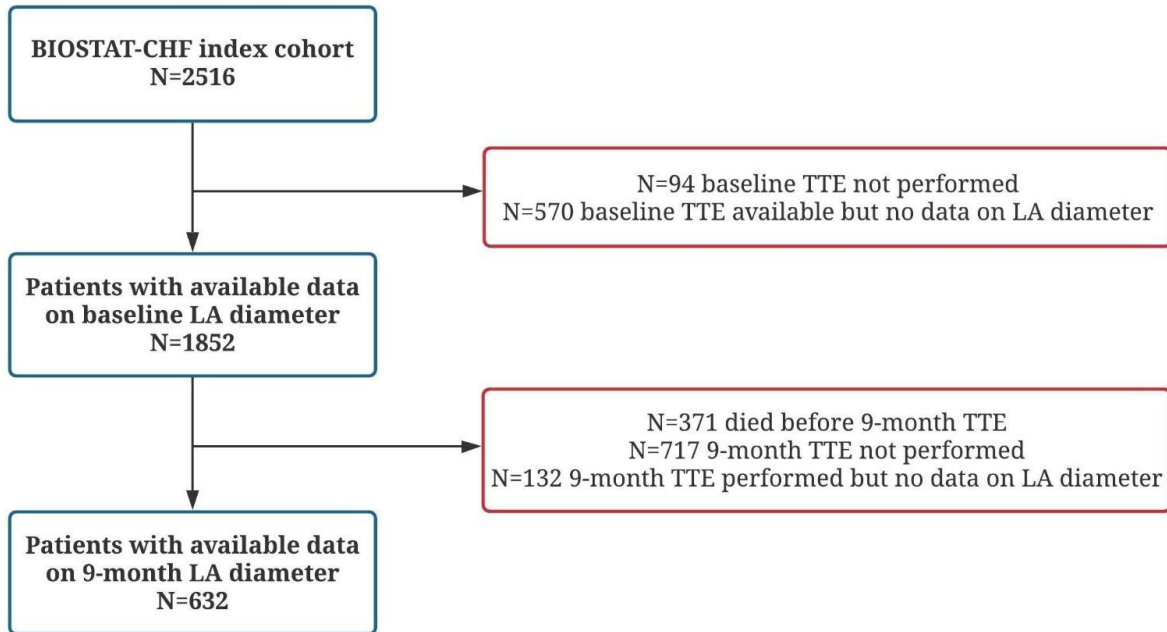
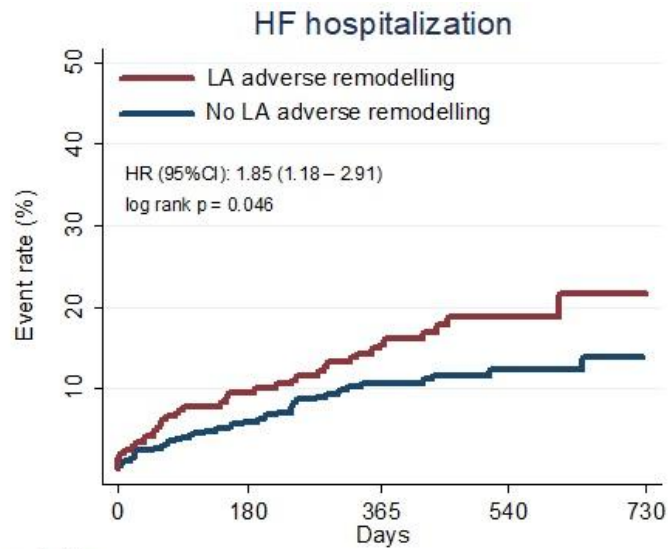


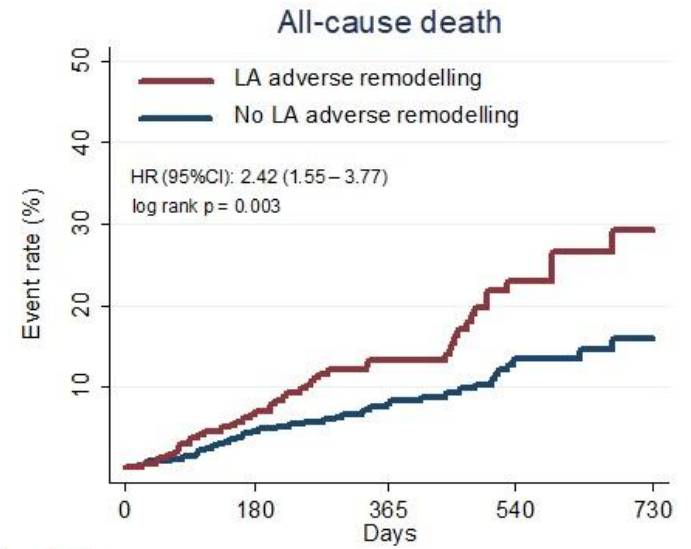
Supplemental Material



Supplement Figure 1. Study population.



	0	180	365	540	730
No LA adverse remodelling	385	333	234	108	24
LA adverse remodelling	247	199	131	49	18



	0	180	365	540	730
No LA adverse remodelling	385	349	253	122	33
LA adverse remodelling	247	218	150	59	23

Supplemental Figure 2. Kaplan-Meier estimates of All cause death and HF hospitalization in patients with and without LA adverse remodelling.

Reported the unadjusted HR (95%CI). HR: hazard ratio; 95%CI: 95% confidence interval.

Supplemental Table 1. Baseline clinical characteristics in the index cohort stratified by available LA assessment at 9-month.

	No LA assessment at 9-Month (n=1884)	LA assessment at 9-Month (n=632)	p-value
Death	571 (30.3%)	86 (13.6%)	< 0.001
Age (years)	69.9 ± 11.7	65.8 ± 12.1	< 0.001
Female	529 (28.1%)	141 (22.3%)	0.005
BMI (kg/m ²)	27.8 ± 5.6	28.0 ± 5.0	0.51
HF hospitalization in last year	628 (33.3%)	166 (26.3%)	< 0.001
Smoking			0.013
- Past	909 (48.3%)	311 (49.2%)	
- Current	245 (13.0%)	108 (17.1%)	
Medical history			
Hypertension	1157 (61.4%)	412 (65.2%)	0.09
Diabetes mellitus	638 (33.9%)	181 (28.6%)	0.015
Atrial fibrillation	912 (48.4%)	231 (36.6%)	< 0.001
HF primary ischemic etiology	842 (45.5%)	284 (45.6%)	0.97
Heart valve disease	141 (7.6%)	49 (7.9%)	0.48
Peripheral artery disease	223 (11.8%)	50 (7.9%)	0.006
COPD	343 (18.2%)	93 (14.7%)	0.045
Stroke	188 (10.0%)	45 (7.1%)	0.032
Current malignancy	86 (4.6%)	11 (1.7%)	0.001
CKD	956 (54.0%)	251 (42.6%)	< 0.001
Device therapy			< 0.001
Pacemaker	146 (7.7%)	37 (5.9%)	
ICD	166 (8.8%)	39 (6.2%)	
CRT-P	38 (2.0%)	11 (1.7%)	
CRT-D	147 (7.8%)	26 (4.1%)	
NYHA functional class			< 0.001
I	43 (2.4%)	13 (2.1%)	
II	571 (31.3%)	297 (47.6%)	
III	961 (52.7%)	267 (42.8%)	
IV	247 (13.6%)	47 (7.5%)	
Clinical profile			
Peripheral oedema	514 (32.9%)	110 (20.4%)	< 0.001
Hepatomegaly	279 (14.9%)	79 (12.5%)	0.14
SBP (mmHg)	123.9 ± 21.9	127.2 ± 21.8	0.001
DBP (mmHg)	74.1 ± 13.6	77.3 ± 12.4	< 0.001
HR (bpm)	82.8 ± 21.5	80.8 ± 20.9	0.047
Type of visit			< 0.001
Inpatient hospitalization	440 (23.4%)	245 (38.8%)	
Outpatient clinic	1351 (71.7%)	343 (54.3%)	
HF therapy			
ACEi/ARB at baseline	1306 (69.3%)	514 (81.3%)	< 0.001
ACEi/ARB fraction target dose at 3 months (%)	0.45 ± 0.37	0.54 ± 0.42	< 0.001
ACEi/ARB at 9 month	1559 (82.7%)	594 (94.0%)	< 0.001
β-blocker at baseline	1561 (82.9%)	532 (84.2%)	0.44
β-blocker fraction target dose at 3	0.36 ± 0.31	0.36 ± 0.29	0.59

months (%)			
β-blocker at 9 months	1681 (89.2%)	608 (96.2%)	0.060
MRA use	975 (51.8%)	364 (57.6%)	0.011
Loop diuretic use	1873 (99.4%)	631 (99.8%)	0.18
Digoxin use	363 (19.3%)	128 (20.3%)	0.59

Data are presented as n (%) and mean ± standard deviation. ACEi = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; BMI = body mass index; CKD = chronic kidney disease; COPD = chronic obstructive pulmonary disease; CRT-D = cardiac resynchronization therapy with defibrillator; CRT-P = cardiac resynchronization therapy with pacemaker; DBP = diastolic blood pressure; HF = heart failure; HR = heart rate; ICD = implantable cardioverter-defibrillator; MRA = mineralocorticoid receptor antagonist; NYHA = New York Heart Association; SBP = systolic blood pressure.

Supplemental table 2. Unadjusted association of baseline determinants with LA adverse remodelling.

	OR (95% CI)	p	Z
Baseline LA diameter (mm)	0.92 (0.90 – 0.94)	< 0.001	6.2
ACEi or ARB dose at 3 months	0.64 (0.43 – 0.97)	0.035	2.1
LV remodelling			
- Concentric remodelling	1.68 (0.48 – 5.86)	0.41	0.8
- Concentric hypertrophy	1.11 (0.55 – 2.24)	0.77	0.29
- Eccentric hypertrophy	1.47 (0.95 – 2.26)	0.081	1.7
HF primary ischemic aetiology	1.71 (1.23 – 2.37)	0.001	3.2
Men	0.85 (0.57 – 1.25)	0.42	0.8
Age	1.02 (1.00 – 1.03)	0.001	3.3
eGFR CKD-EPI (mL/min/1.73 m ²)	0.99 (0.98 – 1.00)	0.11	1.5
History of atrial fibrillation	1.28 (0.92 – 1.78)	0.14	1.5
Baseline LVEF (%)	1.00 (0.98 – 1.02)	0.62	0.4
Baseline moderate-severe mitral regurgitation (%)	0.85 (0.61 – 1.17)	0.33	0.9
NYHA Class			
- II	1.34 (0.40 – 4.46)	0.63	0.4
- III	1.48 (0.44 – 4.9)	0.63	0.4
- IV	2.34 (0.63 – 8.69)	0.63	0.4

OR: odds ratio; 95%CI: confidence interval; eGFR = estimated glomerular filtration rate; NYHA = New York Heart Association; HF: heart failure; LV: leftventricle; LA: left atrium; ACEi = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker. Overall model AUC: 0.72 (95%CI: 0.67 – 0.76)

Supplemental Table 3. Association of LA adverse remodelling and the analyzed endpoints excluding HFpEF patients.

	Unadjusted			Adjusted		
	HR (95% CI)	p	Z	HR (95% CI)	p	Z
All cause death or HF hospitalization						
LA Adverse remodelling	2.02 (1.41 – 2.89)	< 0.001	3.8	1.77 (1.24 – 2.53)	0.002	3.1
Δ LA Change *	1.60 (1.34 – 1.92)	< 0.001	5.1	1.33 (1.11 - 1.59)	0.002	3.1
HF hospitalization						
LA Adverse remodelling	1.91 (1.19 – 3.05)	0.007	2.7	1.70 (1.06 – 2.72)	0.025	2.2
Δ LA Change *	1.61 (1.29 – 2.03)	< 0.001	4.1	1.38 (1.10 - 1.74)	0.005	2.7
All cause death						
LA Adverse remodelling	2.48 (1.56 – 3.95)	< 0.001	3.9	2.26 (1.42 – 3.59)	0.001	3.5
Δ LA Change *	1.55 (1.22 - 1.97)	< 0.001	3.5	1.28 (1.00 - 1.63)	0.045	2.0

Unadjusted and adjusted analysis accounted for baseline LA diameter. Adjusted model was adjusted for the risk model of BIOSTAT-CHF which contains age, previous hospitalization for HF, systolic blood pressure, presence of peripheral oedema, N-terminal pro-B-type natriuretic peptide (NT-proBNP), haemoglobin, sodium, high-density lipoprotein, and the use of β blockers at baseline * HR are shown for 5 mm increase among patients with positive LA change.