Supplemental material

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Heart

SUPPLEMENTAL MATERIALS

Supplemental Figure 1. Study flowchart

1152 patients who underwent TEER

→ Primary MR: 405 patients
LVEF >50%: 242 patients

504 patients with secondary MR and LVEF of <50%

→ Unavailable information of medication: 19 patients
In-hospital death: 22 patients

463 patients who were included to the analysis

GDMT patients
228 patients

Non-GDMT patients
235 patients
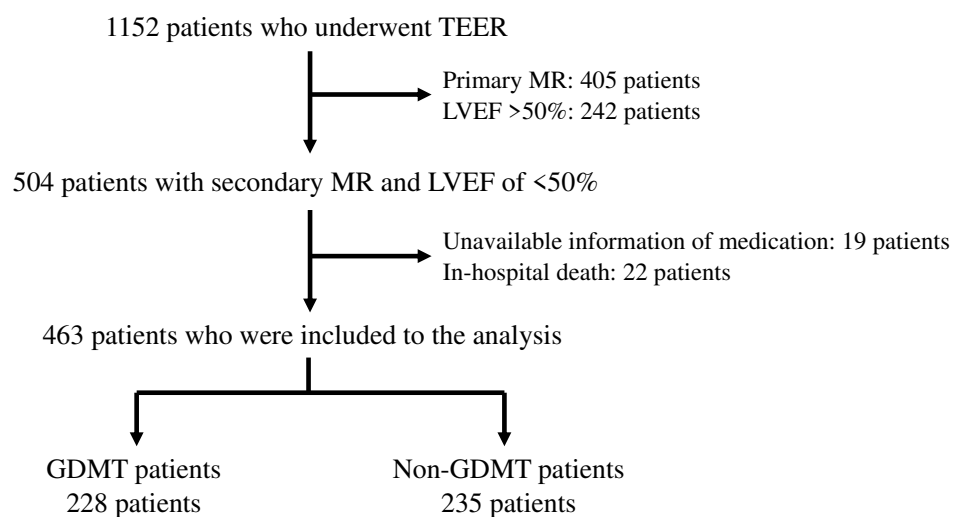
Legend: Study flowchart in the present study. TEER = transcatheter edge-to-edge mitral valve repair; MR = mitral regurgitation; LVEF = left-ventricular ejection fraction; GDMT = guideline-directed medical therapy

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Supplemental Figure 2. Distribution of propensity scores for guideline-directed medical therapy
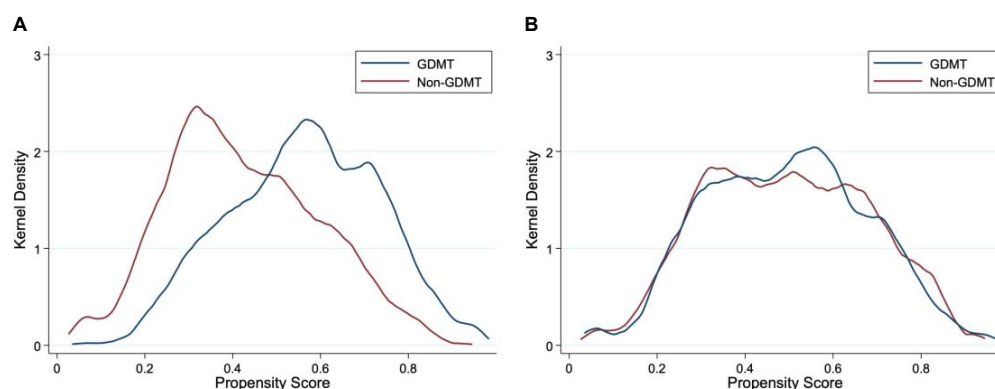
Legend: Kernel density plots showing the distributions of propensity scores in patients who received guideline-directed medical therapy (GDMT) and those who did not (A) before and (B) after inverse probability of treatment weighting.

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Supplemental Figure 3. Standardized differences of patient characteristics before and after inverse probability of treatment weighting
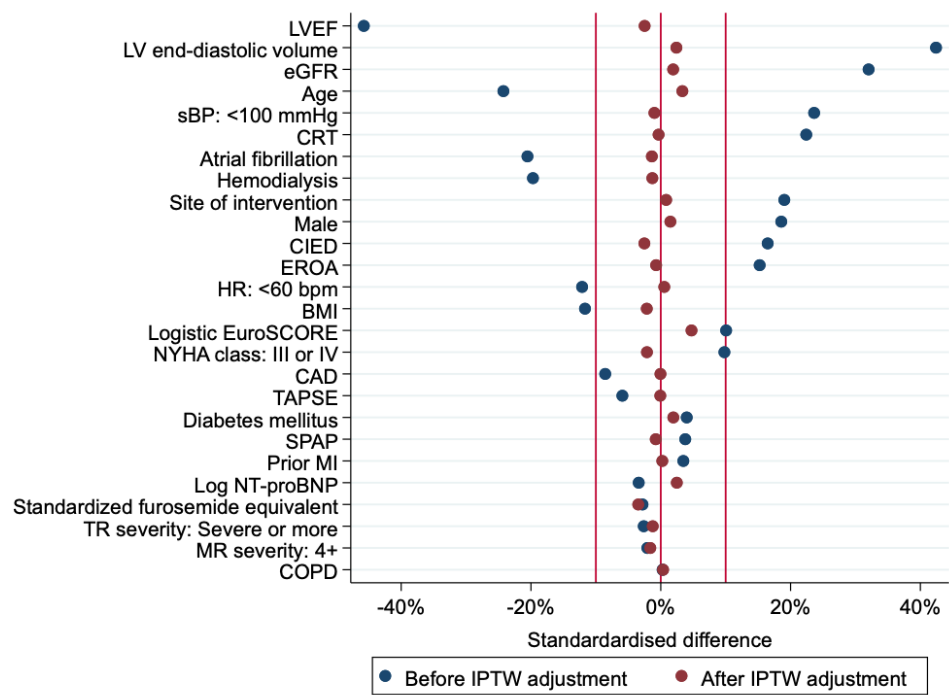
Legend: The standardized differences were smaller after inverse probability of treatment weighting. BMI = body mass index; CAD = coronary artery disease; MI = myocardial infarction; COPD = chronic obstructive pulmonary disease; NYHA = New York Heart Association; CIED = cardiac implantable electronic device; CRT = cardiac resynchronization therapy; COPD = chronic obstructive pulmonary disease; eGFR = estimated glomerular filtration rate; BP = blood pressure; HR = heart rate; EuroSCORE = European System for Cardiac Operative Risk Evaluation; MR = mitral regurgitation; EROA = effective regurgitant orifice area; LVEF = left ventricular ejection fraction; LVEDV = left ventricular end-diastolic volume; LVESV = left ventricular end-systolic volume; SPAP = systolic pulmonary artery pressure; TAPSE = tricuspid annular plane systolic excursion; TR = tricuspid regurgitation. NT-proBNP = N-terminal pro-B-type natriuretic peptide, TMVR = transcatheter mitral valve repair.

Supplemental Table 1. Percentage of missing values in baseline variables

	N=463
Age, n (%)	0 (0.0)
Male, n (%)	0 (0.0)
BMI, n (%)	32 (6.9)
Diabetes, n (%)	0 (0.0)
CAD, n (%)	1 (0.2)
Prior MI, n (%)	0 (0.0)
COPD, n (%)	0 (0.0)
CIED, n (%)	0 (0.0)
NYHA class, n (%)	0 (0.0)
Atrial fibrillation, n (%)	1 (0.2)
Systolic BP, n (%)	41 (8.9)
HR, n (%)	39 (8.4)
Logistic EuroSCORE, n (%)	0 (0.0)
Site of intervention, n (%)	0 (0.0)
eGFR, n (%)	5 (1.1)
Hemodialysis, n (%)	0 (0.0)
NT-proBNP, n (%)	45 (9.7)
MR severity, n (%)	5 (1.1)
EROA, n (%)	40 (8.6)
LVEF, n (%)	0 (0.0)
LVEDV, n (%)	45 (9.7)
SPAP, n (%)	45 (9.7)
TAPSE, n (%)	35 (7.6)
TR severe or more, n (%)	6 (1.3)
Standardized furosemide equivalent, n (%)	1 (0.2)
Post-procedural LVEF, n (%)	43 (9.3)
Residual MR, n (%)	5 (1.1)

Values are number (%).

Legends: BMI = body mass index; CAD = coronary artery disease; MI = myocardial infarction;

COPD = chronic obstructive pulmonary disease; NYHA = New York Heart Association; CIED

= cardiac implantable electronic device; eGFR = estimated glomerular filtration rate; BP = blood pressure; HR = heart rate; EuroSCORE = European System for Cardiac Operative Risk Evaluation; MR = mitral regurgitation; EROA = effective regurgitant orifice area; LVEF = left ventricular ejection fraction; LVEDV = left ventricular end-diastolic volume; SPAP = systolic pulmonary artery pressure; TAPSE = tricuspid annular plane systolic excursion; TR = tricuspid regurgitation.

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Supplemental Table 2. Procedural and post-procedural findings

	All	GDMT	Non-GDMT	
	n=463	n=228	n=235	p value
Procedural findings				
Number of clips	1.5 ± 0.7	1.6 ± 0.7	1.5 ± 0.6	0.325
Technical success, %	98.7	98.7	98.7	1.000
Post-procedural findings				
Residual MR				
0 or 1+, %	74.7	74.0	75.3	0.767
2+, %	19.9	22.4	17.6	0.749
3+ or more, %	5.4	3.6	7.1	0.141
Mean MVPG, mmHg	3.1 [2.2, 4.4]	3.1 [2.1, 4.3]	3.1 [2.2, 4.7]	0.805
LVEF, %	32.1 [25.0, 41.0]	29.2 [23.2, 36.6]	35.6 [27.5, 45.1]	<0.001

Values are either %, mean ± SD, or median [interquartile range].

Legend: GDMT = guideline-directed medical therapy; MR = mitral regurgitation; MVPG = mitral valvular pressure gradient; LVEF = left-ventricular ejection fraction.

Supplemental Table 3. Medical therapy for heart failure before the procedure

	All	GDMT	Non-GDMT	
	n=463	n=228	n=235	p value
GDMT	46.0	89.0	4.3	<0.001
Beta-blocker, %				<0.001
None	10.8	4.4	17.0	
1% to 24%	8.0	8.8	7.2	
25% to 49%	24.2	28.1	20.4	
50% to 99%	37.4	37.3	37.5	
100%	19.7	21.5	17.9	
RAS inhibitor, %				<0.001
None	22.5	6.6	37.9	
1% to 24%	12.1	17.1	7.2	
25% to 49%	28.1	33.8	22.6	
50% to 99%	25.5	30.7	20.4	
100%	11.9	11.8	11.9	
MRA, %	56.8	91.7	23.0	<0.001
Loop diuretics, %	84.0	89.5	78.7	0.002
Standardized furosemide equivalent, mg/day	30 [20, 60]	40 [20, 60]	30 [10, 60]	0.100

Values are either % or median [interquartile range].

Legends: GDMT = guideline-directed medical therapy; RAS = renin-angiotensin system; MRA = mineralocorticoid receptor antagonist.

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Supplemental Table 4. Univariate and multivariable Cox-proportional hazard analysis for all-cause mortality within two years in the non-weighted population

	Univariate analysis			Multivariable analysis		
	HR	95%CI	p value	HR	95%CI	p value
GDMT	0.58	0.38 - 0.89	0.012	0.52	0.33 - 0.81	0.004
Age, years	1.04	1.01 - 1.06	0.004	1.04	1.01 - 1.07	0.014
Male	1.37	0.84 - 2.23	0.206			
BMI, kg/m^2	0.98	0.94 - 1.03	0.436			
CAD	1.36	0.86 - 2.16	0.185			
Prior MI	1.13	0.75 - 1.71	0.560			
Diabetes mellitus	1.50	0.99 - 2.28	0.053	1.57	1.03 - 2.40	0.036
Atrial fibrillation	0.73	0.48 - 1.10	0.135			
eGFR, ml/min/1.73m^2	0.98	0.97 - 0.99	0.003	1.00	0.99 - 1.02	0.482
Hemodialysis	2.13	0.67 - 6.74	0.197			
NYHA class: III or IV	1.79	0.93 - 3.45	0.082	1.36	0.69 - 2.66	0.370
CIED	0.96	0.64 - 1.44	0.840			
CRT	1.16	0.70 - 1.92	0.570			
COPD	1.02	0.60 - 1.75	0.935			
Logistic EuroSCORE, %	1.00	0.99 - 1.02	0.506			
Log NT-proBNP	1.80	1.50 - 2.17	<0.001	1.59	1.24 - 2.03	<0.001
Site of intervention						
University Hospital Bonn	1 [Ref.]					
University Hospital Düsseldorf	0.72	0.43 - 1.20	0.202			
University Hospital Cologne	1.03	0.64 - 1.66	0.917			
LVEF, %	0.99	0.96 - 1.01	0.362			
LVEDV, ml	1.00	0.99 - 1.00	0.949			
EROA, mm^2	1.00	0.98 - 1.02	0.834			
MPG, mmHg	0.98	0.80 - 1.19	0.804			
TAPSE, mm	0.94	0.90 - 0.99	0.022	0.98	0.93 - 1.04	0.518
SPAP, mmHg	1.00	0.98 - 1.01	0.752			
Standardized furosemide equivalent, mg/day	1.00	1.00 - 1.01	0.001	1.00	0.99 - 1.01	0.137

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Residual MR: 2+ or more	1.58	1.04 - 2.41	0.032	1.28	0.83 - 1.98	0.266
Post-procedural LVEF, %	0.98	0.96 - 0.99	0.035	0.98	0.96 - 1.00	0.115

Legend: GDMT = guideline-directed medical therapy; BMI = body mass index; CAD = coronary artery disease; MI = myocardial infarction; NYHA = New York Heart Association; CIED = cardiac implantable electronic device; CRT = cardiac resynchronization therapy; COPD = chronic obstructive pulmonary disease; eGFR = estimated glomerular filtration rate; EuroSCORE = European System for Cardiac Operative Risk Evaluation; MR = mitral regurgitation; EROA = effective regurgitant orifice area; MPG = mean pressure gradient; LVEF = left ventricular ejection fraction; LVEDV = left ventricular end-diastolic volume; SPAP = systolic pulmonary artery pressure; TAPSE = tricuspid annular plane systolic excursion; TR = tricuspid regurgitation.

Supplemental Table 5. Echocardiographic assessments at one year after transcatheter edge-to-edge mitral valve repair

	All	GDMT	Non-GDMT	
	n=192	n=108	n=84	p value
LVEF, %	33.2 [25.8, 41.6]	31.0 [24.3, 37.0]	38.0 [30.0, 45.0]	0.001
LVEDV, ml	184 [133, 240]	189 [136, 250]	177 [125, 226]*	0.118
LVESV, ml	117 [79, 172]	129 [85, 184]	108 [74, 153]*	0.018
LVRR, %	33.9	40.2	26.8	0.038

Values are either % or median [interquartile range]. * p<0.05 vs. baseline

Legend: LVEF = left-ventricular ejection fraction; LVEDV = left-ventricular end-diastolic volume;

LVESV = left-ventricular end-systolic volume; LVRR = left-ventricular reverse remodeling.

Supplemental Table 6. Medical therapies at three months and one year after transcatheter edge-to-edge mitral valve repair

	All	GDMT	Non-GDMT	p value
At 3 months	n=243	n=131	n=112	
GDMT, %	49.4	85.5	7.1	<0.001
Beta-blockers, %				0.088
None	4.9	1.5	8.9	
1% to 24%	7.4	6.1	8.9	
25% to 49%	27.2	29.0	25.0	
50% to 99%	37.5	38.9	35.7	
100%	23.1	24.4	21.4	
RAAS inhibitors, %				<0.001
None	21.0	6.1	38.4	
1% to 24%	17.7	23.7	10.7	
25% to 49%	23.5	26.0	20.5	
50% to 99%	30.9	35.9	25.0	
100%	7.0	8.4	5.4	
MRAs, %	60.1	90.8*	24.1	<0.001
Loop diuretic, %	92.6	93.9	91.1	0.393
Standardized furosemide equivalent, mg/day	40 [20, 60]	40 [20, 75]	35 [20, 60]	0.209
At 1 year	n=195	n=109	n=86	
GDMT, %	49.2	77.1	14.0	<0.001
Beta-blockers, %				0.365
None	5.6	2.8	9.3	
1% to 24%	10.8	11.0	10.5	
25% to 49%	28.7	31.2	25.6	
50% to 99%	39.5	38.5	40.7	
100%	15.4	16.5	14.0	
RAS inhibitors, %				0.003
None	18.5	9.2	30.2	
1% to 24%	21.0	23.9	17.4	
25% to 49%	23.1	22.0	24.4	

50% to 99%	28.2	33.9	20.9	
100%	9.2	11.0	7.0	
MRAs, %	60.0	83.5*	30.2*	<0.001
Loop diuretics, %	90.3	94.5	84.9	0.025
Standardized furosemide equivalent, md/day	40 [20, 60]	40 [20, 60]	30 [10, 50]	0.059

Values are either percent or median [interquartile range]. * p<0.05 vs. baseline.

Legend: GDMT = guideline-directed medical therapy; RAS = renin-angiotensin- system; MRA = mineralocorticoid receptor antagonist.

Supplemental Table 7. Comparison of baseline characteristics between patients with completed and lost follow-up

	Completed follow-up n=249	Lost follow-up n=219	p value
Age, years	74 ± 9	74 ± 9	0.651
Female, %	71.5	73.8	0.573
BMI, kg/m^2	26.0 ± 4.5	26.3 ± 4.9	0.523
Diabetes, %	35.3	32.7	0.552
Hypertension, %	75.5	80.4	0.209
CAD, %	68.7	65.7	0.501
Prior MI, %	43.0	42.1	0.842
Prior CABG, %	35.3	36	0.886
COPD, %	15.3	21	0.107
CIED, %	55.0	56.1	0.820
CRT, %	16.9	22	0.165
NYHA class III/IV, %	83.5	79.9	0.313
Atrial fibrillation, %	61.0	63.4	0.606
Systolic BP, mmHg	118 ± 20	120 ± 17	0.317
SBP <100 mmHg, %	11.3	7.6	0.233
Diastolic BP, mmHg	68 ± 11	70 ± 11	0.072
HR, bpm	73 ± 13	75 ± 13	0.067
HR <60 bpm, %	11.8	7.7	0.192
Logistic EuroSCORE, %	19.5 [10.9, 32.0]	20.8 [11.7, 35.4]	0.532
Site of intervention			0.001
University Hospital Bonn, %	45.8	36.5	
University Hospital Düsseldorf, %	33.7	27.1	
University Hospital Cologne, %	20.5	36.5	
eGFR	44.3 [32.4, 62.0]	42.1 [31.5, 58.9]	0.809
>60 ml/min/m^2, %	27.7	24.3	0.681
30 to 60 ml/min/m^2, %	50.6	54.2	
<30 ml/min/m^2, %	21.7	21.5	
Hemodialysis, %	2.4	0.9	0.296

NT-proBNP, pg/ml	4526 [2181, 9872]	3510 [1874, 6499]	0.015
Echocardiographic findings			
MR severity			0.534
3+, %	29.7	26.9	
4+, %	70.3	73.1	
EROA, mm^2	25.0 [20.0, 33.0]	28.6 [20.0, 38.0]	0.226
LVEF, %	32.6 [26.0, 40.0]	32.0 [26.0, 40.1]	0.718
40% to 50%, %	25.3	33.6	0.052
LVEDV, ml	168 [134, 219]	179 [138, 218]	0.326
LVESV, ml	116 [84, 152]	123 [89, 157]	0.471
LA volume, ml	101 [80, 124]	100 [78, 125]	0.931
SPAP, mmHg	48 ± 16	49 ± 16	0.404
TAPSE, mm	16 ± 5	18 ± 5	0.011
TR severe or more, %	24.5	26.4	0.637

Values are either %, mean ± SD, or median [interquartile range].

Legends: BMI = body mass index; CAD = coronary artery disease; CABG = coronary artery bypass grafting; MI = myocardial infarction; COPD = chronic obstructive pulmonary disease; NYHA = New York Heart Association; CIED = cardiac implantable electronic device; CRT = cardiac resynchronization therapy; eGFR = estimated glomerular filtration rate; BP = blood pressure; HR = heart rate; EuroSCORE = European System for Cardiac Operative Risk Evaluation; MR = mitral regurgitation; EROA = effective regurgitant orifice area; LVEF = left ventricular ejection fraction; LVEDV = left ventricular end-diastolic volume; LVESV = left ventricular end-systolic volume; LA = left atrium; SPAP = systolic pulmonary artery pressure; TAPSE = tricuspid annular plane systolic excursion; TR = tricuspid regurgitation.