Five-year clinical outcomes after percutaneous edge-to-edge mitral valve repair: Insights from the multicenter GRASP-IT registry

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Background Limited evidence is available on 5-year clinical outcomes after percutaneous edge-to-edge mitral valve repair.

Methods The Getting Reduction of mitrAl inSufficiency by Percutaneous clip implantation in ITaly (GRASP-IT) is a multicenter registry including 304 consecutive patients undergoing Mitraclip between October 2008 and October 2013 at 4 Italian centers. Primary end point (all-cause mortality) and secondary end point (all-cause mortality or heart failure [HF] hospitalization) were evaluated up to 5 years and between 1 and 5 years.

Results Cumulative incidence of the primary and secondary end points at 1, 2, 3, 4, and 5 years were 15.1%, 26.4%, 35.5%, 42.1%, and 47.3% and 29.1%, 41.7%, 49.8%, 56%, and 62.3%, respectively. Landmark analysis between 1 and 5 years showed an incidence of primary and secondary end point of 37.9% and 46.8%, respectively. Five-year event rates were significantly higher in patients with functional ischemic mitral regurgitation (MR) compared to other etiologies. MR recurrence and left ventricular ejection fraction <30% were associated with an increased risk of both primary and secondary end points. EuroSCORE II >5% was associated with an increased risk of 5-year mortality. Ischemic etiology of MR, baseline serum creatinine >1.5 mg/dL, chronic obstructive pulmonary disease, and previous HF hospitalizations were independent predictors of 5-year secondary end point.

Conclusions At 5-year follow-up after Mitraclip, nearly half of patients died and almost two thirds died or were admitted for HF. MR recurrence, ischemic etiology, high comorbidity burden (ie, EuroSCORE II >5%, chronic obstructive pulmonary disease), and advanced cardiomyopathy (ie, left ventricular ejection fraction <30%, prior HF admission, creatinine >1.5 mg/dL) significantly increase the relative risk of 5-year clinical events. (Am Heart J 2019;217:32-41.)

Mitraclip is the most widely used device for transcatheter mitral valve repair. It has been showed safe and effective in reducing mitral regurgitation (MR), improving symptoms and quality of life in patients at high risk for surgical interventions.[1-4]

Long-term results from EVEREST II trial have been reported showing a cumulative incidence of 5-year mortality, reoperation, and MR recurrence (MRr) in Mitraclip arm of 20.8%, 27.9%, and 12.3%, respectively.[5] However, as well known, the EVEREST II population, including patients suitable for surgery and mostly affected by primary MR, is highly different compared to that treated in daily practice.

Recently, 2 randomized trials comparing Mitraclip to medical therapy alone in patients with functional MR (FMR) have shown different results: comparable 1-year events (mortality and hospitalizations) in the Percutaneous Repair with the MitraClip Device for Severe Functional/Secondary Mitral Regurgitation (MITRA-FR)[6] and prognostic benefit up to 2 years after Mitraclip in the Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients with Functional Mitral Regurgitation (COAPT).[7] A complementary interpretation of these 2 studies has been proposed concluding that Mitraclip would improve prognosis in selected patients with truly severe MR and not too advanced cardiomyopathy.[8,9] However, long-term results from these 2 trials are not available yet.

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Limited evidence is available about 5-year clinical outcomes after Mitraclip in the real-world setting.[10-12] Thus, we aim at investigating 5-year events and independent predictors of long-term prognosis in a large real-world population undergoing Mitraclip implantation.

Methods

Study population and data collection

The Getting Reduction of mitrAl inSufficiency by Percutaneous clip implantation in ITaly (GRASP-IT) is a retrospective multicenter registry with prospective collection of follow-up data. Details about the registry and previous results have been published earlier.[13] Briefly, consecutive patients with symptomatic moderate-to-severe or severe MR undergoing Mitraclip implantation between October 2008 and October 2013 at 4 Italian centers have been included. Baseline demographic, laboratory, clinical, and echocardiographic parameters, as well as procedural and follow-up data, were entered into a dedicated computerized database.

Clinical follow-up was obtained by clinical visits and/or through telephone contacts. Referring cardiologists, general practitioners, and patients were contacted whenever necessary for further information. Death and hospitalization, with relative cause, were recorded up to 5-year follow-up.

All data provided by each site were anonymized, centrally collected, and assessed for quality.

The local ethics committee at each center approved the use of clinical data for the study, and all patients provided written informed consent. No extramural funding was used to support this work.

End points and definitions

As previously reported,[13] primary end point was all-cause mortality, whereas secondary end point was the composite of all-cause mortality and hospitalization due to heart failure (HF). For the purpose of the present analysis, these 2 end points were evaluated up to 5-year follow-up and by means of a landmark analysis between 1 and 5 years.

Cardiovascular (CV) mortality has also been reported and included periprocedural death (if occurring within 30 days of the intervention or beyond 30 days in the patient not yet discharged) and any death occurring due to HF, myocardial infarction (MI), major bleeding, thromboembolism, stroke, arrhythmia, cardiovascular infection, or tamponade; sudden and/or unexpected death; and death of unknown cause.[14]

Hospitalization for HF was defined as admission to an inpatient unit or ward in the hospital for ≥24 hours because of symptoms, signs, and/or laboratory evidence of worsening HF and administration of intravenous or mechanical HF therapies.[14]

Occurrence of surgical mitral valve replacement, heart transplantation, and left ventricular assistance device (LVAD) implantation has also been detected and reported.

MR recurrence was defined as documentation of MR >2+ within 2 years of Mitraclip procedure; thus, it also included procedural failure (MR >2+ after Mitraclip procedure).

Of note, procedural outcomes and acute complications have already been reported.[13]

Statistical analysis

Continuous variables following a normal distribution, according to Kolmogorov-Smirnov and the Shapiro-Wilk tests, were reported as mean ± SD and compared using the Student *t* test, whereas those without a normal distribution were presented as median (interquartile range [IQR]) and compared with the Mann-Whitney test. Categorical variables were reported as counts and percentages and compared using the χ^2 or Fisher exact tests, as appropriate. Cumulative incidence of primary and secondary end points was estimated by means of Kaplan-Meier plots and compared using log-rank test. Univariate and multivariable analyses for the study end points were performed using a Cox regression model. The proportional hazards assumption was tested and satisfied in all cases using Schoenfeld residuals. Continuous variables were dichotomized as needed based on best receiver operating characteristics (ROC) cutoff values. To avoid overfitting, only variables that in the univariate analysis were differently distributed at an α level of .10 were entered in a multivariable stepwise Cox regression model to calculate independent predictors of 5-year all-cause mortality and composite end point. Collinearity in the multivariable model was tested using the variance inflation factor. The results of univariate and multivariable analyses were reported as hazard ratio (HR) and corresponding 95% CI. For all analyses, a 2-sided *P* value <.05 was considered to be significant. All statistical analyses were performed using the SPSS software, version 21 (SPSS Inc, Chicago, IL).

Results

Among 304 patients included in the registry, 129 died within 5-year follow-up at a median of 590 days (IQR: 251-1080). Eighty-three of them died for CV causes at a median of 675 days (IQR: 220-1080). Hospitalization due to HF occurred in 88 patients at a median follow-up of 367 days (IQR: 145-872). Seven patients underwent surgical mitral valve replacement at a median of 605 days (IQR: 400-1329), and 8 received heart transplantation or LVAD at a median of 496 days (IQR: 153-942). Median follow-up was 1843 days (IQR: 1200-2170). A complete 5-year clinical follow-up has been reached in 95.4% of the population.

Baseline features according to vital status at 5 years were showed in Table I.

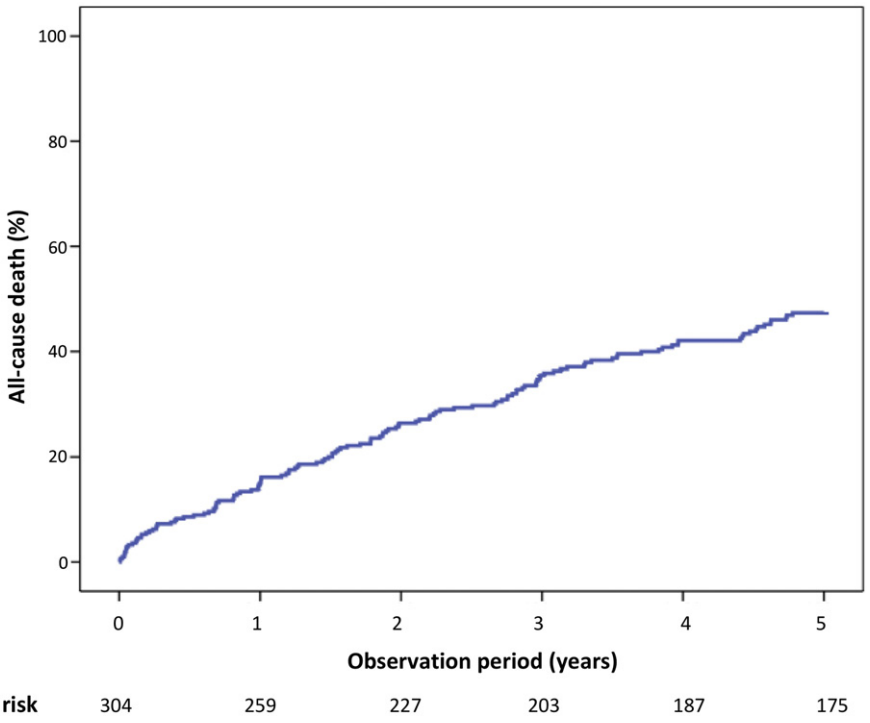
Compared to patients who were alive at 5 years after Mitraclip, those who died were more likely to have diabetes mellitus, coronary artery disease, previous HF hospitalization, functional ischemic etiology of MR, advanced HF symptoms, and lower ejection fraction. As expected, a

Table I. Baseline characteristics

	Overall (304)	Died (129)	Alive (175)	*P* value
Age (y), mean ± SD	72 ± 10	73 ± 10	71 ± 10	.093
Sex (male), n (%)	194 (63.8)	89 (69.0)	105 (60)	.117
BMI (kg/m^2), mean ± SD	25 ± 4	25 ± 4	26 ± 4	.821
EuroSCORE II (%), mean ± SD	8 ± 7	11 ± 9	7 ± 5	<.001
Diabetes mellitus, n (%)	105 (34.5)	56 (43.4)	49 (28)	.007
Hypertension, n (%)	205 (67.4)	86 (28.3)	119 (68)	.806
CAD, n (%)	165 (54.3)	81 (62.8)	82 (46.9)	.007
Prior CABG, n (%)	68 (22.4)	35 (27.1)	33 (18.9)	.096
Prior PCI, n (%)	101 (33.2)	49 (38.0)	52 (29.7)	.141
Atrial fibrillation, n (%)	125 (41.2)	54 (41.9)	70 (40)	.813
COPD, n (%)	66 (21.7)	34 (26.4)	32 (17.5)	.121
Creatinine (mg/dL), mean ± SD	1.5 ± 0.9	1.5 ± 0.7	1.5 ± 1.1	.914
Prior HF, n (%)	200 (65.8)	95 (73.6)	105 (60)	.015
NYHA IV, n (%)	52 (17.1)	28 (21.7)	20 (11.4)	.017
LVEDD (mm), mean ± SD	63 ± 12	64 ± 11	62 ± 12	.128
LVESD (mm), mean ± SD	48 ± 14	49 ± 13	47 ± 15	.307
LVEDV (mL), mean ± SD	174 ± 83	181 ± 71	172 ± 91	.342
LVESV (mL), mean ± SD	116 ± 75	123 ± 64	115 ± 81	.373
LVEF (%), mean ± SD	37 ± 14	35 ± 13	39 ± 14	.025
PAPs (mm Hg), mean ± SD	48 ± 13	48 ± 12	48 ± 14	.926
MR etiology				.015
Primary, n (%)	56 (22.5)	24 (18.6)	40 (22.9)	
Ischemic, n (%)	112 (45)	70 (54.3)	66 (37.7)	
Nonischemic, n (%)	81 (32.5)	35 (27.1)	69 (39.4)	
MRr, n (%)	68 (22.4)	36 (27.9)	32 (18.3)	.025

BMI, body mass index; *CAD*, coronary artery disease; *CABG*, coronary artery bypass graft; *PCI*, percutaneous coronary intervention; *NYHA*, New York Heart Association; *LVEDD*, left ventricular end-diastolic diameter; *LVESD*, left ventricular end-systolic diameter; *LVEDV*, left ventricular end-diastolic volume; *LVESV*, left ventricular end-systolic volume.

Figure 1



Kaplan-Meier survival estimates for the occurrence of primary end point. Legend: Cumulative incidence of mortality up to 5 years.

higher calculated risk profile was observed in these patients compared to those who were alive at 5 years (mean EuroSCORE II 11% ± 9% vs 6% ± 5%, respectively; $P < .001$). Finally, patients who died within 5 years were more likely to have procedure failure of MRr compared to patients who did not.

Primary end point

Cumulative incidence of all-cause mortality at 1, 2, 3, 4, and 5 years was 15.1%, 26.4%, 35.5%, 42.1%, and 47.3%, respectively (Figure 1). Cardiovascular mortality occurred in 9.5% of patients at 1 year, in 17% at 2 years, 24.4% at 3 years, 28.9% at 4 years, and 34.3% at 5 years.

Landmark analysis between 1 and 5 years showed a cumulative incidence of primary end point of 37.9% at a median of 974 days (IQR: 631-1264).

A significantly higher cumulative incidence of 5-year all-cause death was observed in patients with ischemic FMR compared to those with nonischemic FMR and primary MR (57.9% vs 38.2% and 40.3%, respectively; log-rank $P = .009$) (Figure 2, *A*) and in patients who had procedural failure or MRr compared to those who did not (61.3% vs 41.6%, respectively; log-rank $P = .005$) (Figure 2, *B*).

Secondary end point

Cumulative incidence of composite end point including all-cause death and hospitalization due to HF at 1, 2, 3, 4, and 5 years was 29.1%, 41.7%, 49.8%, 56%, and 62.3%, respectively (Figure 3). Hospitalization due to HF occurred in 18.6% of patients at 1 year, 24.5% at 2 years, 29% at 3 years, 32.5% at 4 years, and 37.9% at 5 years.

Landmark analysis between 1 and 5 years showed a cumulative incidence of secondary end point of 46.8% at a median of 867 days (IQR: 651-1283).

Cumulative incidence of 5-year secondary end point was significantly higher among patients with functional ischemic MR compared to functional nonischemic and primary MR (71.7% vs 55.7% and 53.3%, respectively; log-rank $P = .015$) (Figure 4, *A*) and in patients who experienced procedural failure or MRr compared to those who did not (73.1% vs 58.2%; log-rank $P = .002$) (Figure 4, *B*).

Predictors of outcomes

At the multivariable analysis, independent predictors of both primary and secondary end point were procedural failure or MRr and left ventricular ejection fraction (LVEF) less than 30% that were associated with an about 2-fold increased risk of 5-year events (Tables II and III).

Baseline EuroSCORE II >5% significantly increased the relative risk of 5-year mortality (Table II). A trend toward an increased relative risk of 5-year primary end point was observed for patients with previous HF hospitalization (Table II). Ischemic etiology of MR, history of chronic obstructive pulmonary disease (COPD), baseline creatinine >1.5 mg/dL, and previous HF hospitalization were independent predictors of 5-year secondary end point (Table III). No significant collinearity was detected in the multivariable models.

FMR population

Among 304 patients included in the registry, 240 were affected by FMR, 105 of whom died within 5 years. Cumulative incidence of all-cause mortality at 1, 2, 3, 4, and 5 years was 16.2%, 27.4%, 37.1%, 43.6%, and 49.3%, respectively (Supplementary Figure 1, *A*). Secondary end point occurred in 31.4%, 43.3%, 51.3%, 58.8%, and 64.8% of FMR patients at 1, 2, 3, 4, and 5 years, respectively (Supplementary Figure 1, *B*).

A significantly higher cumulative incidence of 5-year events was observed in patients with MRr compared to those without MRr (primary end point: 73.2% vs 41.6%; log-rank $P < .001$; secondary end point: 84.8% vs 58.7%; log-rank $P < .001$) (Supplementary Figure 2).

Among FMR patients, procedural failure or MRr is associated to an almost 3-fold increased risk of 5-year primary and secondary end point. EuroSCORE II >5% and LVEF <30% were independent predictors of 5-year mortality, whereas ischemic etiology, COPD, and prior HF hospitalization were independent predictors of 5-year composite end point. History of hypertension is associated to a decreased risk of 5-year events (Supplementary Tables I and II).

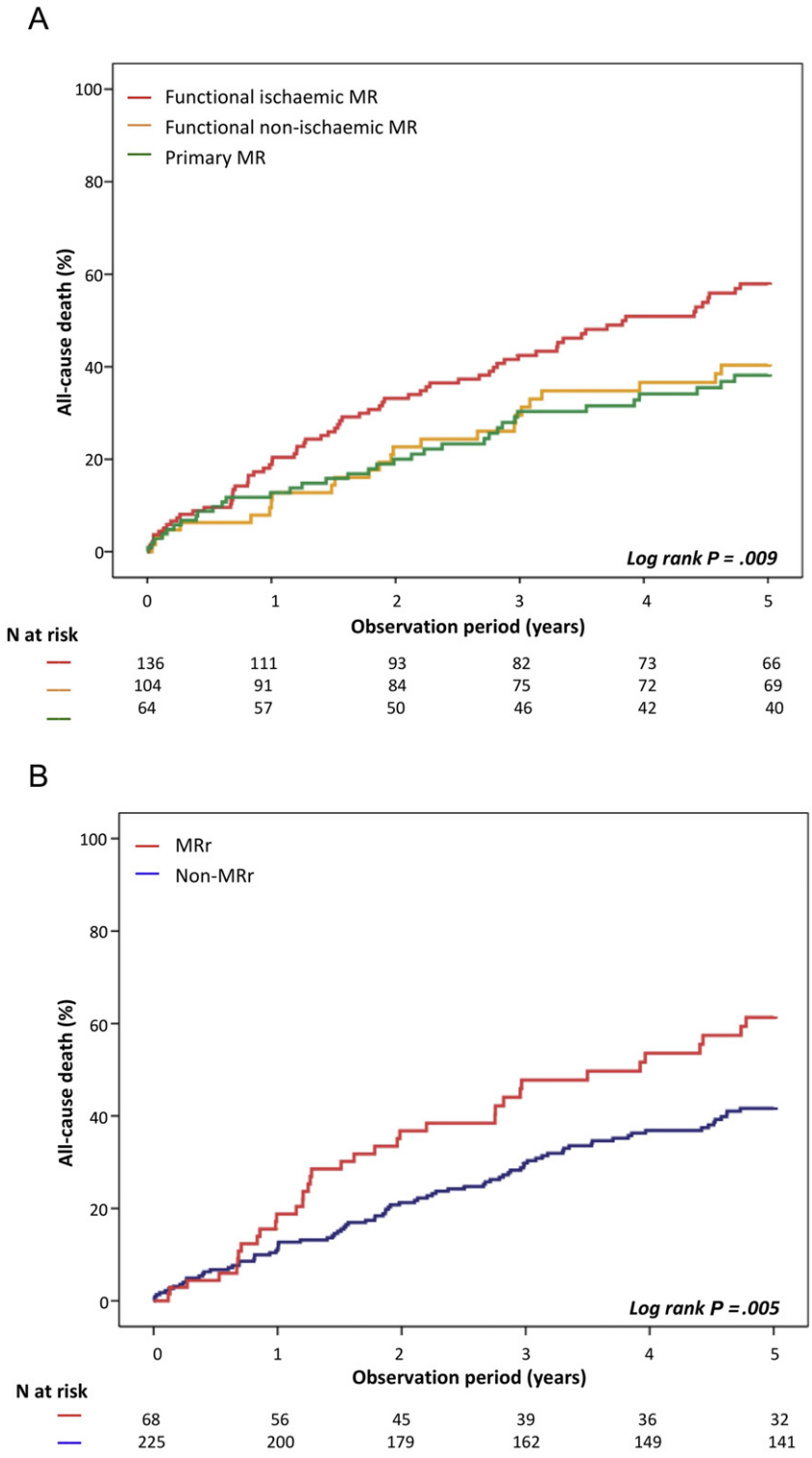
Discussion

The key findings of the present study can be summarized as follows. First, at 5-year follow-up after Mitraclip, almost half of patients died and more than one third were admitted for HF. Second, the cumulative incidence of clinical events had different distribution according to MR etiology and was higher among patients with functional ischemic MR compared to those with functional nonischemic and primary MR. Third, procedural failure or MRr within 2 years was associated to a significantly increased relative risk of 5-year primary and secondary end points. Fourth, EuroSCORE II higher than 5% and severe left ventricular dysfunction (LVEF <30%) were associated to an increased risk of all-cause mortality at 5 years. Finally, ischemic etiology of MR, renal insufficiency at baseline, history of COPD, previous HF hospitalizations, and LVEF<30% were independent predictors of 5-year composite end point.

The GRASP-IT registry is so far the largest real-word multicenter registry that reports complete 5-year clinical outcomes after percutaneous mitral valve repair by Mitraclip.

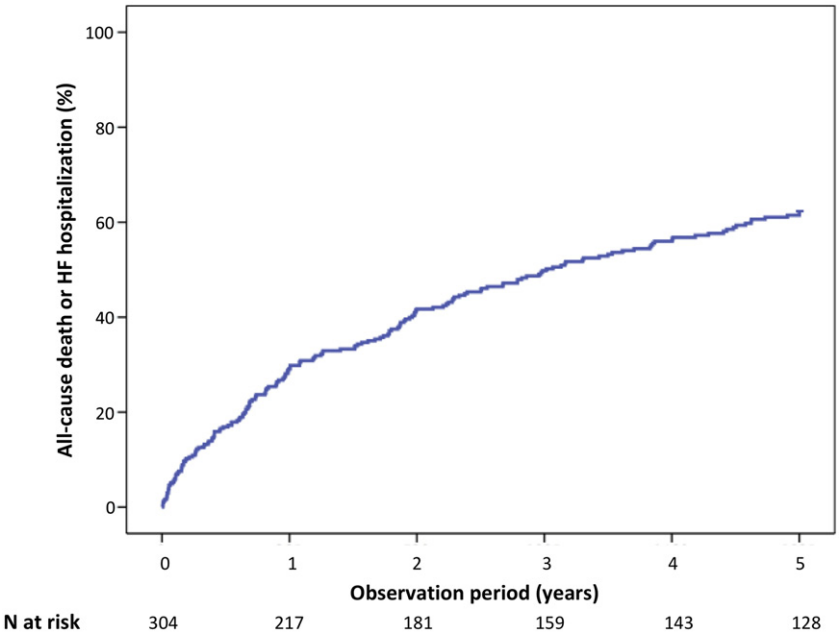
The EVEREST II trial has showed a 5-year mortality in the Mitraclip arm of 20.8%.[5] Nevertheless, the EVEREST II population is highly selected and not comparable to the real-world setting due to its low-risk profile. A more appropriate comparison could be done with EVEREST II High-Risk cohort, including 78 patients, whose 5-year

Figure 2



Kaplan-Meier survival estimates for the occurrence of primary end point stratifying by etiology and mitral regurgitation recurrence. Legend: Cumulative incidence of mortality in patients affected by primary MR, functional nonischemic MR, and functional ischemic MR (**A**) and in patients with and without MRr (**B**).

Figure 3



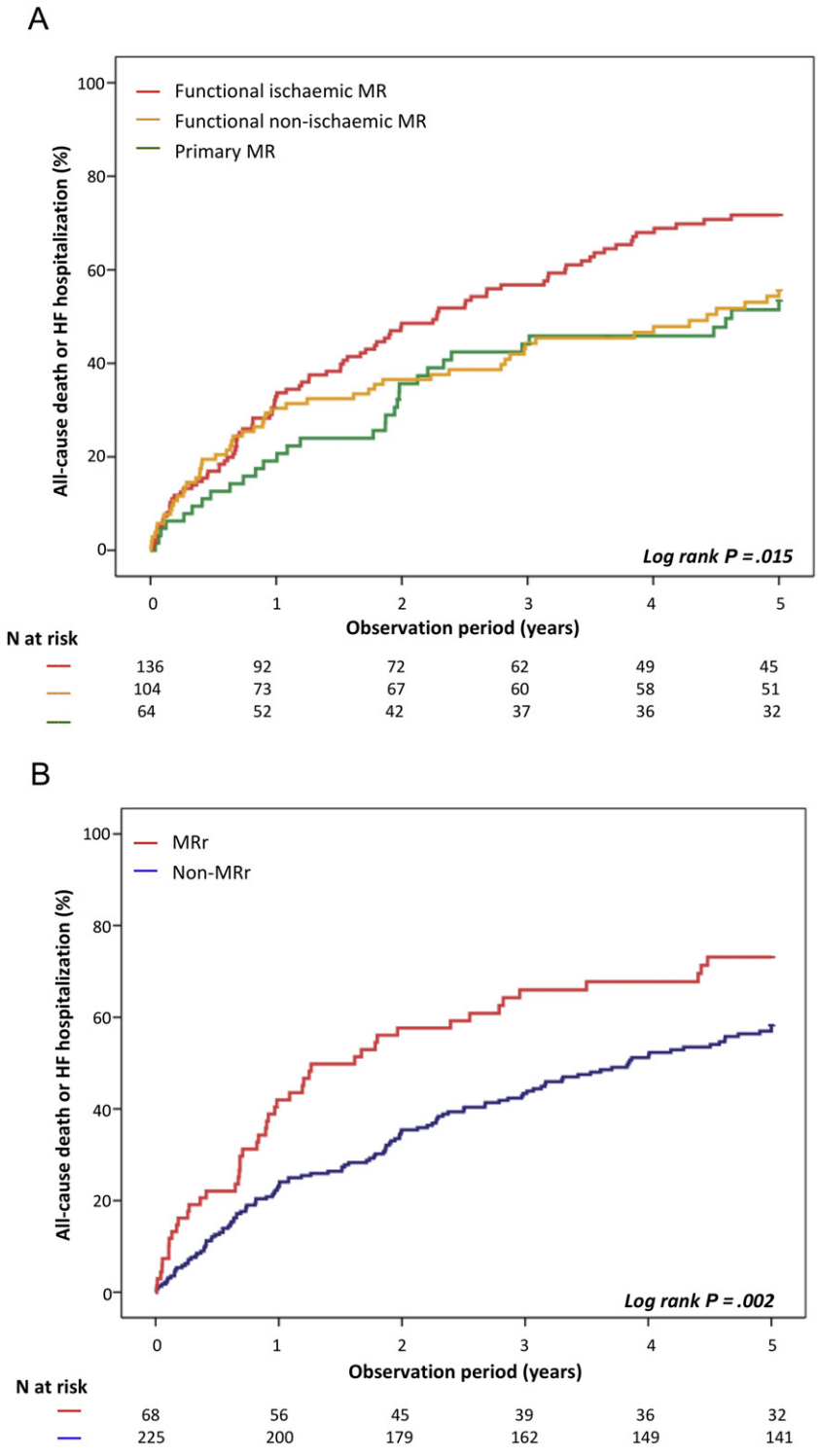
Kaplan-Meier survival estimates for the occurrence of secondary end point. Legend: Cumulative incidence of composite end point including mortality and rehospitalization for HF up to 5 years.

mortality was 53.8%.[10] Buzzatti et al have recently reported a single-center experience showing a cumulative incidence of all-cause death at 5 years after Mitraclip of 46.5% in patients affected by FMR and 42.5% in those with primary MR, and 5-year HF hospitalization rate of 42.1% in FMR and 18.3% in primary MR.[11] Results from a retrospective registry comparing Mitraclip to surgical and medical therapy showed a 5-year incidence of all-cause death of 60.2% in the percutaneous group.[12] Orban et al have previously reported a long-term mortality after Mitraclip of 35.7% at a median of 43 months.[15] TRAMI investigators have published 4-year outcomes showing a mortality rate of 53.1%.[16]

Mortality rate at 5-year follow-up in patients with severe and symptomatic MR who did not undergo mitral valve treatment ranges from 50% to 70%, and HF hospitalization rate reaches 90% in patients alive at 5 years.[12,17-19] Kortland et al have recently reported a propensity-matched analysis showing a 5-year mortality hazard significantly lower in patients treated with Mitraclip compared to those receiving only medical management.[12] Propensity-matched comparison at earlier follow-up has also been reported with favorable results in Mitraclip populations.[20,21] Two recent randomized trials, focusing on FMR and comparing Mitraclip with optimized medical therapy alone, have showed discrepant midterm results.[6,7] The COAPT trial showed a significant advantage in terms of both HF hospitalization (primary end point) and mortality up to 2 years in Mitraclip compared to control group,[7] whereas in MITRA-FR, similar 1-year mortality and HF hospitalization have been observed in interventional and conservative arms.[7] The highly different populations included in the 2 studies could explain the reason for such different results. Selected patients with truly severe MR receiving maximum tolerated dose of medical therapy and without too advanced cardiomyopathy seem to have a midterm prognostic benefit from MR treatment.[8,9] At midterm follow-up, the incidence of events in our real-world population was more similar to that reported in the device arm of COAPT rather than MITRA-FR (1-year mortality: 16% in FMR group of GRASP-IT, 19% in COAPT, and 24% in MITRA-FR; 1-year mortality or HF hospitalization: 31% in FMR group of GRASP-IT, 34% in COAPT, and 55% in MITRA-FR). Long-term results from these 2 trials and data from other ongoing studies will give us further evidence about the role of MR correction in improving long-term prognosis.

Cumulative incidence of 5-year end points was differently distributed in our population based on etiology, with higher values among patients with functional ischemic MR compared to other etiologies. Interestingly, patients with functional nonischemic MR and primary MR seem to have a similar incidence of at long-term events. In addition, ischemic etiology of MR was associated to a 41% increased risk of 5-year composite end point. Previous evidence on the impact of ischemic etiology of MR on prognosis is

Figure 4



Kaplan-Meier survival estimates for the occurrence of secondary end point stratifying by etiology and MRr. Legend: Cumulative incidence of composite end point (mortality and HF rehospitalization) in patients affected by primary MR, functional nonischemic MR, and functional ischemic MR (**A**) and in patients with and without MRr (**B**).

Table II. Predictors of primary end point

	Univariate analysis		Multivariable analysis	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Age >75 y	1.13 (0.80-1.60)	.489		
Sex, male	1.39 (0.96-2.01)	.086	1.34 (0.87-2.05)	.181
BMI >25 kg/m^2	0.86 (0.60-1.22)	.396		
EuroSCORE >5%	2.19 (1.53-3.14)	<.001	2.15 (1.43-3.23)	<.001
Diabetes	1.80 (1.27-2.55)	.001	1.21 (0.79-1.85)	.393
Hypertension	0.86 (0.60-1.24)	.428		
CAD	1.61 (1.12-2.30)	.009	0.77 (0.42-1.42)	.403
Prior CABG	1.38 (0.94-2.04)	.103		
Prior PCI	1.28 (0.90-1.83)	.172		
Atrial fibrillation	1.06 (0.75-1.51)	.741		
COPD	1.39 (0.94-2.05)	.103		
Creatinine >1.5 mg/dL	1.40 (0.96-2.05)	.084	1.19 (0.77-1.85)	.431
Prior HF	1.70 (1.15-2.52)	.008	1.49 (0.96-2.33)	.078
NYHA IV	1.99 (1.31-3.03)	.001	1.29 (0.77-2.17)	.340
LVEDV >160 mL	1.34 (0.94-1.91)	.102		
LVESV >110 mL	1.37 (0.97-1.95)	.078	0.80 (0.48-1.31)	.368
LVEF <30%	1.69 (1.19-2.39)	.003	1.62 (1.10-2.40)	.015
PAPs >50 mm Hg	0.96 (0.66-1.39)	.831		
FMR	1.32 (0.85-2.06)	.218		
Ischemic MR	1.71 (1.21-2.42)	.002	1.14 (0.66-1.97)	.629
MRr	1.73 (1.17-2.56)	.006	2.17 (1.42-3.31)	<.001

Table III. Predictors of secondary end point

	Univariate analysis		Multivariable analysis	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Age >75 y	0.93 (0.70-1.26)	.652		
Sex, male	1.16 (0.85-1.58)	.362		
BMI >25 kg/m^2	0.98 (073-1.33)	.906		
EuroSCORE II >5%	1.53 (1.12-2.10)	.007	1.21 (0.83-1.75)	.324
Diabetes	1.55 (1.14-2.09)	.005	0.91 (0.62-1.35)	.653
Hypertension	0.79 (0.58-1.07)	.132		
CAD	1.48 (1.09-2.00)	.012	0.91 (0.53-1.69)	.804
Prior CABG	1.26 (0.90-1.77)	.181		
Prior PCI	1.20 (0.89-1.63)	.237		
Atrial fibrillation	1.14 (0.84-1.53)	.400		
COPD	1.59 (1.14-2.22)	.007	1.72 (1.17-2.51)	.005
Creatinine >1.5 mg/dL	1.42 (1.02-1.97)	.037	1.54 (1.08-2.19)	.017
Prior HF	2.01 (1.43-2.82)	<.001	1.77 (1.20-2.61)	.004
NYHA IV	2.06 (1.44-2.95)	<.001	1.33 (0.87-2.03)	.192
LVEDV >160 mL	1.43 (1.06-1.95)	.020	0.74 (0.39-1.43)	.373
LVESV >110 mL	1.50 (1.11-2.03)	.008	1.16 (0.75-1.79)	.512
LVEF <30%	1.55 (1.15-2.09)	.004	1.60 (1.13-2.26)	.008
PAPs >50 mm Hg	1.02 (0.74-1.40)	.291		
FMR	1.39 (0.95-2.04)	.080	1.02 (0.58-0.78)	.948
Ischemic MR	1.54 (1.14-2.07)	.005	1.41 (1.01-1.99)	.049
MRr	1.69 (1.21-2.38)	.002	2.20 (1.52-3.19)	<.001

conflicting.[13,22-24] We may speculate that patients with functional ischemic MR having more or less extended "scar" zone could get a poor prognosis due to the absence of substrate for recovering.

Failure of Mitraclip procedure, moderate-to-severe or severe MR at discharge, and MRr during the follow-up have been previously reported as predictors of adverse outcome at midterm follow-up after percutaneous correction of both primary and functional MR.[2,7,11,13,16,25-27] Our finding confirms these previous observations showing that patients who underwent successful Mitraclip procedure with durable result (MR ≤2+ up to 2-year follow-up) had a better long-term outcome compared to patients with procedural failure or MRr within 2 years even after

adjustment for possible confounders. This could be interpreted as an indirect evidence that MR correction may improve long-term prognosis, interrupting the vicious circle that leads to developing or worsening of left ventricular disease.

EuroSCORE II has been previously reported as the best surgical risk score in terms of correlation to mortality up to 3-year follow-up in patients undergoing Mitraclip.[28] In the same cohort, at longest follow-up, we confirmed a strong correlation between EuroSCORE II and primary end point. EuroSCORE II with a cutoff value of 5% emerged as an independent predictor of 5-year mortality. This was expectable given the high comorbidity burden inherent to high EuroSCORE II. More interesting is that, in the multivariable analysis, MRr emerged as an independent predictor of 5-year mortality despite the presence of such a strong competitor.

Severe left ventricular dysfunction, renal insufficiency, and prior HF hospitalization, as surrogate of advanced cardiomyopathy, have also been confirmed to be independent predictors of composite end point[2,16] even at long-term follow-up. Of note, LVEF <30% was also associated with an increased risk of mortality as single end point. Goliasch et al reported that severe FMR did not affect long-term outcome in patients with LVEF <30%.[18] Low LVEF values have already been reported as predictor of poor midterm prognosis in Mitraclip recipients.[2] Thus, a more advanced left ventricular dysfunction may be less likely associated with a favorable recovery after MR correction.

COPD, which also resulted to be associated with an increased risk of secondary end point, has to be considered an important comorbidity leading to higher mortality[5,16] as well as a potential trigger for HF hospitalization when its reactivation occurred.

Limitations

The present study has several limitations. First, it has a retrospective design with lack of a control arm; nevertheless, the inclusion of consecutive patients and the statistical adjustment for baseline imbalance by multivariable model should have minimized potential selection bias. Unfortunately, data about medical therapy changes during the follow-up are not available, and this could have affected our results. Second, the sample size is relatively small; however, 129 primary end points and 176 secondary end points have allowed us to perform a solid multivariable analysis. Third, the study lacks complete echocardiographic follow-up, although it purposefully focuses on hard end points; moreover, the available echocardiographic parameters have not been assessed by a central Core Laboratory but by expert physicians at each center. Finally, additional data such as effective regurgitant orifice area, natriuretic hormone levels, 6-minute walking test distance, and quality of life assessment are not available.

Conclusions

In the GRASP-IT registry, 47% of patients died and 62% died or were admitted for HF at 5 years after Mitraclip. Procedural failure or MRr is one of the main independent predictors of both primary and secondary end points. Ischemic MR etiology, high comorbidity burden (ie, EuroSCORE II >5%, COPD), and advanced cardiomyopathy (ie, severe left ventricular dysfunction, prior HF admission, cardiorenal syndrome) significantly increase the relative risk of 5-year clinical events.

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