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Heart Failure Therapy Optimization in the M-TEER Pathway: a missed opportunity before referral?

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Introduction: Mitral transcatheter edge-to-edge repair (M-TEER) is a treatment option for patients with severe symptomatic secondary mitral regurgitation (SMR), as well as for patients with primary mitral regurgitation (PMR) at high surgical risk. While optimized guideline-directed medical therapy (GDMT) is a formal prerequisite for M-TEER in SMR, heart failure (HF) therapy in PMR patients is guided by general HF recommendations. Real-world data regarding GDMT optimization in setting of the M-TEER procedure are limited.[1-3] The aim of our study was to explore the GDMT patterns in patients referred for the M-TEER procedure at our institution.

Patients and Methods: Our retrospective registry-based study included patients with PMR and SMR who underwent a successful M-TEER procedure at our institution. Use and dosing patterns of the four-pillar HF therapy were compared at screening, after screening, and at discharge after the procedure, with regard for hemodynamic (blood pressure and heart rate) and laboratory parameters (serum creatinine and potassium levels), as possible limitations for up-titration. Optimal GDMT was defined as at least three drug classes at maximally tolerated doses, with documented reasons for any limitation.

Results: We included 42 patients, 35 with SMR and 7 with PMR, **Table 1**. At screening, only 3 patients (7%) received all four drug classes at maximal doses, 14 (33%) received all four classes and 19 (45%)

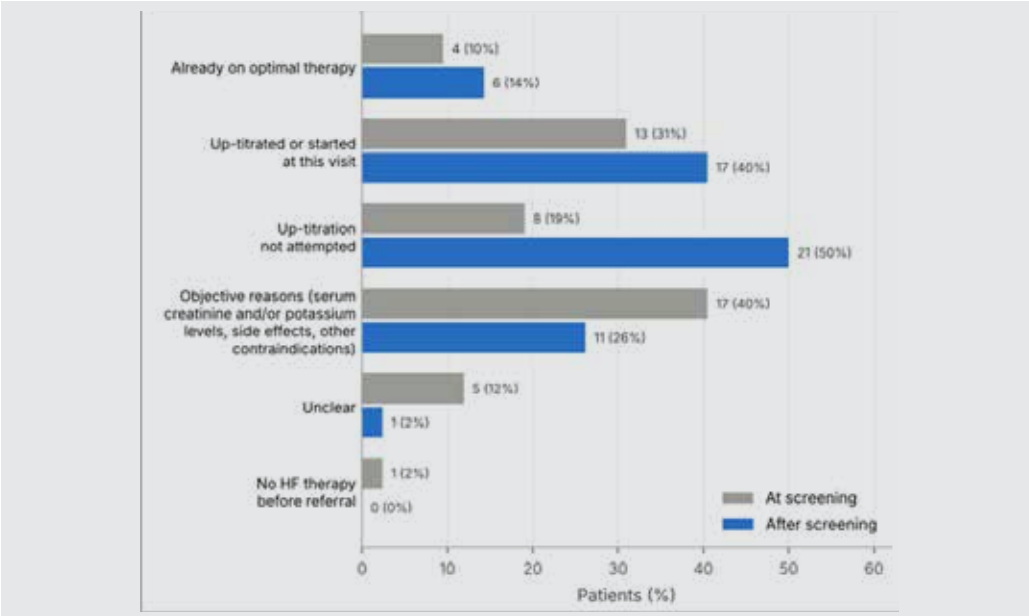


FIGURE 1. Documented status of GDMT optimization at screening and after screening in patients undergoing M-TEER (n=42). Categories are not mutually exclusive.

Abbreviations: CKD – chronic kidney disease; GDMT – guideline-directed medical therapy; HF – heart failure; M-TEER, mitral transcatheter edge-to-edge repair

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TABLE 1. Baseline characteristics at screening (n = 42).

Characteristic	All (n=42)	Primary MR (n=7)	Secondary MR (n=35)	p (primary *vs* secondary)
Demographics and clinical status				
Age, years	74 (67–80)	79 (66–82)	74 (68–79)	0.62
Male	27 (64%)	5 (71%)	22 (63%)	1.00
MR etiology				
Primary	7 (17%)	7 (100%)	0 (0%)	
Secondary	20 (48%)	0 (0%)	20 (57%)	
Predominantly secondary	8 (19%)	0 (0%)	8 (23%)	
Mixed	7 (17%)	0 (0%)	7 (20%)	
LVEF, %	41 (35–55)	50 (44–52)	37 (33–55)	0.15
≤40%	21 (50%)	1 (14%)	20 (57%)	
41–49%	6 (14%)	2 (29%)	4 (11%)	
≥50%	15 (36%)	4 (57%)	11 (31%)	0.23
NYHA class [n=41; primary n=7; secondary n=34]				0.71
I	3 (7%)	0 (0%)	3 (9%)	
II	23 (55%)	4 (57%)	19 (54%)	
III	15 (36%)	3 (43%)	12 (34%)	
IV	1 (2%)	0 (0%)	1 (3%)	
≥1 HF hospitalization in previous 12 months	22 (52%)	2 (29%)	20 (57%)	0.23
ICD / CRT-D	14 (33%)	0 (0%)	14 (40%)	0.08
Rhythm at screening				
Sinus rhythm	15 (36%)	5 (71%)	10 (29%)	
Atrial fibrillation/flutter	17 (40%)	1 (14%)	16 (46%)	
Paced rhythm	6 (14%)	1 (14%)	5 (14%)	
CRT	3 (7%)	0 (0%)	3 (9%)	
Unknown	1 (2%)	0 (0%)	1 (3%)	
Vital signs at screening				
Systolic blood pressure, mmHg	129 (110–148) [n=40]	130 (113–142)	128 (110–147) [n=33]	0.83
Diastolic blood pressure, mmHg	80 (70–90) [n=40]	80 (75–90)	80 (70–90) [n=33]	0.62
Systolic blood pressure <100 mmHg	0 (0%)	0 (0%)	0 (0%)	
Heart rate, bpm	80 (70–87) [n=41]	77 (68–86) [n=6]	80 (70–88)	0.58
Heart rate <60 bpm	1 (2%)	0 (0%)	1 (3%)	
Laboratory at screening				
NT-proBNP, pg/mL	3284 (1047–7042) [n=30]	2072 (1496–2647) [n=2]	4030 (1168–7696) [n=28]	0.46
Creatinine, µmol/L	118 (90–154)	87 (84–90)	129 (107–160)	0.008
eGFR, mL/min/1.73 m²	42.8 (35.3–67.1)	76.0 (67.5–77.5)	42.3 (33.9–58.1)	0.008
eGFR <30 mL/min/1.73 m²	5 (12%)	0 (0%)	5 (14%)	0.57
Potassium, mmol/L	4.3 (4.0–4.7)	4.3 (4.1–4.9)	4.3 (4.0–4.6)	0.67
Potassium >5.0 mmol/L	4 (10%)	0 (0%)	4 (11%)	1.00
Sodium, mmol/L	139 (138–141)	138 (138–140)	139 (138–141)	0.62
Hemoglobin, g/L	137 (123–147) [n=40]	137 (121–144)	137 (123–147) [n=33]	0.87
Pathway				
Time from screening to M-TEER, days	98 (72–142)	109 (68–126)	97 (78–143)	1.00

Values are median (interquartile range) or n (%). Where data were incomplete, the number of patients with available data is shown in brackets. NT-proBNP excludes one value at the assay ceiling (35001 pg/mL). Primary vs secondary comparisons use Fisher's exact test or the Mann–Whitney U test.

Abbreviations: CRT, cardiac resynchronization therapy; CRT-D, cardiac resynchronization therapy defibrillator; eGFR, estimated glomerular filtration rate; HF, heart failure; ICD, implantable cardioverter-defibrillator; LVEF, left ventricular ejection fraction; M-TEER, mitral transcatheter edge-to-edge repair; MR, mitral regurgitation; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association.

were on optimal GDMT. Up-titration had never been attempted in 8 patients (19%), while intolerance or objective contraindications limited therapy in 17 (40%). From screening to discharge, therapy was optimized in 33 patients (79%). Four-pillar therapy increased from 33% to 57% (p=0.021), and from 43% to 81% in patients with LVEF ≤40% (p=0.008). Optimal GDMT increased from 45% at screening to 57% after screening and 74% at discharge (p=0.002) (**Table 2** and **Figure 1**). In the SMR group, optimal GDMT increased from 49% to 77% (p=0.006) and four-pillar therapy from 37% to 66% (p=0.013). Compared with SMR, despite 6 of 7 (86%) PMR patients had a documented heart failure diagnosis at screening, they less often received SGLT2 inhibitors (29% vs 89%, p=0.003) and four-pillar therapy (14% vs 66%, p=0.031).

TABLE 2. GDMT of the whole cohort (n = 42) at screening, after screening and at discharge.

	Screening	After screening	Discharge	p (screening vs after)	p (screening vs discharge)
Drug classes					
Beta-blocker	37 (88%)	38 (90%)	39 (93%)	1.00	0.62
ACEi / ARB / ARNI	30 (71%)	33 (79%)	34 (81%)	0.38	0.34
ACEi	16 (38%)	16 (38%)	14 (33%)	1.00	0.77
ARB	2 (5%)	3 (7%)	3 (7%)	1.00	1.00
ARNI	12 (29%)	14 (33%)	17 (40%)	0.50	0.06
MRA	30 (71%)	32 (76%)	37 (88%)	0.62	0.016
SGLT2 inhibitor	26 (62%)	31 (74%)	33 (79%)	0.06	0.039
Dose intensity					
Beta-blocker ≥50% of target dose	21 (50%)	28 (67%)	30 (71%)	0.039	0.004
ACEi/ARB/ARNI ≥50% of target dose	14 (33%)	18 (43%)	25 (60%)	0.22	0.013
MRA ≥25 mg	29 (69%)	31 (74%)	37 (88%)	0.62	0.008
Beta-blocker at target dose	2 (5%)	6 (14%)	3 (7%)	0.12	1.00
ACEi/ARB/ARNI at target dose	4 (10%)	5 (12%)	5 (12%)	1.00	1.00
Overall GDMT					
Number of drug classes					
0–1	3 (7%)	1 (2%)	2 (5%)		
2	11 (26%)	8 (19%)	3 (7%)		
3	14 (33%)	15 (36%)	13 (31%)		
4 (four-pillar therapy)	14 (33%)	18 (43%)	24 (57%)	0.22	0.021
Number of classes, median (IQR)	3 (2–4)	3 (3–4)	4 (3–4)	0.013	0.003
Four-pillar therapy, LVEF ≤40% [n=21]	9 (43%)	10 (48%)	17 (81%)	1.00	0.008
All four classes at maximal doses	3 (7%)	12 (29%)	–	0.004	–
Optimal GDMT*	19 (45%)	24 (57%)	31 (74%)	0.27	0.002
Diuretics					
Furosemide dose, mg/day	60 (40–125)	60 (40–125)	102 (45–125)	0.11	0.017

Abbreviations: ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor–neprilysin inhibitor; GDMT, guideline-directed medical therapy; IQR, interquartile range; LVEF, left ventricular ejection fraction; MRA, mineralocorticoid receptor antagonist; SGLT2, sodium-glucose cotransporter 2.

Conclusion: GDMT remains suboptimal both before and after screening for M-TEER. HF therapy optimization is paramount regardless of MR etiology; therefore, efforts should be made to implement a structured clinical algorithm for GDMT optimization prior to the procedure.

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