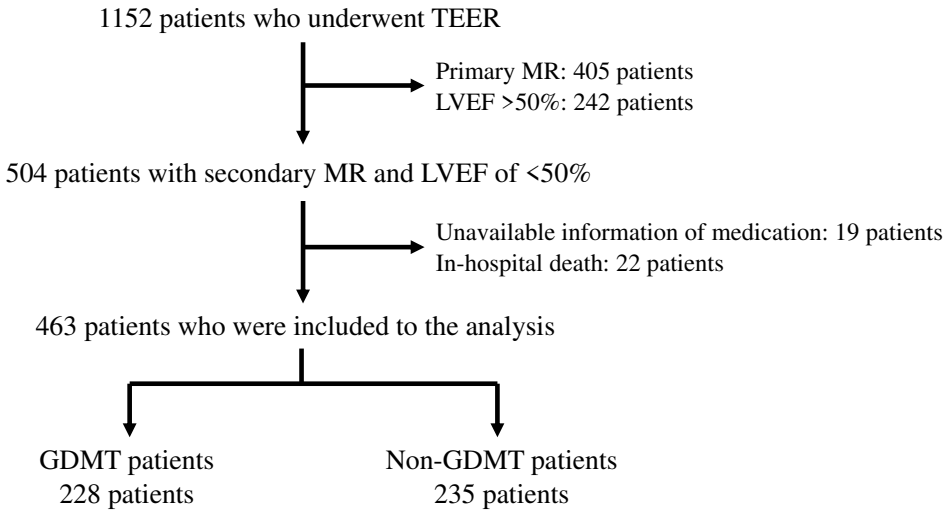
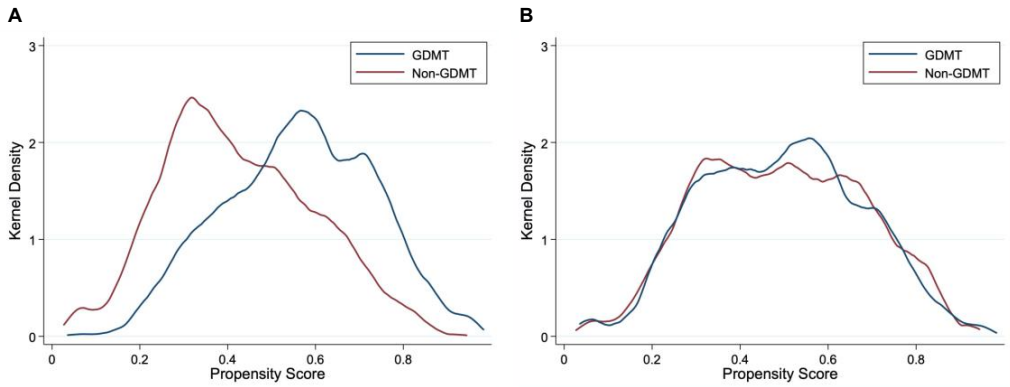
SUPPLEMENTAL MATERIALS

Supplemental Figure 1. Study flowchart



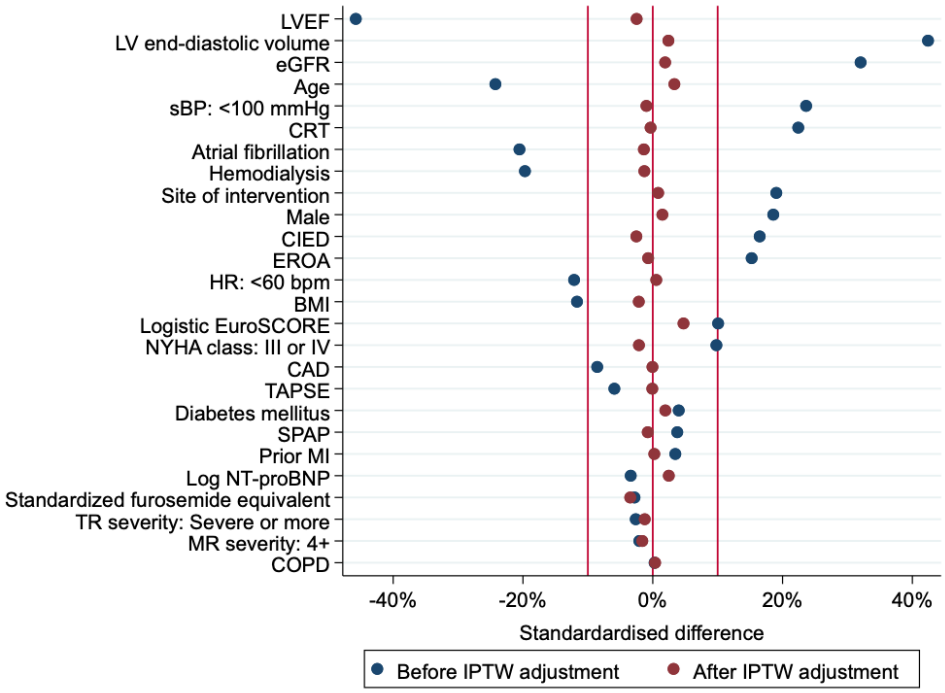
Legend: Study flowchart in the present study. TEER = transcatheter edge-to-edge mitral valve repair; MR = mitral regurgitation; LVEF = left-ventricular ejection fraction; GDMT = guideline-directed medical therapy

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.

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.

Supplemental Table 2. Procedural and post-procedural findings

	All n=463	GDMT n=228	Non-GDMT 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.

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

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 n=192	GDMT n=108	Non-GDMT 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.