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ORIGINAL INVESTIGATIONS

Predictors of Clinical Response to Transcatheter Reduction of Secondary Mitral Regurgitation

The COAPT Trial

Paul A. Grayburn, MD,[a] Anna Sannino, MD,[a] David J. Cohen, MD, MSc,[b] Saibal Kar, MD,[c,d] D. Scott Lim, MD,[e] Jacob M. Mishell, MD,[f] Brian K. Whisenant, MD,[g] Michael J. Rinaldi, MD,[h] Samir R. Kapadia, MD,[i] Vivek Rajagopal, MD,[j] Aaron Crowley, MA,[k] Lak N. Kotinkaduwa, PhD,[k] JoAnn Lindenfeld, MD,[l] William T. Abraham, MD,[m] Michael J. Mack, MD,[a] Gregg W. Stone, MD[k,n]

ABSTRACT

BACKGROUND Transcatheter mitral valve repair with the MitraClip results in marked clinical improvement in some but not all patients with secondary mitral regurgitation (MR) and heart failure (HF).

OBJECTIVES This study sought to evaluate the clinical predictors of a major response to treatment in the COAPT trial.

METHODS Patients with HF and severe MR who were symptomatic on maximally tolerated guideline-directed medical therapy (GDMT) were randomly assigned to MitraClip plus GDMT or GDMT alone. Super-responders were defined as those alive without HF hospitalization and with ≥20-point improvement in the Kansas City Cardiomyopathy Questionnaire overall summary (KCCQ-OS) score at 12 months. Responders were defined as those alive without HF hospitalization and with a 5 to <20-point KCCQ-OS improvement at 12 months. Nonresponders were those who either died, were hospitalized for HF, or had <5-point improvement in KCCQ-OS at 12 months.

RESULTS Among 614 enrolled patients, 41 (6.7%) had missing KCCQ-OS data and could not be classified. At 12 months, there were 79 super-responders (27.2%), 55 responders (19.0%), and 156 nonresponders (53.8%) in the MitraClip arm compared with 29 super-responders (10.2%), 46 responders (16.3%), and 208 nonresponders (73.5%) in the GDMT-alone arm (overall $p < 0.0001$). Independent baseline predictors of clinical responder status were lower serum creatinine and KCCQ-OS scores and treatment assignment to MitraClip. MR grade and estimated right ventricular systolic pressure at 30 days were improved to a greater degree in super-responders and responders but not in nonresponders.

CONCLUSIONS Baseline predictors of clinical super-responders in patients with HF and severe secondary MR in the COAPT trial were lower serum creatinine, KCCQ-OS score and MitraClip treatment. Improved MR severity and reduced right ventricular systolic pressure at 30 days are associated with a long-term favorable clinical response after transcatheter mitral valve repair. (Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients With Functional Mitral Regurgitation [COAPT]; NCT01626079)
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From the [a]Baylor Heart and Vascular Institute, Baylor University Medical Center, Dallas, Texas; [b]University of Missouri-Kansas City School of Medicine, Kansas City, Missouri; [c]Los Robles Regional Medical Center, Thousand Oaks, California; [d]Bakersfield Heart Hospital, Bakersfield, California; [e]Division of Cardiology, University of Virginia, Charlottesville, Virginia; [f]Kaiser Permanente-San Francisco Hospital, San Francisco, California; [g]Intermountain Heart Center, Salt Lake City, Utah; [h]Sanger Heart & Vascular Institute/Atrium Health, Charlotte, North Carolina; [i]Cleveland Clinic, Cleveland, Ohio; [j]Piedmont Hospital, Atlanta, Georgia; [k]Clinical Trials Center, Cardiovascular Research Foundation, New York, New York; [l]Vanderbilt Heart and

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ABBREVIATIONS AND ACRONYMS

CI = confidence interval

CRT = cardiac resynchronization therapy

GDMT = guideline-directed medical therapy

HF = heart failure

KCCQ-OS = Kansas City Cardiomyopathy Questionnaire overall summary

LV = left ventricular

MR = mitral regurgitation

OR = odds ratio

RVSP = right ventricular systolic pressure

TMVr = transcatheter mitral valve repair

Two randomized clinical trials of edge-to-edge transcatheter mitral valve repair (TMVr) with the MitraClip compared with guideline-directed medical therapy (GDMT) in patients with heart failure (HF) and secondary mitral regurgitation (MR) have shown different results. In the COAPT (Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients with Functional Mitral Regurgitation) trial, treatment of secondary MR with the MitraClip reduced HF hospitalizations at 2 years and demonstrated a substantial survival benefit (1). Conversely, no difference in death or HF hospitalization at 1 year was present after MitraClip treatment for secondary MR in the MITRA-FR (Multicentre Randomized Study of Percutaneous Mitral Valve Repair MitraClip Device in Patients With Severe Secondary Mitral Regurgitation) trial (2). These discordant results may in part be explained by enrollment of different patient populations in the 2 trials, indicating that there are some patients who benefit from TMVr and others who do not (3–6). This phenomenon is not unique to TMVr but has also been described for cardiac resynchronization therapy (CRT) for HF, wherein approximately one-third of patients do not respond in terms of reduced HF symptoms or improved left ventricular (LV) function or reverse LV remodeling (7–9). Conversely, there are a group of patients, termed "super-responders," who demonstrate marked improvement in symptoms along with nearly complete recovery of LV function after CRT (9). Experienced operators have also observed a divergence of clinical response to MR reduction with TMVr ranging from nonresponders to super-responders; however, no study has formally evaluated the incidence and predictors of clinical response after TMVr in HF, in part because of limited collection of quality-of-life data in large registries. We therefore performed a post hoc analysis to evaluate the clinical predictors of a major response to treatment in the COAPT trial.

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METHODS

Details of the COAPT study protocol and main results have been previously published (1). Briefly, patients with established HF and severe (3+ or 4+) secondary MR with LV ejection fraction 20% to 50% and LV end-systolic diameter <70 mm were eligible for enrollment if they remained symptomatic on maximally tolerated doses of GDMT for HF. The Institutional Review Board at each participating site approved the study, and all patients provided informed, written consent to participate. Appropriate titration of antineurohormonal medications along with either CRT and/or coronary revascularization, when indicated, were to be performed before randomization and validated by a central eligibility committee. Subjects were then randomly assigned to TMVr with the

Vascular Institute, Nashville, Tennessee; [m]Division of Cardiovascular Medicine, The Ohio State University, Columbus, Ohio; and [n]The Zena and Michael A. Wiener Cardiovascular Institute, Icahn School of Medicine at Mount Sinai, New York, New York. The COAPT trial was sponsored by Abbott (Santa Clara, California). Dr. Grayburn has received consulting fees from Abbott Vascular, Edwards Lifesciences, W.L. Gore, Medtronic, and 4C Medical; and has received grant support from Abbott Vascular, Boston Scientific, Cardiovalve, Edwards Lifesciences, W.L. Gore, Medtronic, and Neochord. Dr. Cohen has received research grant support from Abbott, Medtronic, Edwards Lifesciences, and Boston Scientific; and has received consulting income from Abbott, Medtronic, Edwards Lifesciences, and Boston Scientific. Dr. Kar has received consulting fees/served on the Advisory Board of Boston Scientific; has received consulting fees/stock equity from Valcare; and has received consulting fees from W.L. Gore and Medtronic. Dr. Lim has received research grant support from Abbott, Edwards, Medtronic, and Gore; has served as a consultant for Abbott, Edwards, Keystone Heart, Pipeline, Siemens, Valgen, and Venus; has served on the advisory board of Ancora and Venus; and has received equity from 510Kardiac and Venus. Dr. Whisenant has served as a consultant for Edwards Lifesciences, Boston Scientific, Gore, and Neochord. Dr. Rinaldi has served on the advisory board of Abbott, Boston Scientific, Cordis, and 4C Medical; has taught courses at Abbott and Edwards; has served as a consultant for Abbott, Boston, Edwards, and Cordis; and has received research support/grant from Boston Scientific. Dr. Kapadia has received stock options from Navigate Cardiac Structures, Inc. Dr. Lindenfeld has received research grant support from AstraZeneca; and has received consulting income from Abbott Vascular, AstraZeneca, CVRx, Edwards Lifesciences, Impulse Dynamics, Boehringer Ingelheim, and V-Wave. Dr. Abraham has received research grant support and consulting income from Abbott Vascular. Dr. Mack has served as co-primary investigator for the PARTNER Trial for Edwards Lifesciences and COAPT trial for Abbott; and has served as study chair for the APOLLO trial for Medtronic. Dr. Stone has received consulting income from Neovasc, Gore, Ancora, and Valfix; and has equity/options from Cardiac Success, Ancora, and Valfix. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose. Francesco Maisano, MD, served as Guest Associate Editor for this paper. P.K. Shah, MD, served as Guest Editor-in-Chief for this paper.
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MitraClip (Abbott, Santa Clara, California) plus GDMT (device arm) or GDMT alone (control arm). Before performing any analyses, we prospectively defined response groups based on modification of the clinical composite score for treatment response in HF (10), which focuses on vital status, HF hospitalization, and symptoms. For the latter, we used the change in Kansas City Cardiomyopathy Questionnaire overall summary (KCCQ-OS) score from baseline to 12-month follow-up. Changes in KCCQ-OS of 5, 10, or 20 points are associated with small, moderate, or large improvements in HF symptom status (11). Therefore, we defined nonresponders as those who within 12 months died, were hospitalized for HF, or had a <5-point improvement in KCCQ-OS from baseline. Responders were defined as those who were alive without HF hospitalization and had a 5 to <20-point KCCQ-OS improvement at 12 months. Super-responders were defined as those who were alive without HF hospitalization and had a ≥20-point improvement in KCCQ-OS at 12 months.

We first compared baseline demographic and clinical variables across all 3 responder groups to determine clinical variables associated with response to TMVr in patients with secondary MR. We then analyzed predictors of response separately in device and control arms. Because the results of the subsequent analysis demonstrated that treatment assignment was the most prominent predictor of response group, we further investigated the impact of a reduction in MR severity and estimated right ventricular systolic pressure (RVSP) at 30 days across response groups.

STATISTICAL ANALYSIS. Categorical data are reported as frequency and percentage and were compared by the chi-square test. Continuous data are reported as mean ± SD and were compared by analysis of variance. Responder status (super-responder vs. responder vs. nonresponder) was modeled using multivariable multinomial logistic regression models. Candidate predictors of responder status included those identified a priori based on prior historical relationships to outcomes (age, creatinine, Society of Thoracic Surgery predicted risk of mortality score for replacement and repair, MR severity [qualitative], effective regurgitant orifice area, LV end-diastolic and end-systolic volumes and ejection fraction, left atrial volume, RVSP) plus variables that were statistically significant on univariate analysis (as shown in **Table 1**). A 2-sided p value of <0.05 was selected as the threshold for statistical significance. All analyses were performed with SAS version 9.4 (SAS Institute, Cary, North Carolina).

RESULTS

Among the 614 enrolled subjects in the COAPT trial, 41 (6.7%) had missing KCCQ-OS data and could not be classified. The **Central Illustration (A)** shows the breakdown of vital status, HF hospitalization, and change in KCCQ-OS score at 12 months in the remaining 573 subjects randomized to MitraClip plus GDMT versus GDMT alone. There were 79 super-responders (27.2%), 55 responders (19.0%), and 156 nonresponders (53.8%) at 12 months in the device arm and 29 super-responders (10.2%), 46 responders (16.3%), and 208 nonresponders (73.5%) at 12 months in the control arm (p<0.0001).

COMPARISON OF BASELINE VARIABLES ACROSS RESPONSE GROUPS. **Table 1** shows baseline demographic, clinical, and selected echocardiographic characteristics of the super-responders, responders, and nonresponders in both treatment groups combined. A more detailed listing of the baseline echocardiographic measures in these groups is shown in Supplemental Table 1. By univariable analysis, there were significant differences between responder groups for prior stroke, KCCQ-OS score, serum creatinine, RVSP, and treatment assignment. **Table 2** shows the results of multivariable analysis in both treatment groups combined. Comparing super-responders and nonresponders, only treatment assignment (GDMT alone compared with MitraClip: odds ratio [OR]: 3.40; 95% confidence interval [CI]: 1.97 to 5.90; p < 0.0001), serum creatinine (per 1 mg/dl: OR: 0.66; 95% CI: 0.47 to 0.93; p = 0.018), and KCCQ-OS score (per 5 points: OR: 0.86; 95% CI: 0.80 to 0.91; p < 0.0001) were statistically significant. Comparing responders and nonresponders, only treatment assignment (GDMT alone compared with MitraClip: OR: 1.72; 95% CI: 1.02 to 2.92; p = 0.043) was statistically significant. In the overall model, treatment assignment, serum creatinine and baseline KCCQ-OS were statistically significant.

Super-responders were more likely to have ≤1+ residual MR at 30 days than responders or nonresponders (**Central Illustration, B**). Conversely, nonresponders were more likely to have severe (>2+) residual MR at 30 days. Both super-responders and responders had a significant decrease in estimated RVSP at 30 days, whereas nonresponders did not (**Central Illustration, C**).

COMPARISON OF RESPONDER GROUPS BY TREATMENT ARM. Supplemental Tables 2 and 3 show the unadjusted baseline predictors of super-responders, responders, and nonresponders in the device and

TABLE 1 Baseline Characteristics According to 1-Year Responder Status in All Patients

	Super-Responder (n = 108)	Responder (n = 101)	Nonresponder (n = 364)	p Value
Age, yrs	71.6 ± 12.3	72.9 ± 10.4	71.9 ± 11.1	0.65
Male	60.2 (65/108)	64.4 (65/101)	64.8 (236/364)	0.67
Race				
White	73.1 (79/108)	74.3 (75/101)	74.7 (272/364)	0.95
Black	18.5 (20/108)	10.9 (11/101)	13.7 (50/364)	0.27
Hispanic or Latino	4.6 (5/108)	9.9 (10/101)	6.3 (23/364)	0.29
Body mass index, kg/m^2	26.0 ± 5.2	27.1 ± 5.7	27.3 ± 6.2	0.15
Systolic blood pressure, mm Hg	111.1 ± 16.3	112.5 ± 16.9	110.9 ± 17.3	0.73
Diastolic blood pressure, mm Hg	66.4 ± 9.9	63.9 ± 8.5	64.2 ± 9.7	0.09
Heart rate, beats/min	74.9 ± 12.3	73.0 ± 14.1	74.3 ± 12.4	0.54
HFH within 12 months	53.7 (58/108)	59.4 (60/101)	57.1 (208/364)	0.70
Ischemic cardiomyopathy	61.1 (66/108)	58.4 (59/101)	60.7 (221/364)	0.90
Prior stroke	18.5 (20/108)	9.9 (10/101)	9.9 (36/364)	0.04
Coronary artery disease	73.1 (79/108)	64.4 (65/101)	74.5 (271/364)	0.13
Hypertension	77.8 (84/108)	83.2 (84/101)	80.5 (293/364)	0.62
Hypercholesterolemia	55.6 (60/108)	47.5 (48/101)	54.9 (200/364)	0.38
Chronic obstructive pulmonary disease	21.3 (23/108)	23.8 (24/101)	22.5 (82/364)	0.91
Atrial fibrillation	50.9 (55/108)	58.4 (59/101)	52.5 (191/364)	0.50
Diabetes	35.2 (38/108)	35.6 (36/101)	37.4 (136/364)	0.89
Peripheral vascular disease	13.0 (14/108)	15.8 (16/101)	19.0 (69/364)	0.32
Anemia	19.4 (21/108)	26.7 (27/101)	24.2 (88/364)	0.44
History of major bleeds	3.7 (4/108)	12.9 (13/101)	6.6 (24/364)	0.03
Prior coronary artery bypass grafting	40.7 (44/108)	33.7 (34/101)	41.2 (150/364)	0.38
Prior percutaneous coronary intervention	48.1 (52/108)	45.5 (46/101)	45.6 (166/364)	0.89
Prior defibrillator	63.9 (69/108)	56.4 (57/101)	62.9 (229/364)	0.45
Prior cardiac resynchronization therapy	34.3 (37/108)	35.6 (36/101)	37.4 (136/364)	0.83
STS replacement score	7.3 ± 5.1	7.3 ± 4.5	8.4 ± 6.2	0.07
STS repair score	4.9 ± 4.2	4.8 ± 3.6	6.0 ± 5.9	0.06
KCCQ-OS score	42.4 ± 16.9	57.9 ± 21.5	55.0 ± 24.0	<0.0001
Serum creatinine, mg/dl	1.5 ± 1.0	1.6 ± 0.6	1.9 ± 1.5	0.007
Elevated BNP or NT-proBNP	90.5 (95/105)	93.9 (92/98)	94.5 (326/345)	0.34
Moderate-to-severe (3+) MR	52.8 (57/108)	61.0 (61/100)	51.4 (187/364)	0.23
Severe (4+) MR	47.2 (51/108)	39.0 (39/100)	48.6 (177/364)	0.23
Effective regurgitant orifice area, cm^2	0.39 ± 0.12	0.39 ± 0.13	0.41 ± 0.17	0.32
Estimated RVSP, mm Hg	42.1 ± 13.5	41.9 ± 12.4	45.4 ± 13.3	0.02
LV ejection fraction, %	31.3 ± 10.0	32.6 ± 10.0	30.8 ± 8.8	0.27
LV end-diastolic volume, ml	187.0 ± 65.3	180.6 ± 73.4	197.6 ± 71.5	0.08
LV end-systolic volume, ml	130.8 ± 55.7	124.7 ± 60.7	138.7 ± 57.8	0.09
Left atrial volume, ml	87.4 ± 36.6	88.1 ± 32.1	93.6 ± 44.1	0.26
Randomized to MitraClip	73.1 (79/108)	54.5 (55/101)	42.9 (156/364)	<0.0001

Values are mean ± SD or % (n/N).

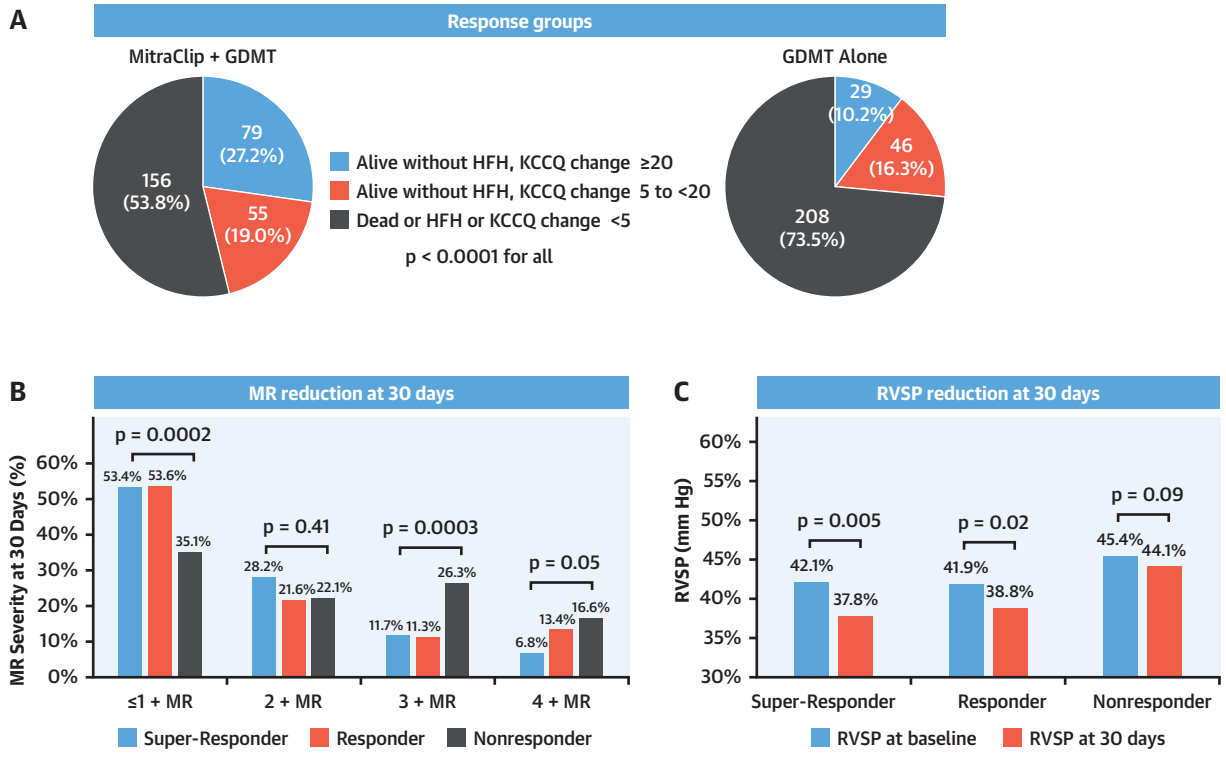
BNP = brain natriuretic peptide; HFH = heart failure hospitalization; ITT = intention-to-treat; KCCQ-OS = Kansas City Cardiomyopathy Questionnaire overall summary; LV = left ventricular; MR = mitral regurgitation; NT-proBNP = N-terminal pro b-type natriuretic peptide; RVSP = right ventricular systolic pressure; STS = Society of Thoracic Surgeons.

control arms, respectively, and Tables 3 and 4 show the multivariable predictors of response in these groups. Among MitraClip-assigned patients, only baseline KCCQ-OS was an independent predictor of super-responders and responders ($p < 0.0001$). In the control arm, there were no predictors of super-responders, responders, and nonresponders by multivariate analysis in the overall model, although baseline KCCQ-OS and serum creatinine level predicted super-responders.

DISCUSSION

The principal finding of the study is that among patients with HF and severe MR enrolled in the COAPT trial, the therapeutic response within 12 months was predicted by only 3 baseline parameters: lower serum creatinine and KCCQ-OS score and treatment assignment to TMVr with the MitraClip plus GDMT, rather than GDMT alone. Super-responders were more likely to be assigned to TMVr plus GDMT, and conversely,

CENTRAL ILLUSTRATION **Clinical Response to Treatment in the COAPT Trial**



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(A) Response categories in the device arm (MitraClip + guideline-directed medical therapy [GDMT]) versus the control arm (GDMT alone). Nonresponders (death, heart failure hospitalization [HFH], or change in Kansas City Cardiomyopathy Questionnaire [KCCQ] overall summary [OS] <5 points) are shown in **gray**; responders (alive without HFH with KCCQ-OS improvement 5 to <20 points) are shown in **red**; super-responders (alive without HFH and KCCQ-OS improvement ≥20 points) are shown in **blue** for GDMT plus TMVr **(left pie chart)** and GDMT alone **(right pie chart)**. **(B)** Change in mitral regurgitation (MR) severity at 30 days in responders and nonresponders. Core laboratory-adjudicated reduction in MR severity at 30 days for super-responders **(blue bars)**, responders **(red bars)**, and nonresponders **(gray bars)**. Super-responders were more likely to have mild (1+) MR and less likely to have severe (3+ or 4+) MR. **(C)** Change in right ventricular systolic pressure (RVSP) from baseline to 30 days in responders and nonresponders. Core laboratory-adjudicated reduction in RVSP at 30 days for super-responders **(blue bars)**, responders **(red bars)**, and nonresponders **(gray bars)**. There were statistically significant reductions in RVSP in super-responders and responders, but not nonresponders.

nonresponders were more likely to be assigned to GDMT alone. This finding was corroborated by the 30-day change in MR severity and estimated RVSP, suggesting that the mechanism underlying clinical response to TMVr is MR reduction. Nevertheless, 10% of patients randomized to GDMT alone were super-responders. This finding may reflect the well-known dynamic nature of MR (12–14) and the potential for secondary MR to improve over time with neurohormonal antagonists (15,16). Although an eligibility committee verified that patients were on appropriate doses of medical therapy before randomization with dosage stability for at least 30 days, it is possible that neurohormonal antagonists may continue to improve secondary MR severity beyond 30 days. Although few major changes were made in either treatment group during follow-up (1), detailed analysis of these patients in terms of more modest adjustments in medications pre- and post-randomization is warranted.

It is not surprising that lower baseline KCCQ-OS score was a predictor of responder status. A super-responder was defined as being alive without HF hospitalization and with a ≥20 point improvement in KCCQ-OS at 12 months. This definition is similar to the clinical composite score for classifying response to HF treatments proposed by Packer (10), but substitutes KCCQ-OS for New York Heart Association functional class. In COAPT, patients were selected for having symptoms despite maximally tolerated HF medications and were further enriched for HF events by either having: 1) an HF hospitalization within the prior 12 months; or 2) a corrected brain natriuretic

TABLE 2 Multivariable Predictors of 1-Year Responders in All Patients

	Super-Responder Versus Nonresponders		Responder Versus Nonresponders		
	Odds Ratio (95% CI)	p Value	Odds Ratio (95% CI)	p Value	Overall p Value
Randomized treatment (MitraClip vs. GDMT)	3.40 (1.97–5.90)	<0.0001	1.72 (1.02–2.92)	0.043	<0.0001
Serum creatinine (per 1 mg/dl)	0.66 (0.47–0.93)	0.018	0.76 (0.56–1.03)	0.08	0.022
RVSP (per 5 mm Hg)	0.92 (0.83–1.03)	0.14	0.91 (0.82–1.01)	0.08	0.11
LVEDV (per 10 ml)	1.00 (0.96–1.03)	0.85	0.97 (0.94–1.01)	0.2	0.44
EROA (per 0.1 cm^2)	0.85 (0.68–1.06)	0.14	0.91 (0.74–1.13)	0.41	0.29
Baseline KCCQ-OS score (per 5 U)	0.86 (0.80–0.91)	<0.0001	1.02 (0.96–1.09)	0.46	<0.0001
MR severity (4+ vs. 3+)	1.10 (0.60–2.02)	0.77	0.90 (0.49–1.66)	0.74	0.88

CI = confidence interval; EROA = effective regurgitant orifice area; KCCQ-OS = Kansas City Cardiomyopathy Questionnaire overall summary; LVEDV = left ventricular end-diastolic volume; other abbreviations as in Table 1.

peptide ≥300 pg/ml or a corrected NT-pro brain natriuretic peptide ≥1,500 pg/ml (defined as a 4% reduction for every increase of 1 kg/m^2 of body mass index above 20 kg/m^2). As reported by Arnold et al. (17), the mean KCCQ-OS score in COAPT was 53 ± 23 (consistent with at least moderate HF symptoms) and improved significantly in the TMVr but not the control group within 30 days, changes that persisted during 24-month follow-up. Importantly, the findings of COAPT, including this substudy, are applicable to symptomatic patients meeting the entry criteria for the study. There is currently no evidence supporting the treatment of asymptomatic patients with severe secondary MR.

Beside treatment assignment and lower baseline KCCQ-OS scores (i.e., worse HF symptoms), there were no significant differences between response groups in demographic and medical history variables, except for prior stroke, which was more common in super-responders. This finding is likely spurious given absence of mechanistic explanation. Super-responders also had lower serum creatinine, lower RVSP, and a trend toward smaller LV end-diastolic volumes. These findings are physiologically plausible and are consistent with previous registry data (18–24), although most registries were confounded by a mixture of patients with primary and secondary MR. Only serum creatinine and baseline KCCQ-OS remained statistically significant after multivariable adjustment. However, COAPT inclusion/exclusion criteria limited the range of LV size and MR severity. It is possible that a pooled analysis of COAPT and MITRA-FR data would yield different results.

The fact that treatment assignment to MitraClip was such a powerful predictor of favorable clinical response is consistent with the reduction of MR severity by TMVr. This is supported by the finding that there were substantial reductions in MR severity and RVSP at 30 days in responders. In a large registry of secondary MR with core laboratory adjudication of MR severity, residual severe (3+ or 4+) MR was a strong predictor of 1-year mortality (22). In COAPT, only 5% of patients had residual severe MR after TMVr. The findings of this study are therefore applicable in a setting of experienced operators with high MitraClip device success (25).

STUDY LIMITATIONS. This is a post hoc analysis of COAPT that was not pre-specified. We defined responder groups based on vital status, HF hospitalization, and KCCQ-OS at 12 months. KCCQ-OS was

TABLE 3 Multivariable Predictors of 1-Year Responders in the Device Arm

	Super-Responder Versus Nonresponders		Responder Versus Nonresponders		
	Odds Ratio (95% CI)	p Value	Odds Ratio (95% CI)	p Value	Overall p Value
Serum creatinine (per 1 mg/dl)	0.76 (0.53–1.09)	0.14	0.75 (0.48–1.16)	0.20	0.19
RVSP (per 5 mm Hg)	0.91 (0.79–1.04)	0.16	0.86 (0.74–1.01)	0.059	0.11
LVEDV (per 10 ml)	1.00 (0.96–1.05)	0.86	0.98 (0.93–1.04)	0.47	0.73
EROA (per 0.1 cm^2)	0.76 (0.56–1.02)	0.07	0.97 (0.74–1.28)	0.84	0.19
Baseline KCCQ-OS score (per 5 U)	0.86 (0.80–0.93)	0.0003	1.07 (0.98–1.16)	0.14	<0.0001
MR severity (4+ vs. 3+)	1.19 (0.54–2.61)	0.66	0.83 (0.35–1.96)	0.67	0.78

Abbreviations as in Tables 1 and 2.

TABLE 4 Multivariable Predictors of 1-Year Responders in the Control Arm

	Super-Responder Versus Nonresponder		Responder Versus Nonresponder		
	Odds Ratio (95% CI)	p Value	Odds Ratio (95% CI)	p Value	Overall p Value
Serum creatinine (per 1 mg/dl)	0.41 (0.18–0.90)	0.027	0.75 (0.48–1.18)	0.22	0.052
EROA (per 0.1 cm^2)	1.00 (0.74–1.36)	0.98	0.84 (0.59–1.21)	0.36	0.65
Baseline KCCQ-OS score (per 5 U)	0.85 (0.77–0.95)	0.005	0.98 (0.90–1.07)	0.68	0.018
LVEDV (per 10 ml)	0.98 (0.92–1.05)	0.61	0.97 (0.92–1.03)	0.33	0.59
MR severity (4+ vs. 3+)	1.01 (0.39–2.65)	0.98	1.10 (0.45–2.70)	0.84	0.98
RVSP (per 5 mm Hg)	0.97 (0.81–1.16)	0.73	0.95 (0.82–1.11)	0.53	0.80

Abbreviations as in Tables 1 and 2.

missing at 1 year in 6.7% of survivors, which may have added some imprecision. Other variables included in the analysis (e.g., effective regurgitant orifice area, LV end-diastolic volume, RVSP) also had missing data for various reasons. Our analysis focused on baseline predictors of responder status; change in various parameters from baseline to 30 days, 1 year, or 2 years was not analyzed, primarily due to survivorship bias and missing data in nonsurvivors. It is possible that patients with severely dilated left ventricles and/or very low LV ejection fraction may be less likely to have a favorable response to MitraClip treatment, but we could not identify these predictors because COAPT excluded patients with LV end-systolic diameter >7 cm or LV ejection fraction <20%. Finally, we have not considered anatomic or technical variables that might have influenced TMVr success rates; however, device success (25) was 95% in COAPT, so it is unlikely that our results would have been significantly different.

CONCLUSIONS

The principal predictors of clinical super-responders at 12 months in COAPT were lower baseline KCCQ-OS score, lower serum creatinine, and assignment to TMVr with the MitraClip plus GDMT rather than GDMT alone. Treatment with the MitraClip was the strongest predictor of improved clinical outcomes at 12 months in patients with HF with severe secondary MR and was associated with improved MR severity and reduced RVSP at 30 days.

ADDRESS FOR CORRESPONDENCE: Dr. Paul A. Grayburn, BSW Research Institute, Suite 500, 1100 Allied Drive, Plano, Texas 75093. E-mail: paul.grayburn@BSWHealth.org. Twitter: @GreggWStone, @djc795.

PERSPECTIVES

COMPETENCY IN PATIENT CARE AND PROCEDURAL SKILLS: The benefit of TMVr is related to baseline renal function and heart failure severity and reflects the degree of improvement in MR and associated pulmonary hypertension in the first month after intervention.

TRANSLATIONAL OUTLOOK: Future studies should focus on optimizing patient selection, device design, and the technique of intervention to enhance long-term clinical outcomes.

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KEY WORDS COAPT trial, heart failure, MitraClip, mitral regurgitation

APPENDIX For supplemental tables, please see the online version of this paper.