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Age-Related Outcomes After Transcatheter Mitral Valve Repair in Patients With Heart Failure

Analysis From COAPT

Chris Song, MD,[a,*] Mahesh V. Madhavan, MD, MS,[b,c,*] JoAnn Lindenfeld, MD,[d] William T. Abraham, MD,[e] Saibal Kar, MD,[f,g] D. Scott Lim, MD,[h] Paul A. Grayburn, MD,[i] Samir R. Kapadia, MD,[j] Lak N. Kotinkaduwa, PHD,[b] Michael J. Mack, MD,[k] Gregg W. Stone, MD[a,b]

ABSTRACT

OBJECTIVES The aim of this study was to assess the impact of age on outcomes in patients undergoing transcatheter edge-to-edge repair (TEER) from the COAPT (Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients with Functional Mitral Regurgitation) trial.

BACKGROUND In the COAPT trial, TEER with the MitraClip device in patients with heart failure (HF) and moderate to severe or severe secondary mitral regurgitation (SMR) reduced the risk for HF hospitalization (HFH) and all-cause mortality compared with maximally tolerated guideline-directed medical therapy (GDMT) alone. There are limited data regarding the effectiveness of MitraClip therapy in elderly patients.

METHODS Patients (n = 614) were grouped by median age at randomization (74 years) and by MitraClip treatment vs GDMT alone. The primary endpoint was the 2-year rate of death or HFH assessed by multivariable Cox regression.

RESULTS Death or HFH within 2 years occurred less frequently after treatment with the MitraClip vs GDMT alone in patients <74 years of age (37.3% vs 64.5%; adjusted HR: 0.41; 95% CI: 0.29-0.59) and ≥74 years of age (51.7% vs 69.6%; adjusted HR: 0.58; 95% CI: 0.42-0.81) (P_{int} = 0.17). Mortality was also consistently reduced with MitraClip treatment in young and elderly patients (P_{int} = 0.42). In contrast, elderly patients treated with the MitraClip vs GDMT alone tended to have a lesser reduction of HFH than younger patients (P_{int} = 0.03). Younger and older patients had similar improvements in quality of life after treatment with the MitraClip compared with GDMT alone.

CONCLUSIONS In the COAPT trial, MitraClip treatment of moderate to severe and severe SMR reduced the composite risk for death or HFH and improved survival and quality of life regardless of age. As such, young and elderly patients with HF and severe SMR benefit from TEER, although elderly patients may not have as great a benefit from the MitraClip device in reducing HFH. (J Am Coll Cardiol Intv 2022;15:397-407) © 2022 Published by Elsevier on behalf of the American College of Cardiology Foundation.

From [a]The Zena and Michael A. Wiener Cardiovascular Institute, Mount Sinai Hospital, Icahn School of Medicine at Mount Sinai, New York, New York, USA; [b]Clinical Trials Center, Cardiovascular Research Foundation, New York, New York, USA; [c]NewYork-Presbyterian Hospital/Columbia University Irving Medical Center, New York, New York, USA; [d]Advanced Heart Failure and Cardiac Transplantation Section, Vanderbilt Heart and Vascular Institute, Nashville, Tennessee, USA; [e]Departments of Medicine, Physiology, and Cell Biology, Division of Cardiovascular Medicine, and the Davis Heart and Lung Research Institute, The Ohio State University, Columbus, Ohio, USA; [f]Los Robles Regional Medical Center, Thousand Oaks, California, USA; [g]Bakersfield Heart Hospital, Bakersfield, California, USA; [h]Division of Cardiology, University of Virginia, Charlottesville, Virginia, USA; [i]Baylor University Medical Center, Baylor Heart and Vascular Institute, Dallas, Texas, USA; [j]Department of Cardiovascular Medicine, Heart and Vascular Institute, Cleveland Clinic, Cleveland, Ohio, USA; and the [k]Baylor Scott and White Heart Hospital - Plano, Dallas, Texas, USA. *Drs Song and Madhavan contributed equally to this paper.
The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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ABBREVIATIONS AND ACRONYMS

GDMT = guideline-directed medical therapy

HF = heart failure

HFH = heart failure hospitalization

LV = left ventricular

LVEF = left ventricular ejection fraction

MR = mitral regurgitation

NYHA = New York Heart Association

QoL = quality of life

SMR = secondary mitral regurgitation

TEER = transcatheter edge-to-edge repair

In the COAPT (Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients with Functional Mitral Regurgitation) trial, transcatheter edge-to-edge repair (TEER) of moderate to severe or severe secondary mitral regurgitation (SMR) with the MitraClip device (Abbott) improved survival, reduced the risk for heart failure hospitalization (HFH), and enhanced quality-of-life (QoL) and functional capacity in selected patients with heart failure (HF).[1] Key considerations when selecting patients who will benefit from MitraClip therapy include valvular anatomy, the degree and type of regurgitation, the severity of left ventricular (LV) dysfunction, symptoms, age, and other comorbidities that may contribute to risk for suboptimal procedural and clinical outcomes.[2] Given the prevalence of SMR in elderly patients and the continued growth of the elderly population,[3-6] age is likely to become an increasingly important factor to consider when evaluating patients for medical and device treatment. In this regard, elderly patients with HF have a limited life expectancy, are more likely to be frequently hospitalized for HF, have poor QoL and functional capacity, and have less cardiac reserve compared with younger patients.[7-9]

SEE PAGE 408

To date, there are limited data regarding MitraClip outcomes in elderly patients with SMR.[10-12] In the randomized MITRA-FR (Percutaneous Repair With the MitraClip Device for Severe Functional/Secondary Mitral Regurgitation) trial, no significant interaction was noted between age and the composite outcome of death and unplanned HF hospitalization at 12 months.[13] However, MitraClip treatment did not improve outcomes among the patients recruited in MITRA-FR. We thus sought to assess the impact of age on outcomes in patients undergoing TEER from the COAPT trial.[1]

METHODS

TRIAL DESIGN AND STUDY POPULATION. The study design, protocol, and primary results of the COAPT trial have been previously described in detail.[1] In brief, COAPT was a prospective, international, open-label, multicenter trial that randomized patients with moderate to severe or severe SMR to treatment with the MitraClip device plus maximally tolerated guideline-directed medical therapy (GDMT) (n = 302) or GDMT alone (n = 312). Key eligibility criteria were symptomatic SMR (3+ or 4+ by independent echocardiographic core laboratory assessment); optimized treatment with HF-related GDMT (including cardiac resynchronization therapy if indicated); New York Heart Association (NYHA) functional class II, III, or ambulatory IV; LV ejection fraction (LVEF) between 20% and 50%; LV end-systolic dimension ≤ 7 cm; and the absence of severe pulmonary hypertension or moderate to severe symptomatic right ventricular dysfunction.[1] Follow-up is ongoing at regular intervals through 5 years after randomization; currently, all patients have reached the 2-year follow-up time point. The ethics committee or Institutional Review Board at each participating center approved the trial, and all patients provided written informed consent.

OBJECTIVES AND ENDPOINTS. The main objective of the present analysis was to assess whether the short- and long-term clinical outcomes of TEER with MitraClip plus GDMT vs GDMT alone were influenced by age. Patients were grouped by median age at randomization (74 years). The primary clinical endpoint of the present study was the composite of all-cause death or HFH within 24 months. The primary safety endpoint (as prespecified in the protocol) was freedom from device-related complications at 24 months, defined as device-specific events (single-leaflet device attachment, device embolization, endocarditis or mitral stenosis requiring surgery, or any device-related complication requiring nonelective cardiovascular surgery) or progressive HF-specific events (LV assist device implantation or heart transplantation). Secondary endpoints included the primary safety endpoint at 30 days and death, HFH, QoL improvement as assessed by Kansas City Cardiomyopathy Questionnaire score change from baseline, and NYHA functional class III or IV at 2 years. Definitions of these endpoints have been previously described in detail.[1] An independent events committee reviewed and adjudicated all primary and secondary adverse events.

STATISTICAL ANALYSIS. Comparison of baseline and procedural characteristics, medical history, and clinical events were conducted using the chi-square test or Fisher exact test for binary variables, Student's *t*-test for continuous variables, and log-rank test for time-to-event variables, as appropriate. HRs and 95% CIs were calculated using a Cox proportional hazards model. The significance of the treatment effect of MitraClip therapy plus GDMT vs GDMT alone on binary variables and change in health status measures from baseline to follow-up according to age at randomization was assessed using unadjusted

logistic regression model and analysis of covariance adjusting for baseline value, respectively. Adjusted comparisons of MitraClip therapy plus GDMT vs GDMT alone for the outcomes of the composite rate of death or HFH and death alone were conducted in patients <74 vs ≥74 years of age at randomization using multivariable Cox regression models. The impact of treatment with MitraClip plus GDMT vs GDMT alone on hospitalization events according to age at randomization was assessed using univariable and multivariable Fine-Gray subdistribution models to account for the competing risk for death.

Covariates in the adjusted models were selected on the basis of their known prognostic impact in HF and SMR and their associations with age and that were significantly different in both groups in univariable analysis, including sex, diabetes mellitus, body mass index, chronic kidney disease (defined as estimated creatinine clearance < 30 mL/min), history of atrial fibrillation, previous coronary artery bypass grafting, previous implantable cardiac defibrillator, NYHA functional class, LV end-diastolic dimension, LV end-systolic volume, LVEF, N-terminal pro-brain natriuretic peptide or brain natriuretic peptide, and echocardiographic severity of SMR. Interaction terms were included in the covariate set to assess whether the effect of MitraClip treatment vs GDMT alone differed according to age group. All *P* values are 2-tailed, and *P* values < 0.05 were considered to indicate statistical significance. Statistical analyses were performed using SAS version 9.4 (SAS Institute).

TABLE 1 Baseline Characteristics by Patient Age

	Patient Age		
	<74 y[a]	≥74 y[b]	*P* Value
Age, y	63.4 ± 9.2 (297)	80.5 ± 4.5 (317)	<0.0001
Male	170/297 (57.2)	223/317 (70.3)	0.0007
Body mass index, kg/m^2	28.3 ± 6.9 (292)	25.9 ± 4.4 (313)	<0.0001
Hypertension	226/297 (76.1)	268/317 (84.5)	0.008
Diabetes	130/297 (43.8)	99/317 (31.2)	0.001
History of atrial fibrillation	127/297 (42.8)	200/317 (63.1)	<0.0001
Prior stroke	39/297 (13.1)	33/317 (10.4)	0.29
Prior percutaneous coronary intervention	129/297 (43.4)	154/317 (48.6)	0.20
Prior coronary artery bypass grafting	94/297 (31.6)	153/317 (48.3)	<0.0001
Chronic obstructive pulmonary disease	75/297 (25.3)	68/317 (21.5)	0.27
Chronic kidney disease[c]	40/290 (13.8)	96/311 (30.9)	<0.0001
Peripheral vascular disease	47/297 (15.8)	62/317 (19.6)	0.23
Anemia	67/297 (22.6)	77/317 (24.3)	0.61
Heart failure-related			
NYHA functional class I	0/296 (0.0)	1/317 (0.3)	0.33
NYHA functional class II	126/296 (42.6)	113/317 (35.6)	0.08
NYHA functional class III	143/296 (48.3)	179/317 (56.5)	0.04
NYHA functional class IV ambulatory	27/296 (9.1)	24/317 (7.6)	0.49
HFH within previous 1 y	172/297 (57.9)	179/317 (56.5)	0.72
Previous CRT	100/297 (33.7)	124/317 (39.1)	0.16
Previous implanted defibrillator	126/297 (42.4)	66/317 (20.8)	<0.0001
N-terminal pro-BNP, pg/mL	5,410 ± 8,445 (84)	5,783 ± 6,603 (75)	0.76
BNP, pg/mL	890 ± 920 (201)	1,133 ± 1,320 (216)	0.03

Values are mean ± SD (n) or n/N (%). [a]Age range: 26 to 73 years. [b]Age range: 74 to 94 years. [c]Creatinine clearance < 30 mL/min.

BNP = brain natriuretic peptide; CRT = cardiac resynchronization therapy; HFH = heart failure hospitalization; NT-proBNP = N-terminal pro-brain natriuretic peptide; NYHA = New York Heart Association.

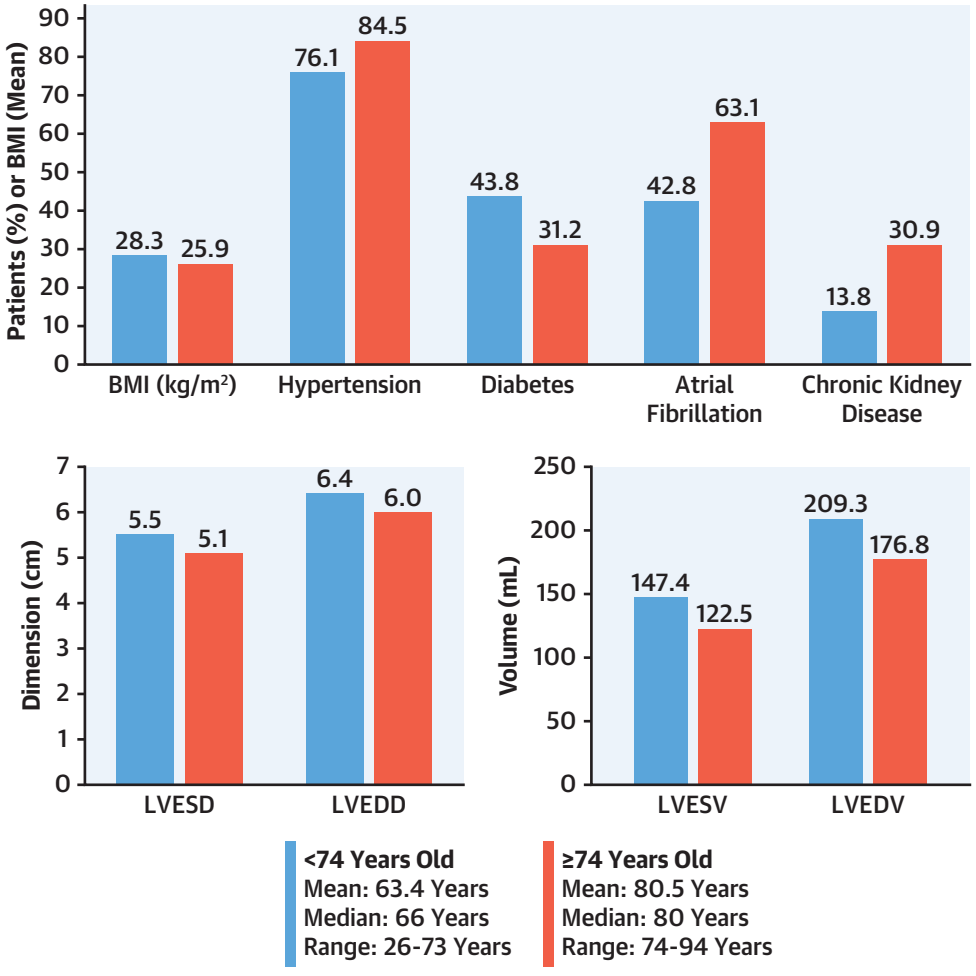
RESULTS

BASELINE CLINICAL CHARACTERISTICS. Among the 614 patients with moderate to severe or severe SMR enrolled in the COAPT trial, 297 (48.4%) were <74 years of age (median group age 66 years; IQR: 59-70 years; range: 26-73 years), and 317 (51.6%) were ≥74 years of age (median group age 80 years; IQR: 77-84 years; range: 74-94 years). As shown in Table 1 and the Central Illustration (left), patients ≥ 74 years of age had significantly higher rates of hypertension, atrial fibrillation, and chronic kidney disease compared with younger patients; however, rates of diabetes mellitus and body mass index were lower in older patients.

ECHOCARDIOGRAPHIC AND PROCEDURAL CHARACTERISTICS. Compared with younger patients, older patients had similar baseline LVEF and mitral regurgitation (MR) severity. Older patients had significantly smaller LV dimensions (Table 2, Central Illustration, left). The number of MitraClip devices implanted was similar between age groups, as was the length of stay after the index procedure (Table 2).

OUTCOMES ACCORDING TO AGE AND TREATMENT. At 2 years, the primary composite endpoint of all-cause death or HFH occurred less frequently after TEER compared with GDMT alone both in patients of younger (37.3% vs 64.5%; unadjusted HR: 0.46, 95% CI: 0.33-0.64) and older (51.7% vs 69.6%; unadjusted HR: 0.65; 95% CI: 0.48-0.87) age (Table 3; Central Illustration, right). There was no significant interaction between age (<74 vs ≥74 years) and randomized treatment (MitraClip plus GDMT vs GDMT alone) with regard to the primary endpoint (P_{int} = 0.10). Both younger and older patients who received MitraClip therapy also had fewer HFHs within 2 years; however, the benefit of MitraClip treatment in reducing HFH, although present, was attenuated in elderly patients compared with younger patients (unadjusted HR: 0.67 [95% CI: 0.48-0.93]; unadjusted HR: 0.37 [95% CI: 0.25-0.55]; P_{int} = 0.03). These outcomes were similar after multivariable adjustment (Figure 1). Younger and older patients had similar improvements in QoL and

CENTRAL ILLUSTRATION **Features and Outcomes According to Age and Treatment**



Song, C. et al. J Am Coll Cardiol Intv. 2022;15(4):397-407.

(Top) Significant baseline clinical and echocardiographic differences in younger patients (<74 years of age; **blue columns**) and older patients (≥74 years of age; **red columns**) ($P < 0.05$ for all comparisons). **(Bottom)** Time-to-first event curves for the composite outcome of death or heart failure hospitalization through 2 years after randomization of younger patients **(blue curves)** and older patients **(red curves)** to MitraClip device plus guideline-directed medical therapy (GDMT) compared with GDMT alone. LVEDD = left ventricular end-diastolic dimension; LVEDV = left ventricular end-diastolic volume; LVESD = left ventricular end-systolic dimension; LVESV = left ventricular end-systolic volume.

Continued on the next page

NYHA functional class after treatment with the MitraClip compared with GDMT alone (Table 3). As a sensitivity analysis, outcomes were analyzed by age in quartiles. The benefits of treatment with the MitraClip compared with GDMT alone were consistent even at the extremes of age (Table 4).

As shown in Table 5, in patients <74 and ≥74 years of age, the primary prespecified safety endpoint of the COAPT trial occurred in 100% and 97.4% of patients, respectively, at 30 days ($P = 0.056$) and in 94.3% and 95.4% of patients, respectively, at 2 years ($P = 0.76$). The reduction in MR grade from baseline was greater at all time periods during follow-up after MitraClip treatment compared with GDMT alone, independent of age (Figure 2).

DISCUSSION

The present analysis from the prospective, randomized COAPT trial is the largest and most extensive

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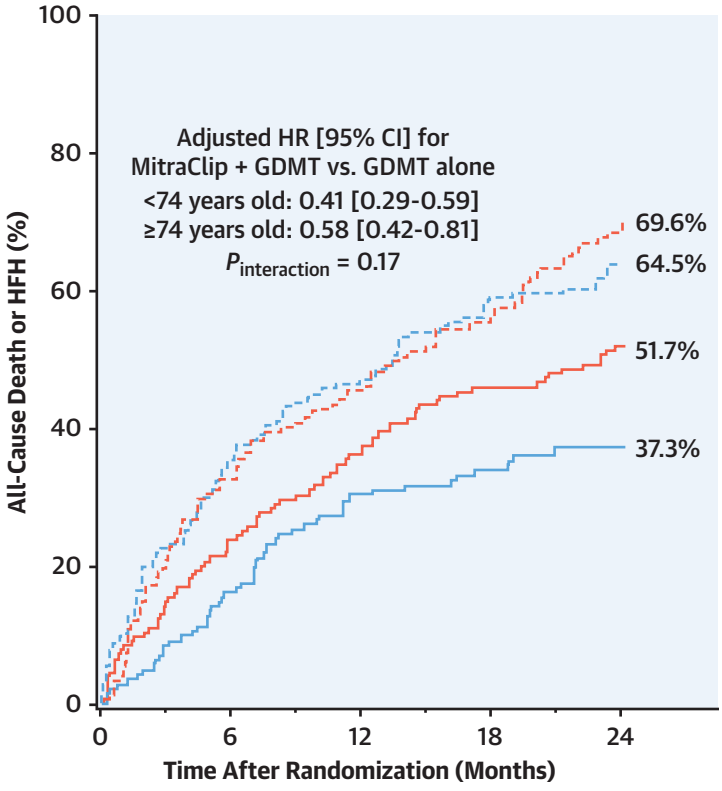


No. at risk:

MitraClip + GDMT: Age <74 Years	145	119	99	93	80
GDMT Alone: Age <74 Years	152	99	78	59	45
MitraClip + GDMT: Age ≥74 Years	157	119	97	83	70
GDMT Alone: Age ≥74 Years	160	107	78	61	42

Song, C. et al. J Am Coll Cardiol Intv. 2022;15(4):397–407.

study to date evaluating the safety and effectiveness of MitraClip therapy for patients with symptomatic HF and severe SMR stratified by age. The principal findings are as follows: 1) MitraClip treatment was comparably safe and effective in both younger and older patients in reducing the composite outcome of all-cause death or HFH within 2 years; 2) similarly, the relative survival benefit, improvements in QoL as assessed by the Kansas City Cardiomyopathy Questionnaire and NYHA functional class, and reduction in MR grade conferred by MitraClip treatment compared with GDMT alone were independent of age; 3) conversely, although both age groups experienced reductions in HFH with MitraClip treatment, this benefit was greater in younger compared with older patients; 4) although MitraClip treatment was safe in both age groups, all device-related complications occurred in patients ≥74 years of age, all within 30 days after implantation.

In the COAPT trial, the 2-year rate of mortality was expectedly higher in patients older compared with those younger than the median age of 74 years treated with GDMT alone (49.1% vs 36.6%). MitraClip treatment consistently reduced mortality in both groups (adjusted HRs for 2-year mortality: 0.64 and 0.50 respectively; P_{int} = 0.42). Conversely, both elderly and younger patients had equivalent 56.5% 2-year rates of HFH with GDMT alone, and although MitraClip treatment significantly reduced HFHs in both age groups, after accounting for baseline covariates and the competing risk for death, the relative reduction in HFH after MitraClip device was somewhat less in older compared with younger patients (adjusted HR: 0.59 vs 0.31; P_{int} = 0.03). Altered

JACC: CARDIOVASCULAR INTERVENTIONS VOL. 15, NO. 4, 2022
FEBRUARY 28, 2022:397–407

TABLE 2 Baseline Echocardiographic Characteristics by Patient Age

	Patient Age		
	<74 y	≥74 y	*P* Value
Moderate to severe MR (3+)	153/296 (51.7)	167/317 (52.7)	0.81
Severe MR (4+)	143/296 (48.3)	150/317 (47.3)	0.81
Effective regurgitant orifice area, cm^2	0.41 ± 0.15 (289)	0.41 ± 0.15 (302)	0.95
Left ventricular end-systolic dimension, cm	5.5 ± 0.9 (292)	5.1 ± 0.8 (315)	<0.0001
Left ventricular end-diastolic dimension, cm	6.4 ± 0.7 (292)	6.0 ± 0.7 (316)	<0.0001
Left ventricular end-systolic volume, mL	147.4 ± 60.8 (282)	122.5 ± 52.9 (292)	<0.0001
Left ventricular end-diastolic volume, mL	209.3 ± 75.6 (282)	176.8 ± 62.5 (292)	<0.0001
Left ventricular ejection fraction, %	30.6 ± 8.8 (283)	32.0 ± 9.8 (292)	0.09
Procedural characteristics			
Number of MitraClip devices implanted			
0	2/139 (1.4)	4/154 (2.6)	0.48
1	49/139 (35.3)	57/154 (37.0)	0.75
2	75/139 (54.0)	82/154 (53.2)	0.90
3	13/139 (9.4)	10/154 (6.5)	0.36
4	0/139 (0.0)	1/154 (0.6)	0.34
Hospital duration after MitraClip implantation, d	2.4 ± 2.3 (139)	2.6 ± 2.3 (154)	0.53

Values are n/N (%) or mean ± SD (n).
MR = mitral regurgitation.

function of cardiomyocytes and cardiac fibroblasts and reduced myocardial compliance due to chronic hypertension and diastolic dysfunction may be factors contributing to this finding in older patients.[14,15] In addition, elderly patients are more likely to have other contributing disease processes, such as atrial fibrillation, which may put them at higher risk for HFH.[16,17] Indeed, older patients were more likely to have baseline atrial fibrillation compared with younger individuals in the present analysis. Other disease processes such as concomitant aortic stenosis, which is also more prevalent in the elderly (but excluded from the present study), may contribute to differences in HFH as well.[18,19] Nonetheless, elderly patients derived substantial benefits in terms of survival and reduction in HFH as well as improved QoL after TEER in the COAPT trial. As such, MitraClip treatment should not be withheld from elderly patients because of concerns of lack of effectiveness. Further studies are warranted to determine whether there is some combination of very advanced age, comorbidities, and cardiac dysfunction that might limit the effectiveness of MitraClip treatment in elderly patients.

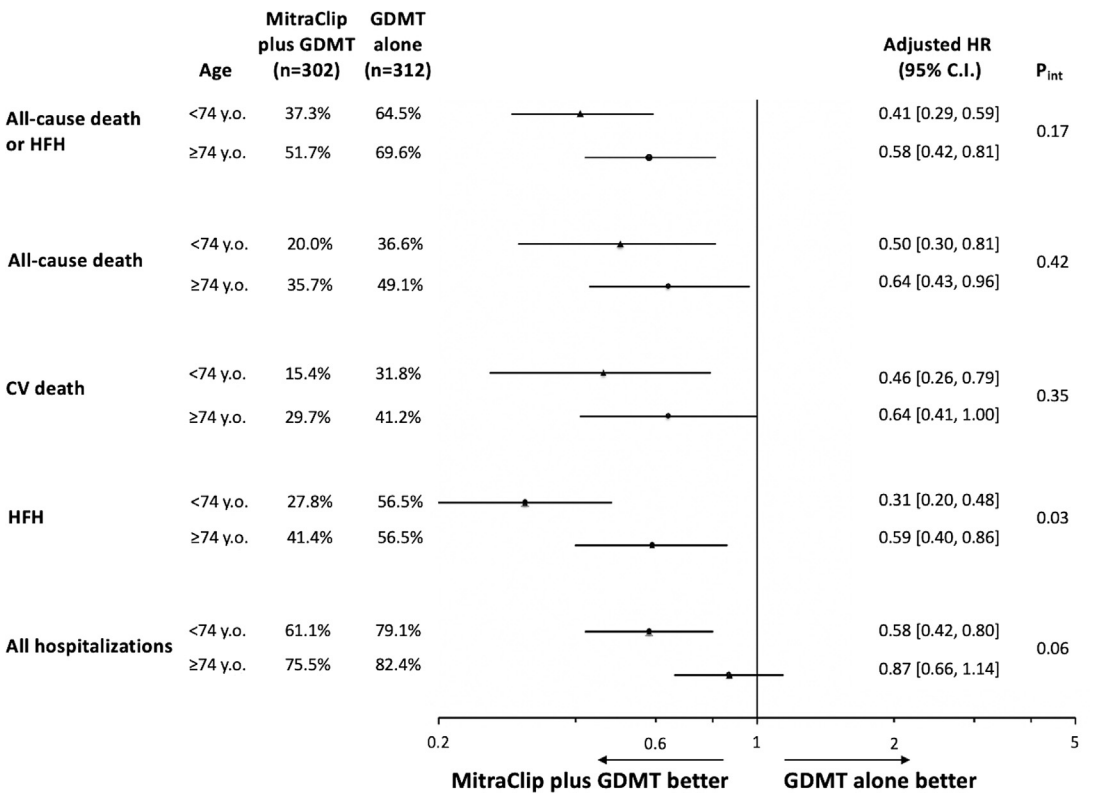
Elderly patients are in general at increased risk for procedural complications and poor short-term clinical outcomes due to frailty and concomitant comorbidities.[20] In the COAPT trial, device-related complications were infrequent; 0% of younger patients compared with 2.6% of older patients had

TABLE 3 Clinical Outcomes Through 2 Years by Randomized Treatment and Patient Age (Unadjusted)

	<74 y (n = 297)			≥74 y (n = 317)			
	MitraClip	GDMT	HR/OR/MD (95% CI)	MitraClip	GDMT	HR/OR/MD (95% CI)	P_{int}[a]
Death or HFH at 2 y	37.3 (53)	64.5 (96)	HR: 0.46 (0.33-0.64)	51.7 (80)	69.6 (105)	HR: 0.65 (0.48-0.87)	0.10
Death	20.0 (28)	36.6 (52)	HR: 0.51 (0.32-0.80)	35.7 (55)	49.1 (73)	HR: 0.70 (0.49-0.99)	0.27
HFH	27.8 (37)	56.5 (81)	HR: 0.37 (0.25-0.55)	41.4 (58)	56.5 (77)	HR: 0.67 (0.48-0.93)	0.03
Change in KCCQ score from baseline to 2 y	17.8 ± 27.1	5.5 ± 25.1	MD: 12.2 (5.3-19.1)	17.0 ± 24.3	0.9 ± 27.9	MD: 14.0 (6.6-21.4)	0.71
NYHA functional class III or IV at 2 y	26.3 (25)	34.2 (27)	OR: 0.69 (0.36-1.32)	35.8 (29)	54.7 (35)	OR: 0.46 (0.24-0.90)	0.40

Values are Kaplan-Meier estimated % (n events) or mean ± SD. [a]Unadjusted interaction *P* values were calculated for time-to-first event variables by proportional hazards regression (for composite death or HFH or death alone) or by the Fine-Gray subdistribution model (for HFH), by logistic regression for NYHA functional class, and by analysis of covariance (adjusted for baseline value) for change in KCCQ score from baseline to follow-up.
GDMT = guideline-directed medical therapy; MD = mean difference; KCCQ = Kansas City Cardiomyopathy Questionnaire; OR = odds ratio; other abbreviations as in Table 1.

FIGURE 1 Forest Plot Showing the Interaction Between Age and Treatment on Multivariable Adjusted 2-Year Outcomes



CV = cardiovascular; GDMT = guideline-directed medical therapy; HFH = heart failure hospitalizations.

adverse outcomes within 30 days, with no device-related complications occurring thereafter through 2 years in either group. In addition, the post-procedural duration of hospitalization was not increased in elderly compared with younger patients. These results extend the findings from other published studies. Lee et al[11] reported that MitraClip treatment was safe in elderly patients (age >80 years), with similar risk for all-cause mortality and risk-free survival as in a younger cohort; however, the number of patients in that study was small (n = 46). Similarly, Taramasso et al[21] showed MitraClip treatment to be safe in octogenarians, but again this study was limited by size (n = 48), and the etiology of MR was degenerative and not functional. Last, the TRAMI (Transcatheter Mitral Valve Interventions) registry showed MitraClip treatment to have similar low rates of in-hospital death, myocardial infarction, and stroke in both elderly (age ≥76 years; n = 525) and young (n = 539) patients (3.5% vs 3.4%; P = 0.93), and there was no impact of age on the short-term efficacy and safety of MitraClip treatment.[12] Thus, although COAPT excluded patients with severe LV dysfunction and end-stage HF, in general MitraClip treatment should not be withheld from elderly patients because of concerns of procedural complications.

STUDY LIMITATIONS. First, although an age-specific subgroup analysis from the COAPT trial was prespecified, subgroup analyses and interaction testing are inherently underpowered; the present outcomes should thus be considered hypothesis generating. Second, age was not a stratification variable for randomization; despite multivariable adjustment for clinical and procedural variables, there remains the potential for unmeasured cofounders within each age cohort.

Third, the 2-year follow-up period is relatively short; longer follow-up may reveal greater differences in outcomes between younger and older patients. Finally, the present study applies only to outcomes of MitraClip therapy in the patients enrolled in COAPT;

TABLE 4 Clinical Outcomes Through 2 Years by Randomized Treatment and Quartiles of Age

	MitraClip Plus GDMT	GDMT Alone	HR/OR/MD (95% CI)	MitraClip Plus GDMT	GDMT Alone	HR/OR/MD (95% CI)	MitraClip Plus GDMT	GDMT Alone	HR/OR/MD (95% CI)
	Death or HFH at 2 y			Death			HFH		
Quartile 1: age 26-66 y (n = 158)	36.3 (30)	59.1 (42)	HR: 0.50 (0.31-0.80)	12.1 (10)	28.9 (20)	HR: 0.40 (0.19-0.86)	32.7 (26)	51.3 (35)	HR: 0.54 (0.33-0.88)
Quartile 2: age 67-73 y (n = 139)	39.0 (23)	69.6 (54)	HR: 0.42 (0.26-0.69)	30.9 (18)	43.7 (32)	HR: 0.64 (0.36-1.14)	20.0 (11)	61.4 (46)	HR: 0.23 (0.11-0.45)
Quartile 3: age 74-80 y (n = 165)	56.8 (47)	69.7 (53)	HR: 0.71 (0.48-1.06)	37.9 (31)	43.2 (32)	HR: 0.87 (0.53-1.42)	45.0 (34)	61.4 (43)	HR: 0.65 (0.42-1.00)
Quartile 4: age 81-94 y (n = 152)	46.0 (33)	69.6 (52)	HR: 0.58 (0.38-0.90)	33.4 (24)	55.0 (41)	HR: 0.57 (0.34-0.94)	37.1 (24)	51.4 (34)	HR: 0.68 (0.40-1.14)
	NYHA Functional Class III or IV at 2 y			Change in KCCQ Score From Baseline to 2 y					
Quartile 1: age 26-66 y (n = 158)	20.7 (12)	34.1 (15)	OR: 0.50 (0.21-1.23)	19.1 ± 23.8	8.2 ± 27.2	MD: 11.4 (2.7-20.1)			
Quartile 2: age 67-73 y (n = 139)	35.1 (13)	34.3 (12)	OR: 1.04 (0.39-2.74)	15.9 ± 31.8	2.3 ± 22.2	MD: 12.9 (1.2-24.6)			
Quartile 3: age 74-80 y (n = 165)	43.6 (17)	48.6 (17)	OR: 0.82 (0.33-2.05)	15.9 ± 25.7	2.2 ± 28.4	MD: 11.5 (0.9-22.0)			
Quartile 4: age 81-94 y (n = 152)	28.6 (12)	62.1 (18)	OR: 0.24 (0.09-0.67)	18.0 ± 23.2	−0.6 ± 27.7	MD: 16.8 (6.1-27.5)			

The interaction *P* values between randomization group and quartiles of age for 2-year outcomes were as follows: $P = 0.39$ for death or HFH at 2 years, $P = 0.39$ for death at 2 years; $P = 0.06$ for HFH at 2 years, $P = 0.88$ for change in KCCQ score from baseline to 2 y, and $P = 0.18$ for NYHA functional class III or IV at 2 years. Unadjusted interaction *P* values were calculated for time-to-first event variables by proportional hazards regression (for composite death or HFH or death alone) or by the Fine-Gray subdistribution model (for HFH), by logistic regression for NYHA functional class, and by analysis of covariance (adjusted for baseline value) for change in KCCQ score from baseline to follow-up.

Abbreviations as in Tables 1 and 3.

additional studies are required to determine whether age influences TEER outcomes in patients who are either less or more ill or have degenerative MR rather than SMR.

CONCLUSIONS

In the COAPT trial, MitraClip treatment of moderate to severe and severe SMR in patients with HF was safe and reduced the 2-year composite risk for death or HFH and improved survival and QoL compared with GDMT alone regardless of age. Although HFH rates were decreased with MitraClip treatment in all age groups, the relative reduction in HFH after TEER was greater in young patients than in the elderly. Nonetheless, young as well as elderly patients with HF and severe SMR substantially benefited from TEER with the MitraClip device. Thus, age should not be an impediment for early referral of selected patients with HF and severe SMR for MitraClip treatment.

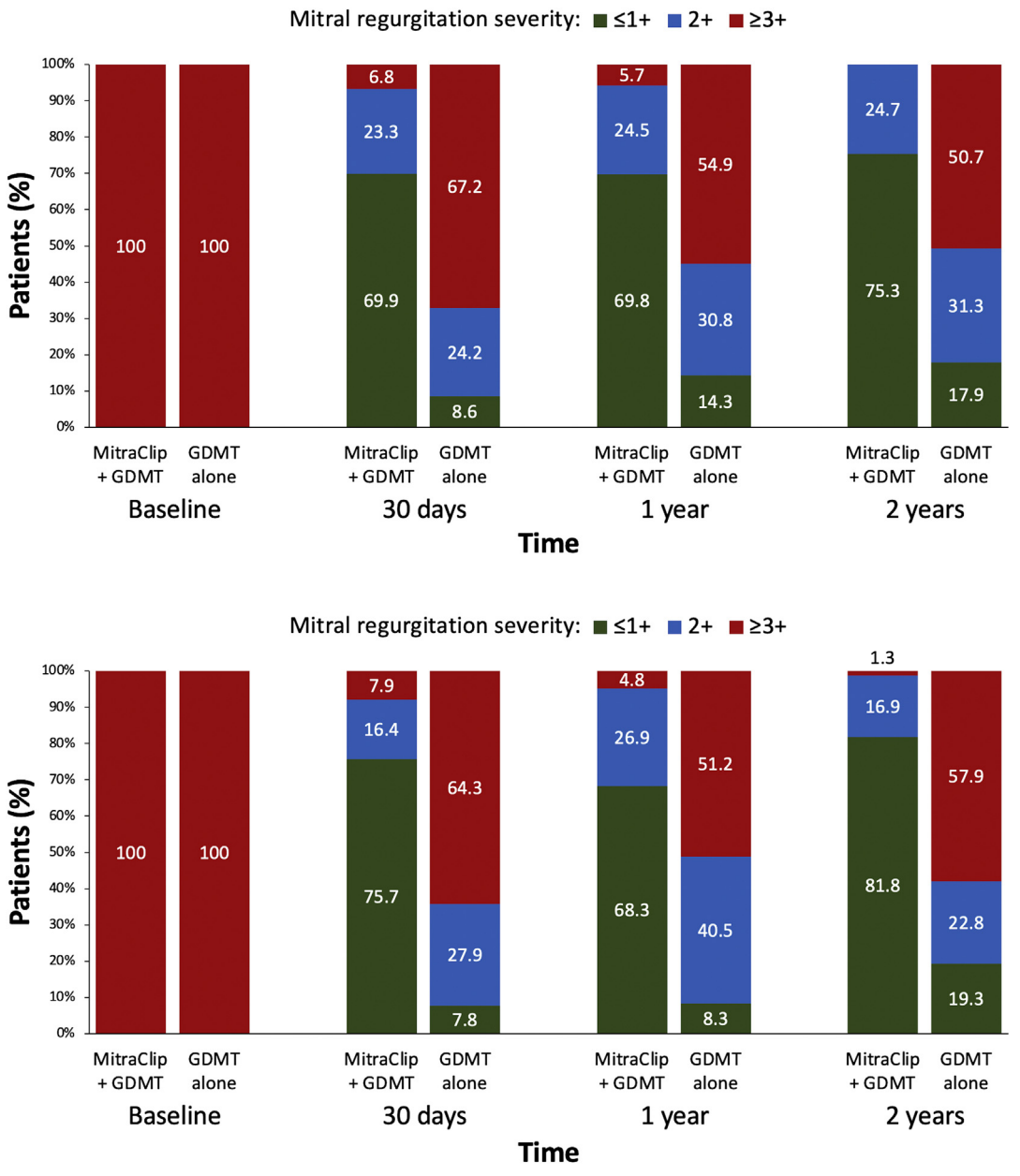
TABLE 5 Prespecified Safety Outcomes in the MitraClip Group

	0-30 d			0-24 mo		
	<74 y (n = 145)	≥74 y (n = 157)	*P* Value	<74 y (n = 145)	≥74 y (n = 157)	*P* Value
Primary safety endpoint	100% (145)	97.4% (153)	0.056	94.3% (138)	95.4% (151)	0.76
Device-related complications	0.0% (0)	2.6% (4)	0.056	0.0% (0)	2.6% (4)	0.056
Single-leaflet device attachment	0.0% (0)	1.3% (2)	–	0.0% (0)	1.3% (2)	–
Device embolization	0.0% (0)	0.6% (1)	–	0.0% (0)	0.6% (1)	–
Endocarditis requiring surgery	0.0% (0)	0.0% (0)	–	0.0% (0)	0.0% (0)	–
Mitral stenosis requiring surgery	0.0% (0)	0.0% (0)	–	0.0% (0)	0.0% (0)	–
Any device-related complication requiring non-elective CV surgery	0.0% (0)	0.6% (1)	–	0.0% (0)	0.6% (1)	–
Progressive heart failure	0.0% (0)	0.0% (0)	–	5.7% (7)	2.0% (2)	0.10
Left ventricular assist device implantation	0.0% (0)	0.0% (0)	–	3.2% (4)	2.0% (2)	–
Heart transplantation	0.0% (0)	0.0% (0)	–	2.5% (3)	0.0% (0)	–

Event rates are Kaplan-Meier time-to-first event estimates expressed as % (n events).

CV = cardiovascular.

FIGURE 2 **Echocardiographic Core Laboratory-Assessed MR Grade at Baseline, 30 Days, 1 Year, and 2 Years in Patients Assigned to Treatment With MitraClip Device Plus GDMT vs GDMT Alone**



(Top) Younger patients (<74 years of age). **(Bottom)** Older patients (≥74 years of age). The proportion of patients with mitral regurgitation (MR) grade ≤1+ and ≤2+ was greater in the MitraClip plus guideline-directed medical therapy (GDMT) group compared with the GDMT alone group at all follow-up periods in both younger and older patients ($P < 0.001$ for all comparisons). Comparing the younger vs older patients treated with the MitraClip plus GDMT, there were no significant differences in the proportion of patients with MR grade ≤1+ or ≤2+ at any follow-up time period ($P > 0.05$ for all comparisons). Similarly, comparing younger vs older patients treated with GDMT alone, there were no significant differences in the proportion of patients with MR grade ≤1+ or ≤2+ at any follow-up time period ($P > 0.05$ for all comparisons).

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ADDRESS FOR CORRESPONDENCE: Dr Gregg W. Stone, Mount Sinai Medical Center, Cardiovascular Research Foundation, 1700 Broadway, 9th Floor, New York, New York 10019, USA. E-mail: gregg.stone@mountsinai.org.@GreggWStone.

PERSPECTIVES

WHAT IS KNOWN? In selected patients with HF and severe SMR, mitral TEER with the MitraClip reduces all-cause mortality and HFH. However, there are limited data regarding the effectiveness of this therapy in elderly patients

WHAT IS NEW? In the COAPT trial, MitraClip treatment reduced death and HFH and improved QoL and functional outcomes in both young and elderly patients.

WHAT IS NEXT? Further studies are warranted to determine whether there is some combination of very advanced age, comorbidities, and cardiac dysfunction that might limit the safety or effectiveness of TEER in elderly patients with HF and severe SMR.

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