Supplementary data

Supplementary Table 1. Main echographic data of the landmark population at 12 months in the MITRA-FR trial.

Characteristics	TMVR group	GDMT group
Echographic data		
Left ventricular ejection fraction, %	33.4±10.7 (n=52)	37.3±11.2 (n=54)
Indexed LVEDV, ml/m2	127.8±33.3 (n=52)	138.4±33.5 (n=54)
Indexed LVESV, ml/m2	831.0±34.4 (n=52)	89.3±33.0 (n=54)
EROA, mm2	11.5±9.6 (n=33)	24.5±14.5 (n=49)
Regurgitant volume, ml	18.1±14.0 (n=34)	39.6±19.5 (n=50)
PASP, mmHg	34.7±12.5 (n=40)	36.5±12.3 (n=43)

EROA: effective regurgitant orifice area; GDMT: guideline-directed medical treatment; LVEDV: left ventricular end-diastolic volume; LVESV: left ventricular end-systolic volume; PASP: pulmonary arterial systolic pressure; TVMR: transcatheter mitral valve repair

Supplementary Table 2. Main characteristics of the landmark population at inclusion in the MITRA-FR trial.

Characteristics	TMVR group (n=113)	GDMT group (n=113)	p-value
Clinical data			
Age, years	69.1±10.4	69.5±9.9	0.83
Age >75 yrs, n (%)	32 (28.3)	37 (32.7)	0.56
Female sex, n (%)	22 (19.5)	32 (28.3)	0.16
Body mass index, kg/m2	25.3±4.5	25.4±3.9	0.80
Systolic blood pressure, mmHg	108.8±16.3	108.4±18.7	0.67
Heart rate, beats/min	72.6±13.1	71.6±12.9	0.37
Medical history			
Ischaemic cardiomyopathy, n (%)	70 (61.9)	64 (56.6)	0.49
Non-ischaemic cardiomyopathy, n (%)	42 (37.2)	46 (40.7)	0.68
Previous myocardial infarction, n (%)	59 (52.2)	40 (35.4)	0.015
Previous coronary revascularisation, n (%)	53 (46.9)	48 (42.5)	0.59
Prior stroke, n (%)	12 (10.6)	7 (6.2)	0.33
Peripheral vascular disease, n (%)	14 (12.4)	10 (8.8)	0.51
History of atrial fibrillation, n (%)	62 (54.9)	63 (55.8)	1.00
Renal insufficiency, n (%)	13 (11.5)	10 (8.8)	0.66
Glomerular filtration rate, ml/min	50.5±20.1	51.4±20.3	0.75
Diabetes mellitus, n (%)	41 (36.3)	31 (27.4)	0.19
Functional status/impact			
NYHA Class III or IV	67 (59.2)	77 (68.1)	0.38
Unplanned hospitalisation for heart failure within 12 months	103 (91.2)	105 (93.8)	0.61
Median BNP* (IQR) ng/litre	721 (391-1,105)	729 (490-1,118)	0.68

Median NT-proBNP* (IQR), ng/litre	2,884 (1,790-4,317)	2,722 (1,703-5,118)	0.91
Echographic data			
Left ventricular ejection fraction, %	33.9±5.9	33.0±6.7	0.38
Indexed LVEDV, ml/m2	132.9±34.4	138.6±32.1	0.19
Indexed LVESV, ml/m2	88.3±29.3	93.8±29.1	0.09
EROA, mm2	30.3±10.4	29.8±10.4	0.73
Regurgitant volume, ml	44.2±13.6	44.5±13.7	0.93
EROA/LVEDV, mm2/100 ml of LVEDV	0.13±0.05	0.12±0.05	0.14
PASP, mmHg	44.1±14.4	44.7±12.9	0.52
Tricuspid regurgitation >moderate, n (%)	21 (20.0)	15 (14.1)	0.60
Risk scores			
Median logistic EuroSCORE II (IQR)	5.6 (3.2-11.0)	5.4 (3.1-9.2)	0.55
Median STS score for mortality (IQR)	3.1 (1.5-5.8)	2.6 (1.3-5.7)	0.44
Medical treatment			
Single implantable cardioverter-defibrillator, n (%)	61 (54.0)	60 (53.1)	1.00
Cardiac resynchronisation therapy-defibrillator, n (%)	64 (56.6)	67 (59.3)	0.78
Single cardiac resynchronisation therapy device, n (%)	29 (25.7)	25 (22.1)	0.64
ACEi/ARB, n (%)	82 (72.6)	83 (73.5)	1.00
Angiotensin receptor and neprilysin inhibitors, n (%)	11 (10.5)	15 (14.2)	0.53
Beta-blockers, n (%)	98 (86.7)	102 (90.3)	0.53
Mineralocorticoid receptor antagonists, n (%)	71 (62.8)	62 (55.4)	0.27
Loop diuretics, n (%)	112 (99.1)	110 (97.3)	0.62

Oral anticoagulants, n (%)	65 (57.5)	69 (61.1)	0.68

Landmark analysis in the selected subgroup of MITRA-FR patients still alive at 12 months (whether they were hospitalised or not for heart failure within the first year).

Plus–minus values are means±SD.

*Brain natriuretic peptide (BNP) was measured in 51 of the 113 patients in the MitraClip group and in 45 of the 113 patients in the control group, and NT-proBNP in 56 and 53 patients, respectively. All the measurements were obtained locally.

ACEi: angiotensin-converting enzyme inhibitor. ARB: angiotensin receptor blocker; EROA: effective regurgitant orifice area; GDMT: guideline-directed medical treatment; IQR: interquartile range; LVEDV: left ventricular end-diastolic volume; LVESV: left ventricular end-systolic volume; NYHA: New York Heart Association; PASP: pulmonary arterial systolic pressure; STS: Society of Thoracic Surgeons; TVMR: transcatheter mitral valve repair

Supplementary Table 3. Main characteristics of the landmark analysis-included and non-included populations, from the MITRA-FR trial overall population.

Characteristics	Landmark population (n=226)	Non-included population (n=78)	p-value
Clinical data			
Age, years	69.3±10.1	73.1±8.8	0.002
Age >75 yrs, n (%)	69 (30.5)	41 (52.6)	0.006
Female sex, n (%)	54 (23.9)	23 (29.5)	0.36
Body mass index, kg/m2	25.4±4.2	24.5±3.4	0.14
Systolic blood pressure, mmHg	108.6±17.5	108.1±15.0	0.77
Heart rate, beats/min	72.1±13.0	73.5±11.4	0.17
Medical history			
Ischaemic cardiomyopathy, n (%)	134 (59.3)	92 (40.7)	1.00
Non-ischaemic cardiomyopathy, n (%)	88 (38.9)	31 (40.3)	0.89
Previous myocardial infarction, n (%)	99 (43.8)	28 (35.9)	0.23
Previous coronary revascularisation, n (%)	101 (44.7)	34 (44.2)	1.00
Prior stroke, n (%)	19 (8.4)	9 (11.5)	0.49
Peripheral vascular disease, n (%)	24 (10.6)	8 (11.3)	1.00
History of atrial fibrillation, n (%)	70 (32.7)	27 (36.0)	0.67
Renal insufficiency, n (%)	23 (10.2)	18 (23.1)	0.006
Glomerular filtration rate, ml/min	50.9±20.1	44.9±18.3	0.02
Diabetes mellitus, n (%)	72 (31.9)	17 (21.8)	0.11
Functional status/impact			
NYHA Class III or IV	144 (63.7)	60 (76.9)	0.02

Unplanned hospitalisation for heart failure within the 12 months	208 (92.4)	75 (96.2)	0.30
Median BNP* (IQR), ng/litre	723 (414-1,111)	1,064 (881-2,950)	0.0001
Median NT-proBNP* (IQR), ng/litre	2,750 (1,757-5,058)	5,932 (3,231-13,248)	<0.0001
Echographic data			
Left ventricular ejection fraction, %	33.5±6.3	31.9±7.1	0.05
Indexed LVEDV, ml/m2	135.7±33.3	134.2±40.5	0.64
Indexed LVESV, ml/m2	91.1±29.3	92.5±33.1	0.87
EROA, mm2	30.1±10.4	33.3±11.3	0.01
Regurgitant volume, ml	44.4±13.6	47.6±13.2	0.03
EROA/LVEDV, mm2/100 ml of LVEDV	0.13±0.05	0.15±0.06	0.002
PASP, mmHg	44.4±13.6	46.5±13.0	0.73
Tricuspid regurgitation >moderate, n (%)	36 (17.1)	16 (22.5)	0.03
Risk scores			
Median logistic EuroSCORE II (IQR)	5.61 (3.2-9.9)	8.20 (4.5-15.3)	0.001
Median STS score for mortality (IQR)	2.99 (1.4-5.8)	4.68 (2.2-8.8)	0.002
Medical treatment			
Single implantable cardioverter-defibrillator, n (%)	121 (53.5)	51 (65.4)	0.08
Cardiac resynchronisation therapy-defibrillator, n (%)	131 (58.0)	55 (70.5)	0.05
Single cardiac resynchronisation therapy device, n (%)	54 (23.9)	27 (35.1)	0.07
ACEi/ARB, n (%)	165 (73.0)	59 (75.6)	0.76

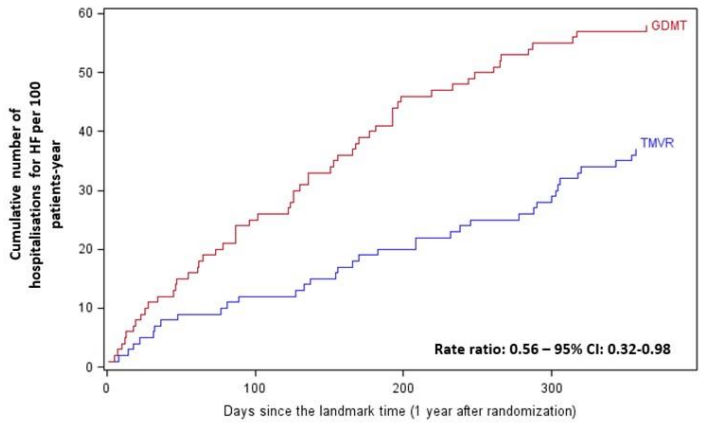
Angiotensin receptor and neprilysin inhibitors, n (%)	26 (12.3)	5 (7.2)	0.27
Beta-blockers, n (%)	200 (88.5)	72 (92.3)	0.39
Mineralocorticoid receptor antagonists, n (%)	133 (59.1)	33 (42.3)	0.01
Loop diuretics, n (%)	222 (98.2)	78 (100)	0.57
Oral anticoagulants, n (%)	134 (59.3)	52 (66.7)	0.28

Landmark analysis in the selected subgroup of MITRA-FR patients still alive at 12 months (whether they were hospitalised or not for heart failure within the first year).

Plus–minus values are means±SD.

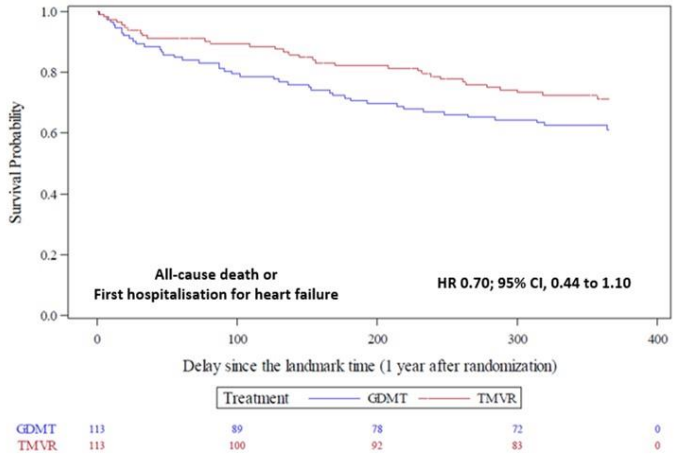
*BNP was measured in 96 of the 226 patients in the Landmark-studied group and in 30 of the 78 patients in the not-included group, and NT-proBNP in 109 and 38 patients, respectively.

ACEi: angiotensin-converting enzyme inhibitor. ARB: angiotensin receptor blocker; EROA: effective regurgitant orifice area; GDMT: guideline-directed medical treatment; IQR: interquartile range; LVEDV: left ventricular end-diastolic volume; LVESV: left ventricular end-systolic volume; NYHA: New York Heart Association; PASP: pulmonary arterial systolic pressure; STS: Society of Thoracic Surgeons; TVMR: transcatheter mitral valve repair

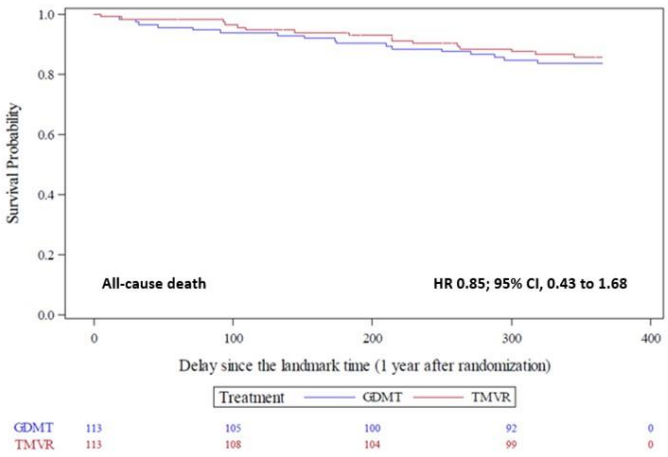


Supplementary Figure 1. Cumulative number of hospitalisations for HF per 100 patient-years. Cumulative rates of recurrent hospitalisations for heart failure in the guideline-directed medical treatment (GDMT) and in the transcatheter mitral valve repair (TMVR) groups between 12 and 24 months after inclusion in the MITRA-FR trial. Landmark analysis in the selected subgroup of MITRA-FR patients still alive at 12 months (whether they were hospitalised or not for heart failure within the first year).

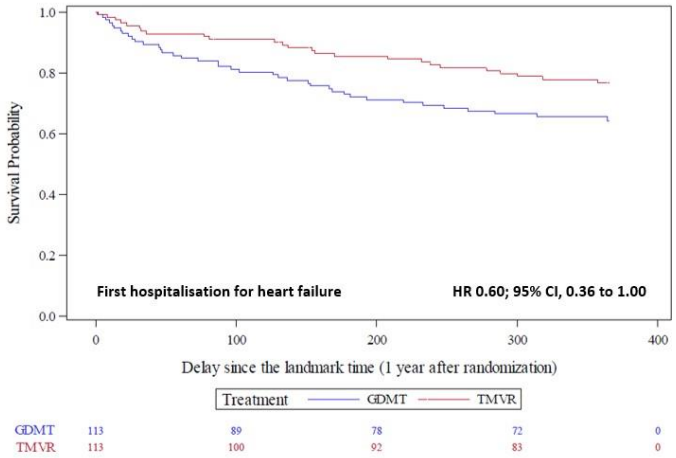
CI: confidence interval



Supplementary Figure 2. Kaplan-Meier estimates for all-cause death or unplanned heart failure hospitalisation in the guideline-directed medical treatment (GDMT) and in the transcatheter mitral valve repair (TMVR) groups between 12 and 24 months after inclusion in the MITRA-FR trial. Landmark analysis in the selected subgroup of MITRA-FR patients still alive at 12 months (whether they were hospitalised or not for heart failure within the first year). CI: confidence interval; HR: hazard ratio



Supplementary Figure 3. Kaplan-Meier estimates for all-cause death in the guideline-directed medical treatment (GDMT) and in the transcatheter mitral valve repair (TMVR) groups between 12 and 24 months after inclusion in the MITRA-FR trial. Landmark analysis in the selected subgroup of MITRA-FR patients still alive at 12 months (whether they were hospitalised or not for heart failure within the first year). CI: confidence interval; HR: hazard ratio



Supplementary Figure 4. Kaplan-Meier estimates for unplanned heart failure hospitalisation in the guideline-directed medical treatment (GDMT) and in the transcatheter mitral valve repair (TMVR) groups between 12 and 24 months after inclusion in the MITRA-FR trial. Landmark analysis in the selected subgroup of MITRA-FR patients still alive at 12 months (whether they were hospitalised or not for heart failure within the first year). CI: confidence interval; HR: hazard ratio