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# Percutaneous mitral valve repair with the MitraClip system in the elderly: One-year outcomes from the GRASP registry☆

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ABSTRACT

*Background:* Although mitral regurgitation (MR) affects a relevant and increasing number of elderly, an optimal management of this high-risk population is challenging.
*Methods and results:* The aim of this prospective, observational study was to compare one-year outcomes of MitraClip therapy in high surgical risk patients with moderate-to-severe or severe MR between patients aged <75 versus ≥75 years. A total of 180 patients were included: 92 were <75 years and 88 were ≥75 years old. At one-year follow-up the primary efficacy endpoint (composite of death, surgery for mitral valve dysfunction and grade 3+ or 4+ MR) occurred in 41 patients (24.5%), with similar rates between those aged <75 years (23.9%) and those ≥75 years (25.2%), $p = 0.912$. A total of 21 (12.2%) deaths were observed within 1 year after the MitraClip procedure, without significant differences in cumulative mortality rates between elderly and younger patients (10.8% vs. 13.3%, respectively, $p = 0.574$). Compared with baseline, the significant reduction in MR severity achieved after the procedure was sustained at one-year follow-up, in both elderly and younger patients and a significant improvement in NYHA functional class was observed in both groups. A total of 18 (10.0%) patients experienced a re-hospitalization for acute heart failure within one-year after the MitraClip procedure, with no significant differences between elderly and younger. At one-year follow-up both elderly and younger patients showed significant reductions in left ventricular volumes, with changes of similar extent between the two subgroups.
*Conclusions:* MitraClip therapy can be considered a viable option also among subsets with more advanced age.


## 1. Introduction

Transcatheter mitral valve repair with the MitraClip System (Abbott Vascular, Santa Clara, CA, USA) may be considered as a therapeutic option for severely symptomatic mitral regurgitation (MR) patients with a prohibitive surgical risk [1]. The MitraClip therapy is based on the edge-to-edge surgical technique and has been successfully used to treat either functional or degenerative MR, showing to reduce regurgitation degree, improve symptoms and lead to left ventricular (LV) reverse remodeling [2–8].

Although MR affects more than one in ten people over the age of 75 years and the rate increases as the population continues to grow old, attention has not been specifically focused on the elderly, who were often denied surgery [9–12]. Actually, an optimal management of elderly patients with severe MR is challenging, due to the high frequency of comorbidities and to the difficulties in balancing survival and functional benefits with perioperative risks. The common view is that, in this age group, mitral valve surgery is related to high early mortality, unclear survival benefit and doubtful satisfactory valve repair because of extensive annular calcification and fragile tissues [13]. Therefore, in daily clinical practice, MitraClip therapy could represent a viable option for elderly patients with MR. Differently from the randomized EVEREST II (Endovascular Valve Edge-to-Edge Repair Study) trial, large real world registries on percutaneous mitral valve repair with the MitraClip System, have included older patients with a larger number of comorbidities [14–18]. However, the influence of age on outcomes after MitraClip treatment has not been clearly defined.

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The aim of this study was to compare one-year outcomes of percutaneous mitral valve repair with the MitraClip System in high surgical risk patients with moderate-to-severe or severe MR aged <75 versus ≥75 years.

## 2. Methods

This was a prospective, observational study of consecutive high surgical risk patients with moderate-to-severe or severe MR who underwent percutaneous mitral valve repair with the MitraClip system from October 2008 to December 2013 at Ferrarotto Hospital (Catania, Italy), as part of the ongoing GRASP (Getting Reduction of Mitral Insufficiency by Percutaneous Clip Implantation) registry [18]. This sub-analysis focused on two subgroups stratified by age at enrollment (<75 or ≥75 years) to address the impact of age on outcomes after MitraClip implantation. High surgical risk was established by consensus between a local independent cardiologist and a cardiac surgeon that conventional surgery would be associated with excessive morbidity and mortality. Surgical risk was based on either the EuroSCORE or the Society of Thoracic Surgeons (STS) mortality risk calculation, or based on the presence of specific surgical risk factors not covered in these risk models. Qualifying inclusion and exclusion criteria for MitraClip therapy, as well as details of the procedure, have been previously reported [18]. All enrolled patients underwent clinical and echocardiographic evaluation at baseline, 1 month, 6 months and 1 year after the procedure of percutaneous mitral valve repair. The baseline and follow-up functional status, assessed according to the New York Heart Association (NYHA) criteria, was also reported. The local ethics committee approved the present study and all patients provided written informed consent.

Throughout the study period MR grade was serially assessed by transthoracic echocardiography, according to the current guidelines, on the base of integrative method and the consensus of 2 or 3 experienced observers [19–20]. To evaluate LV changes in size and function, the following parameters were considered: LV end-diastolic and end-systolic diameter (LVEDD and LVESD, respectively); LV end-diastolic and end-systolic volume (LVEDV and LVESV, respectively), and ejection fraction (EF), performed according to the biplane Simpson's method. Also tricuspid annular plane systolic excursion (TAPSE) was evaluated. Pulmonary artery systolic pressure (PASP) was measured using the gradient derived from the maximal velocity of tricuspid regurgitation.

Acute device success was defined as a residual MR ≤ 2+ after clip implantation. The primary safety endpoint was the rate of major adverse events (MAEs) at 1 month, defined as the composite of death, myocardial infarction, reoperation for failed mitral valve repair, non-elective cardiovascular surgery for adverse events, stroke, renal failure, deep wound infection, mechanical ventilation for >48 h, gastrointestinal complication requiring surgery, new-onset atrial fibrillation, pericardial effusion, septicemia and transfusion ≥ 2 units of blood. The primary efficacy endpoint was the composite of death, surgery for mitral valve dysfunction and grade 3+ or 4+ MR at one-year follow-up. Secondary endpoints were the components of the primary endpoint, re-hospitalization rates and functional NYHA class.

Continuous variables are presented as the mean ± SD or median and interquartile range and were compared using the Student's *t*-test or Mann-Whitney rank sum test for unpaired comparisons, as appropriate, and the Wilcoxon rank sum test for paired comparisons. Categorical variables are expressed as counts and percentages and were compared using the $\chi^2$ test or Fisher exact test, as appropriate. Cumulative event rates were assessed as Kaplan-Meier estimates. Correlations between the echocardiographic measurements were tested, and only those statistically significant were reported, providing the Spearman correlation coefficient. Cox regression analysis was performed to identify independent predictors of one-year mortality after MitraClip therapy. Risk estimates are expressed as hazard ratio (HR) and 95% confidence interval (CI). Candidates variables for the multivariable model were those considered clinically relevant, including chronic kidney disease, diabetes mellitus and EuroSCORE II, plus those with a $p$ value <0.10 at the univariate analysis. Differences were considered statistically significant when $p < 0.05$. Statistical analyses were performed using the Statistical Package for Social Science, version 17.0 (SPSS, Chicago, IL).

## 3. Results

### 3.1. Patient population

A total of 180 patients were included in the present analysis: 92 (51.1%) were aged <75 years and 88 (48.9%) ≥75 years. Baseline demographic and clinical characteristics of the overall population and according to age are listed in Table 1. Comparable baseline features were observed between the two groups, with significant differences in terms of STS score, worst in the older group, NYHA functional class IV and atrial fibrillation, both more common in the older group, male sex, poor LV EF and previous percutaneous intervention, all more frequent in the younger group (Table 1). With regards to etiology, 33 (18.3%) patients presented with degenerative MR and 147 (81.7%) with functional MR; functional MR was more prevalent in both subgroups, with a significant difference between them (Table 1). Baseline echocardiographic characteristics of the overall population and of the two analyzed subgroups are listed in Table 2. Younger patients presented with a poorer and more dilated left ventricle and with lower LV EF (Table 2).

### 3.2. Procedural, clinical and echocardiographic outcomes

Acute device success was achieved in 97.8% of patients. One clip was implanted in 100 (55.5%) patients, two clips in 75 (41.7%) patients, three clips in 4 (2.3%) patients and four in 1 patient (0.5%); comparable distributions were observed in elderly and younger patients. Device implantation time, defined as the time from the guide insertion until clip delivery system removal, was not significantly different between the two subgroups (66.2 ± 34.4 min in patients <75 years and 71.1 ±

**Table 1**
Baseline characteristics within the overall population and in patients aged <75 versus ≥75 years who underwent mitral valve repair with the MitraClip System.

| | Overall population ($n$ = 180) | <75 years ($n$ = 92) | ≥75 years ($n$ = 88) | $p$ value |
|---|---|---|---|---|
| Age, years ± standard deviation | 71.6 ± 9.8 | 64.4 ± 8.6 | 79.2 ± 3.1 | <0.001 |
| Male, % | 61.7 | 69.6 | 53.4 | 0.03 |
| Comorbidities, % | | | | |
| Systemic hypertension | 75.0 | 78.3 | 71.6 | 0.30 |
| Hypercolesterolemia | 51.7 | 53.3 | 50.0 | 0.66 |
| Diabetes mellitus | 35.0 | 40.2 | 29.5 | 0.13 |
| Chronic obstructive pulmonary disease | 21.7 | 22.8 | 20.5 | 0.70 |
| Peripheral artery disease | 10.0 | 9.8 | 10.2 | 0.92 |
| Chronic kidney disease* | 47.8 | 42.4 | 53.4 | 0.14 |
| Atrial fibrillation | 38.3 | 29.3 | 47.7 | 0.01 |
| Prior myocardial infarction | 34.4 | 39.1 | 29.5 | 0.17 |
| Previous percutaneous intervention | 35.6 | 43.5 | 27.3 | 0.02 |
| Previous coronary artery bypass graft | 20.0 | 21.7 | 18.2 | 0.55 |
| Previous heart valve surgery | 11.1 | 9.8 | 12.5 | 0.56 |
| NYHA functional class, % | | | | |
| I | – | | | |
| II | 18.9 | 21.8 | 15.9 | 0.32 |
| III | 70.6 | 72.8 | 68.2 | 0.49 |
| IV | 10.5 | 5.4 | 15.9 | 0.02 |
| LV ejection fraction <30% | 48.3 | 63.0 | 33.0 | <0.001 |
| Functional MR | 81.7 | 89.1 | 73.9 | 0.01 |
| EuroSCORE II | 7.6 ± 6.4 | 7.1 ± 6.0 | 8.2 ± 6.7 | 0.25 |
| STS mortality risk | 6.0 ± 5.8 | 3.8 ± 3.4 | 8.1 ± 6.8 | <0.001 |

MR = mitral regurgitation; NYHA = New York Heart Association; LV = left ventricular; STS = Society of Thoracic Surgeons.
* Estimated glomerular filtration rate < 60 ml/min/1.73 $m^2$.