

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
<i>Echographic data</i>		
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±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)

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).

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
<i>Clinical data</i>			
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/m ²	25.3±4.5	25.4±3.9	0.80
Systolic blood pressure, mm Hg	108.8±16.3	108.4±18.7	0.67
Heart rate, beats/min	72.6±13.1	71.6±12.9	0.37
<i>Medical history</i>			
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
<i>Functional status/impact</i>			
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
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Echographic data

Left ventricular ejection fraction, %	33.9±5.9	33.0±6.7	0.38
Indexed LVEDV, ml/m ²	132.9±34.4	138.6±32.1	0.19
Indexed LVESV, ml/m ²	88.3±29.3	93.8±29.1	0.09
EROA, mm ²	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, mm ² /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
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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 NTproBNP 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	Non-included population	p-value
	(n=226)	(n=78)	
<i>Clinical data</i>			
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/m ²	25.4±4.2	24.5±3.4	0.14
Systolic blood pressure, mm Hg	108.6±17.5	108.1±15.0	0.77
Heart rate, beats/min	72.1±13.0	73.5±11.4	0.17
<i>Medical history</i>			
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
<i>Functional status/impact</i>			
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
<i>Echographic data</i>			
Left ventricular ejection fraction, %	33.5±6.3	31.9±7.1	0.05
Indexed LVEDV, ml/m ²	135.7±33.3	134.2±40.5	0.64
Indexed LVESV, ml/m ²	91.1±29.3	92.5±33.1	0.87
EROA, mm ²	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, mm ² /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
<i>Risk scores</i>			
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
<i>Medical treatment</i>			
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

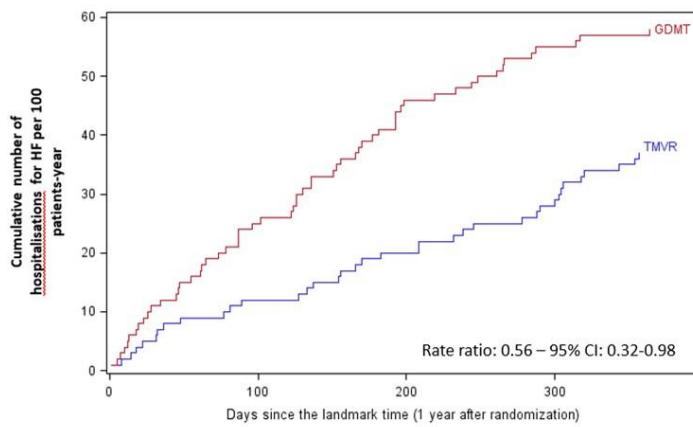
Angiotensin receptor and neprilysin inhibitors, n (%)	26 (12.3)	5 (7.2)	0.27
Beta blockers, n (%)	200 (88.5)	72 (92.3)	0.39
Mineralocorticoid receptor antagonists, n (%)	133 (59.1)	33 (42.3)	0.01
Loop diuretics, n (%)	222 (98.2)	78 (100)	0.57
Oral anticoagulants, n (%)	134 (59.3)	52 (66.7)	0.28

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.

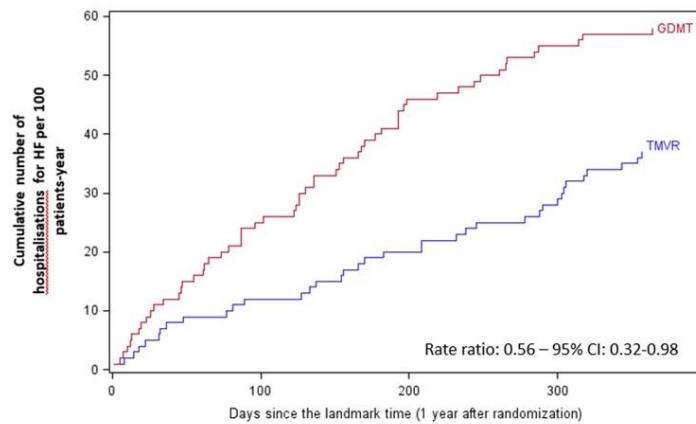
ACEi: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; EROA: effective regurgitant orifice area; GDMT: guideline-directed medical treatment; IQR: interquartile range; LVEDV: left ventricular end-diastolic volume; LVESV: left ventricular end-systolic volume; NYHA: New York Heart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

Figure 1

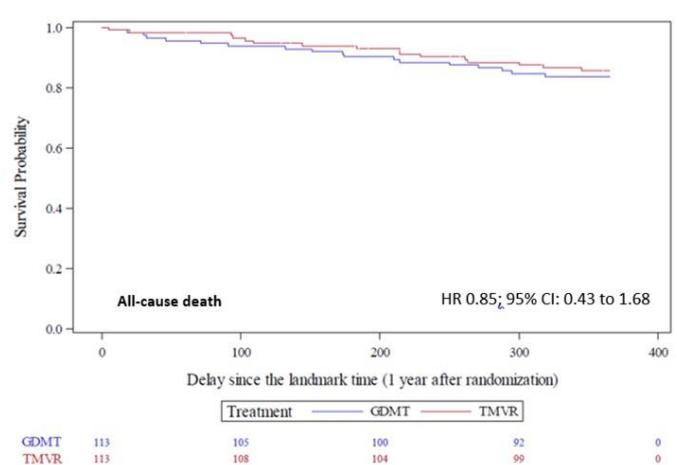


Supplementary Figure 1. Cumulative number of hospitalisations for HF per 100 patient-years. Cumulative rates of recurrent hospitalisations for heart failure in the guideline-directed medical treatment (GDMT) and in the transcatheter mitral valve repair (TMVR) groups between 12 and 24 months after inclusion in the MITRA-FR trial. CI: confidence interval

Figure 1

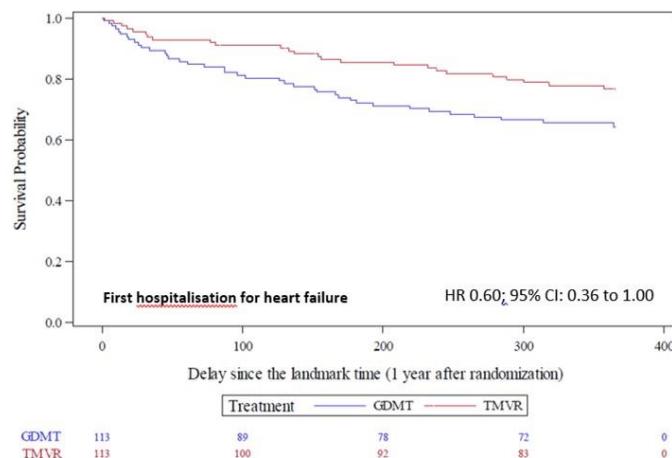


Supplementary Figure 2. Kaplan-Meier estimates for all-cause death or unplanned heart failure hospitalisation in the guideline-directed medical treatment (GDMT) and in the transcatheter mitral valve repair (TMVR) groups between 12 and 24 months after inclusion in the MITRA-FR trial. CI: confidence interval; 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. CI: confidence interval; HR: hazard ratio

Figure 4



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. CI: confidence interval; HR: hazard ratio