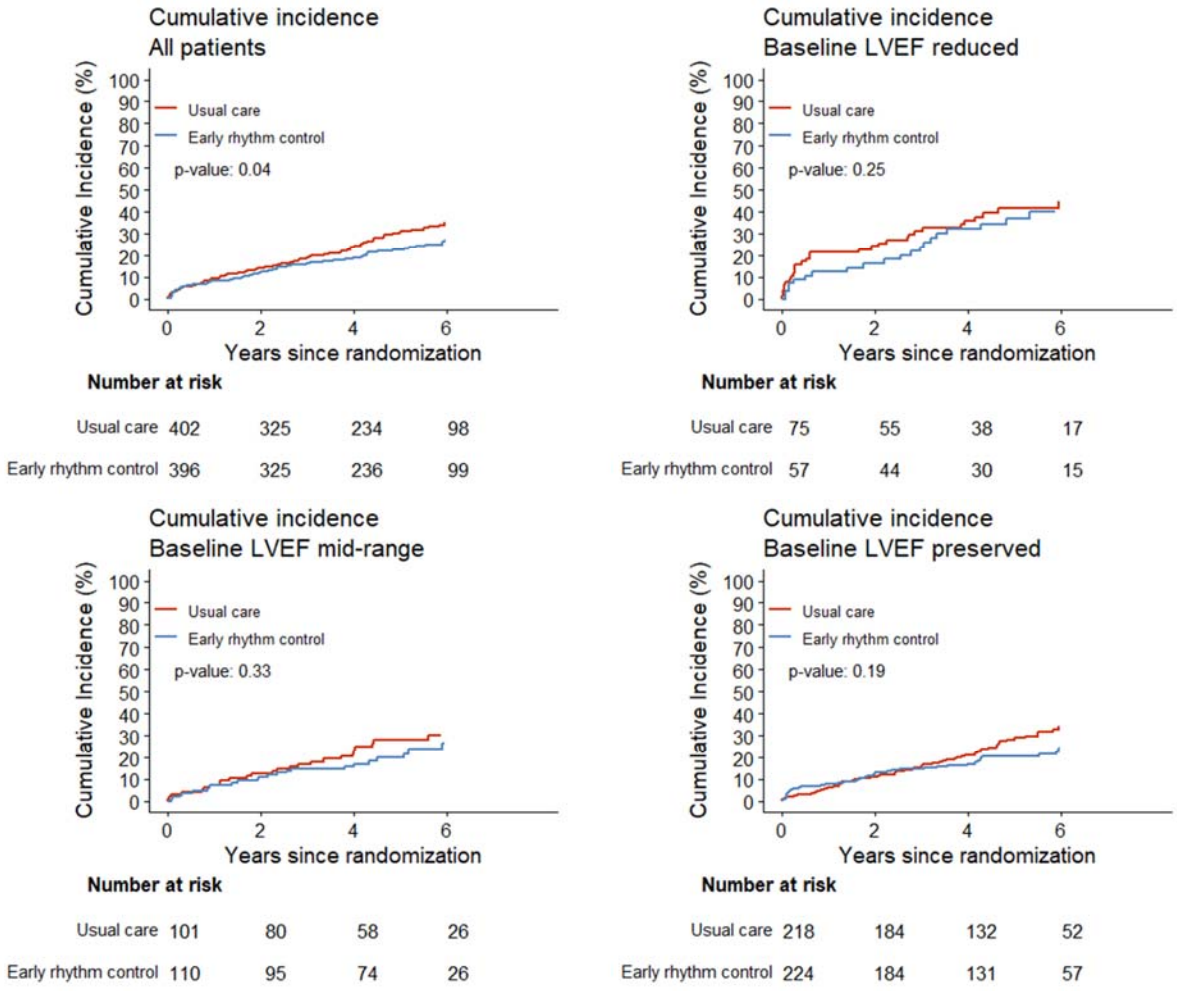


Supplemental Figure II. Forest plot for subgroup analysis of EAST-AFNET4 heart failure patients by randomized groups. Interaction p-value between treatment group and subgroups listed on the left is given.



BMI Body mass index; LVEF Left ventricular function; CAD Coronary artery disease; NYHA class New York Heart Association classification of symptoms in heart failure patients; AF atrial fibrillation; A-site Ablation site; D-site study site without on-site ablation ('drug site'); EAST-AFNET4 indicates Early Treatment for Atrial Fibrillation for Stroke Prevention Trial.

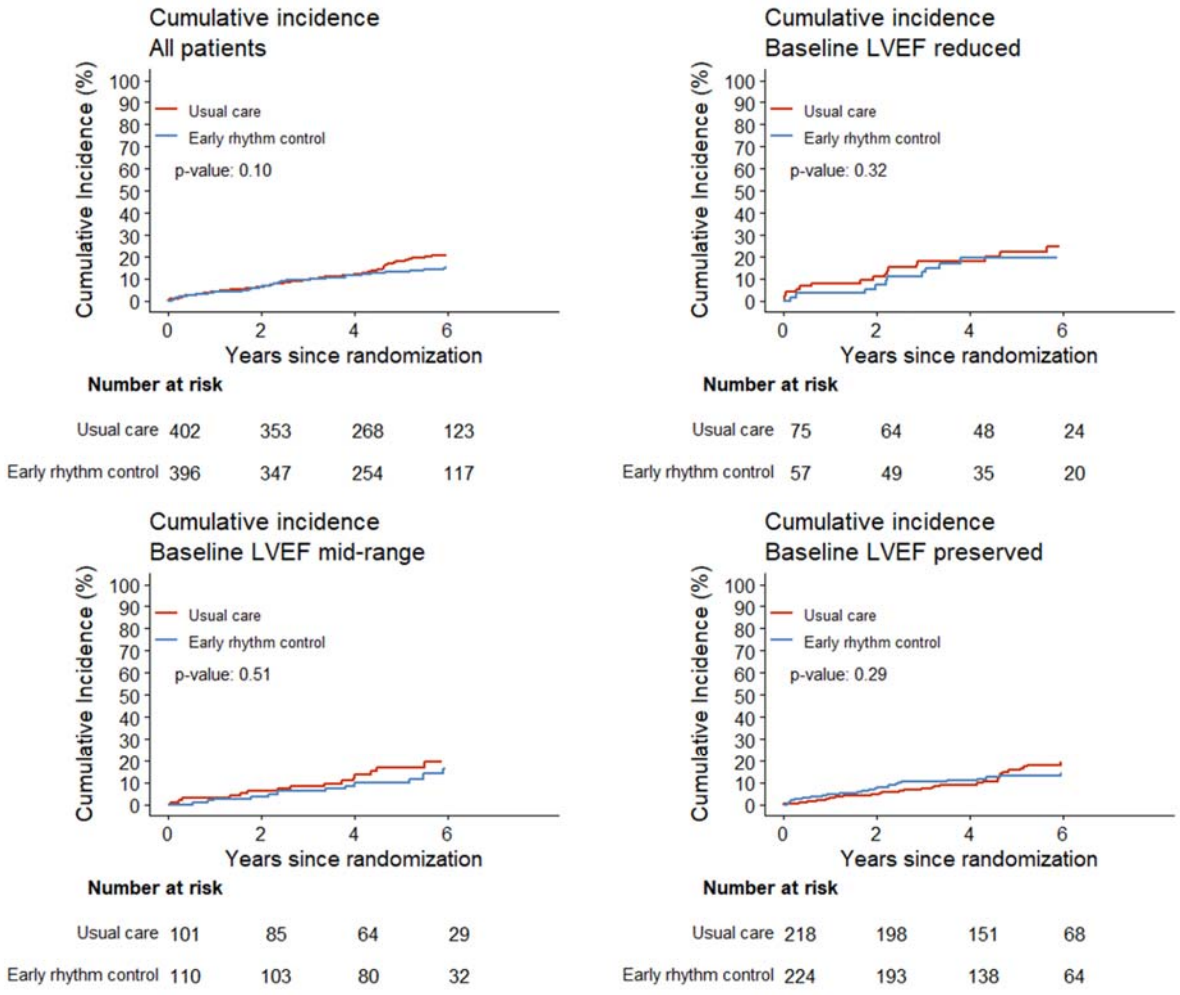
Supplemental Figure III. Outcome of EAST-AFNET4 heart failure patients modelled after the primary endpoint of the CASTLE-AF trial by randomized groups.



Cumulative-Incidence Curves for the effects of early rhythm control on the modelled "CASTLE-AF" like outcome.

LVEF Left ventricular ejection fraction. EAST-AFNET4 indicates Early Treatment for Atrial Fibrillation for Stroke Prevention Trial. CASTLE-AF indicates Catheter Ablation versus Standard Conventional Therapy in Patients with Left Ventricular Dysfunction and Atrial Fibrillation Trial

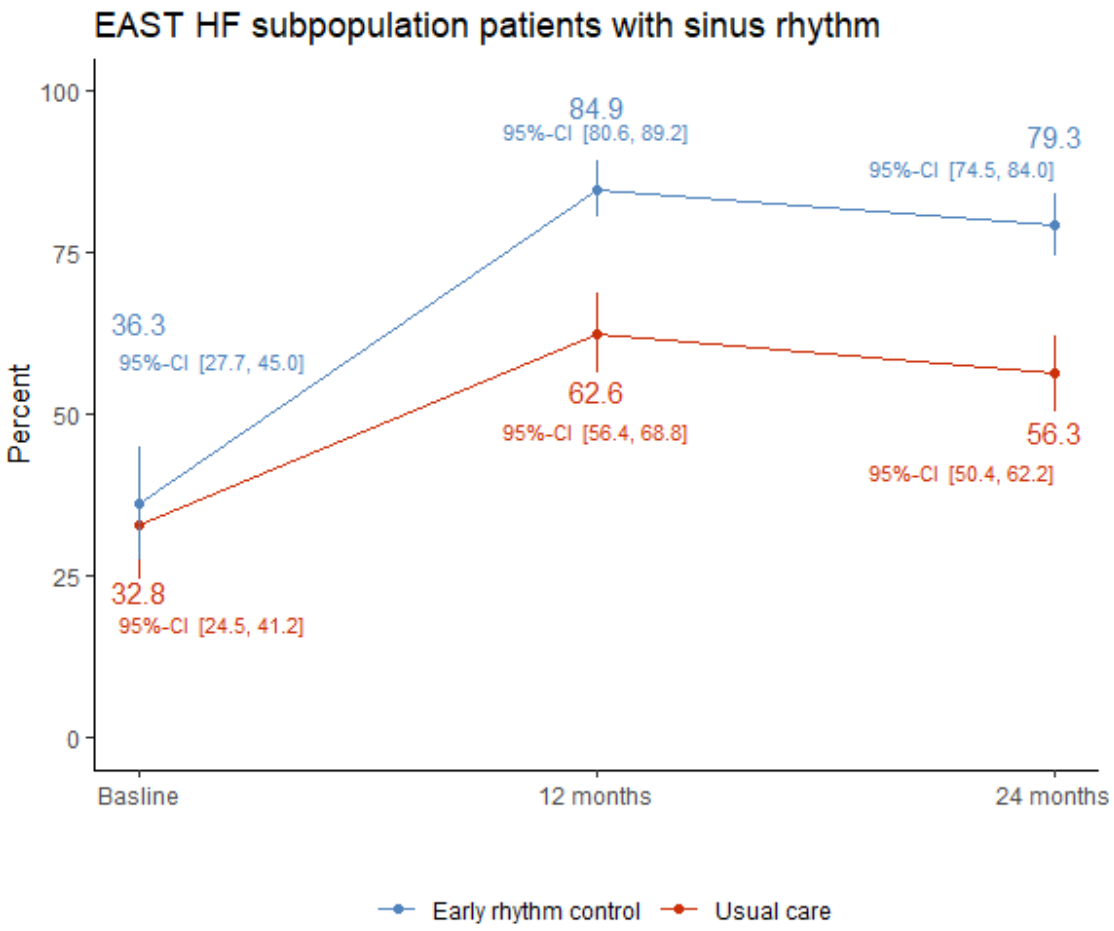
Supplemental Figure IV. Outcome of EAST-AFNET4 heart failure patients using a "CABANA-like" composite endpoint including death, disabling stroke, serious bleeding, or cardiac arrest by randomized groups.



Cumulative-Incidence Curves for the effects of early rhythm control on the modelled "CABANA-like" outcome.

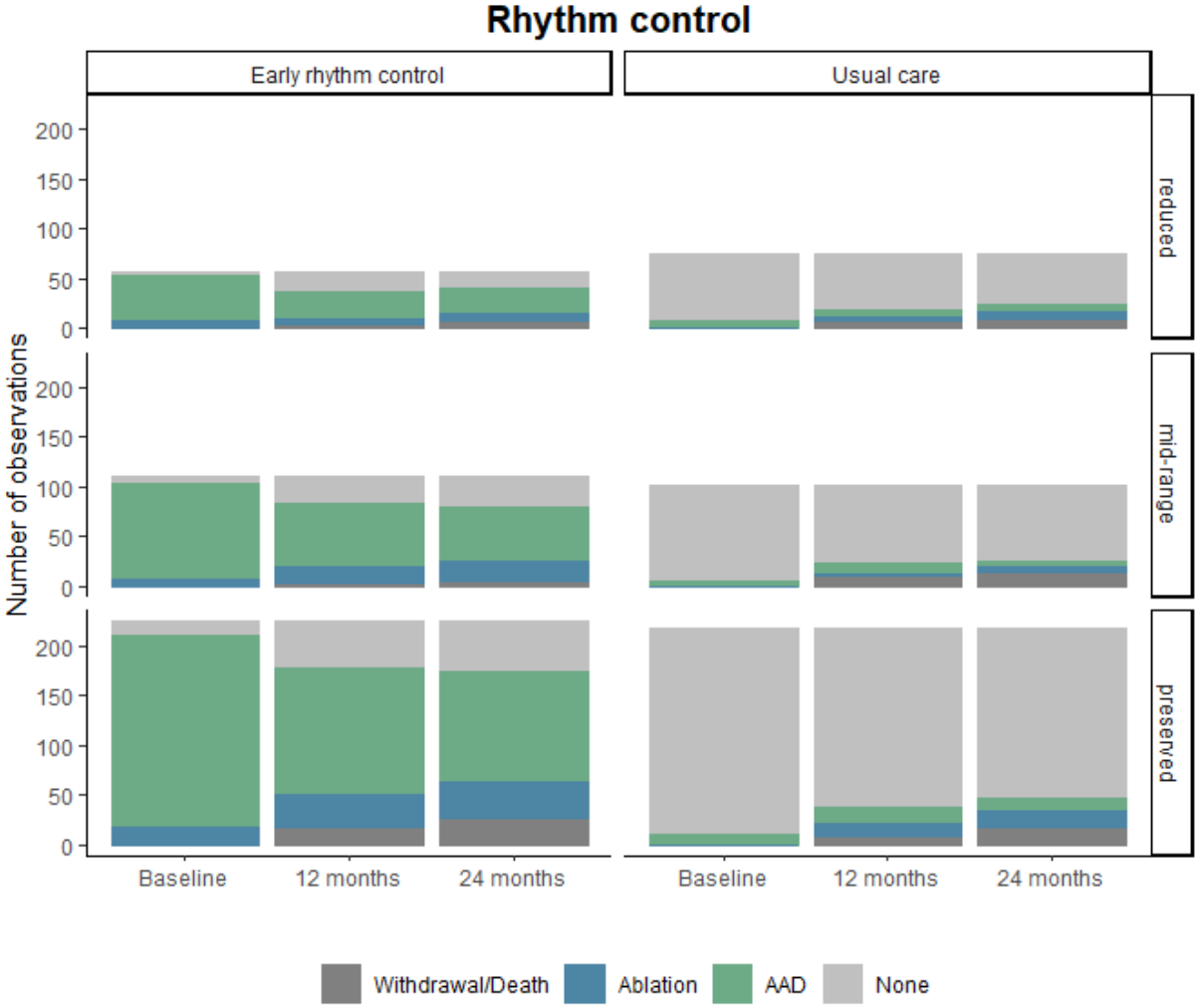
LVEF Left ventricular ejection fraction. EAST-AFNET4 indicates Early Treatment for Atrial Fibrillation for Stroke Prevention Trial. CABANA indicates Catheter Ablation Versus Antiarrhythmic Drug Therapy for Atrial Fibrillation Trial.

Supplemental Figure V. Sinus rhythm of EAST-AFNET4 heart failure patients over time by randomized groups.



HF Heart failure; EAST-AFNET4 indicates Early Treatment for Atrial Fibrillation for Stroke Prevention Trial.

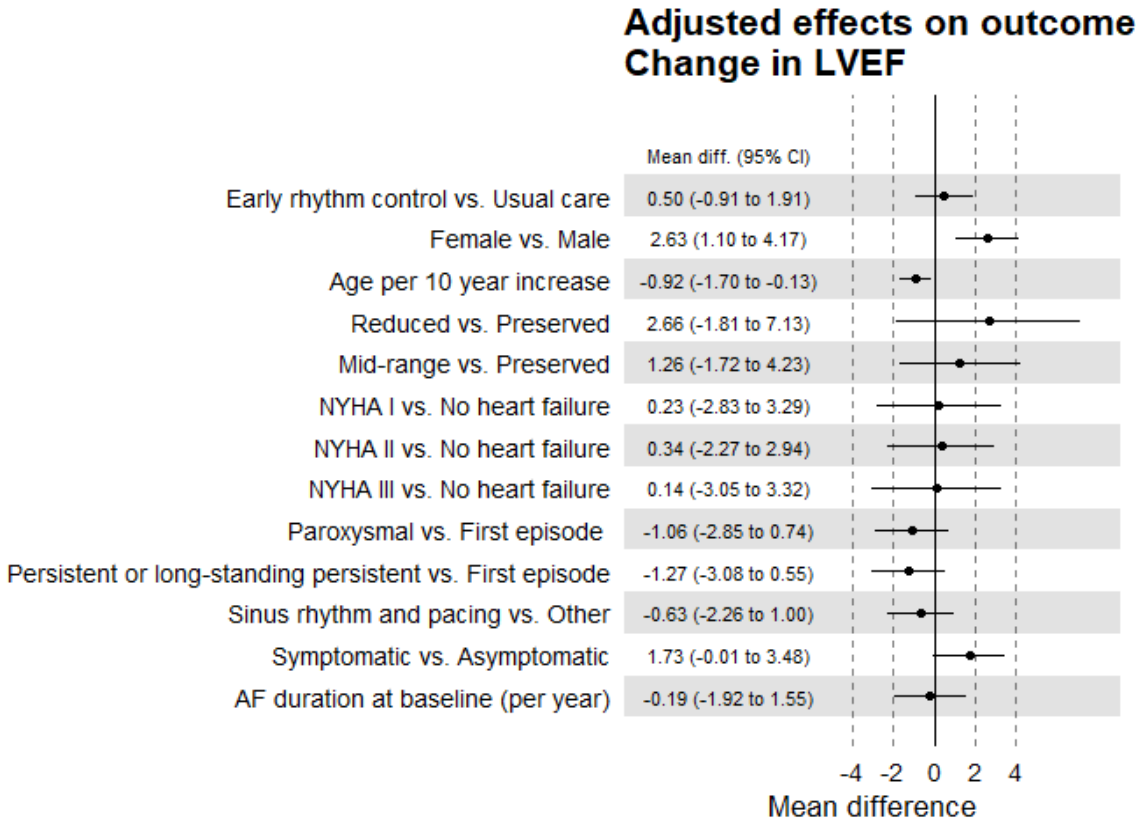
Supplemental Figure VI. Use of atrial fibrillation ablation and antiarrhythmic drugs over time in patients with early rhythm control as compared to usual care.



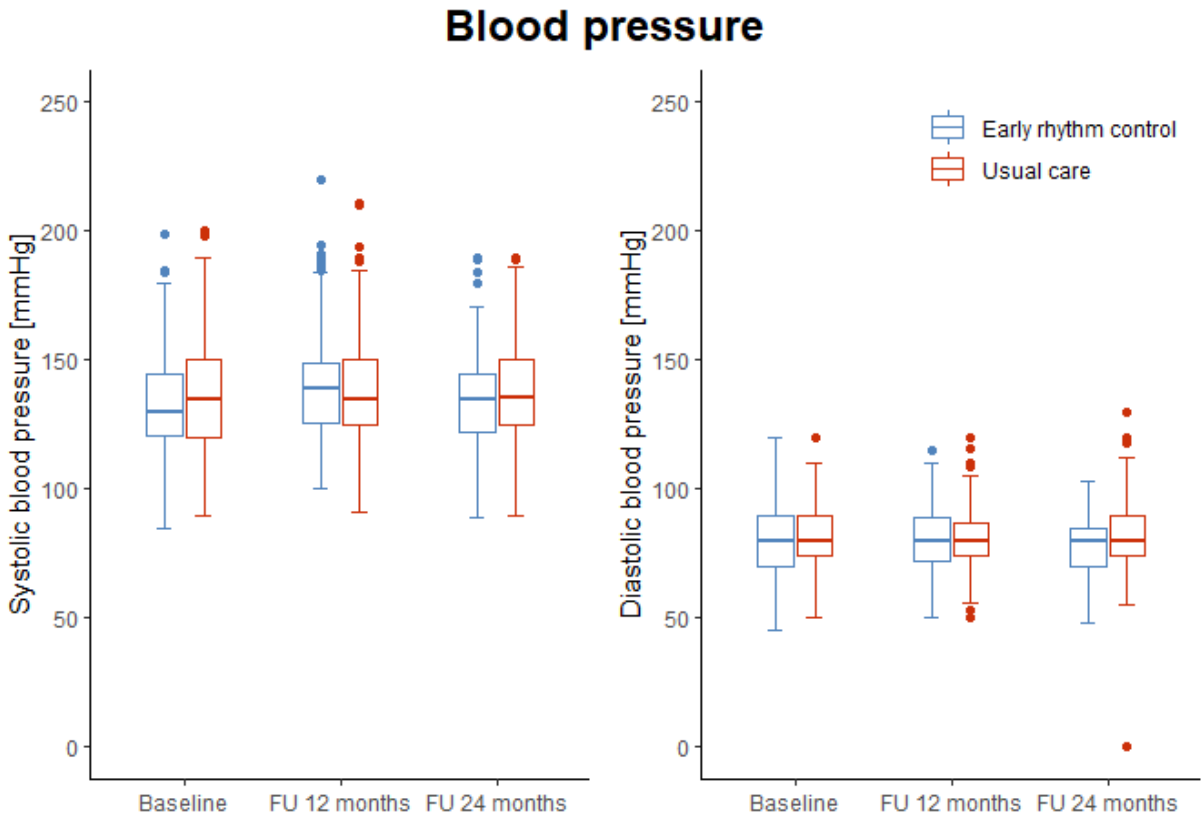
AF Atrial fibrillation; AAD antiarrhythmic drug. The majority of heart failure patients assigned to early rhythm-control therapy was initially treated with antiarrhythmic drugs, most often flecainide in patients with HFpEF and Amiodarone in patients with HFmrEF or HFrEF. At the 2-year follow-up, 257 of the patients (64.9%) who had been randomly assigned to early rhythm control therapy were still receiving rhythm-control therapy (67 patients treated with atrial fibrillation ablation and 190 treated with antiarrhythmic drugs), and only 55 patients (13.7%) who had been randomly assigned to usual care (30 treated with atrial fibrillation ablation and 25 treated with antiarrhythmic drugs). HFpEF Heart failure with preserved ejection fraction; HFmrEF Heart failure with mid-range ejection fraction; HFrEF Heart failure with reduced ejection fraction.

EAST-AFNET4 indicates Early Treatment for Atrial Fibrillation for Stroke Prevention Trial.

Supplemental Figure VII. Changes of left ventricular ejection fraction in the EAST-AFNET4 heart failure patients. Left ventricular function improved in patients randomized to early rhythm control and in patients randomized to usual care, without inter-group differences. Left ventricular ejection fraction improvement was more pronounced in patients with lower baseline ejection fraction. LVEF left ventricular ejection fraction; NYHA class New York Heart Association classification of symptoms in heart failure patients. A multivariable mixed linear regression model was used.



Supplemental Figure VIII. Systolic and diastolic blood pressure of EAST-AFNET4 heart failure patients at baseline and at 12- and 24 months by randomized groups.



EAST-AFNET4 indicates Early Treatment for Atrial Fibrillation for Stroke Prevention Trial.

Supplemental Figure IX. Changes of functional heart failure status estimated according to NYHA class by randomized groups in patients randomized to early rhythm control (**IX a**) and in patients randomized to usual care (**IX b**). Changes in NYHA class were not different between randomized groups. NYHA class New York Heart Association classification of symptoms in heart failure patients.