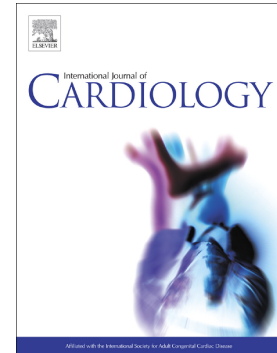


2-year outcomes of MitraClip as a bridge to heart transplantation:
The international MitraBridge registry

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2-year outcomes of MitraClip as a bridge to heart transplantation: the International MitraBridge Registry

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Abstract

Background: In the first report from the MitraBridge registry, MitraClip as a bridge to heart transplantation (HTx) proved to be at 1-year an effective treatment strategy for 119 patients with advanced heart failure (HF) who were potential candidates for HTx. We aimed to determine if benefits of MitraClip procedure as a bridge-to-transplant persist up to 2-years.

Methods: By the end of the enrollment period, a total of 153 advanced HF patients (median age 59 years, left ventricular ejection fraction $26.9\pm 7.7\%$) with significant secondary mitral regurgitation, who were potential candidates for HTx and were treated with MitraClip as a bridge-to-transplant strategy, were included in the MitraBridge registry. The primary endpoint was the 2-year composite adverse events rate of all-cause death, first hospitalization for HF, urgent HTx or LVAD implantation.

Results: Procedural success was achieved in 89.5% of cases. Thirty-day mortality was 0%. At 2-year, Kaplan-Meier estimates of freedom from primary endpoint was 47%. Through 24 months, the annualized rate of HF rehospitalization per patient-year was 44%. After an overall median follow-up time of 26 (9-52) months, elective HTx was successfully performed in 30 cases (21%), 19 patients (13.5%) maintained or obtained the eligibility for transplant, and 32 patients (22.5%) no longer had an indication for HTx because of significant clinical improvement.

Conclusions: After 2-years of follow-up, the use of MitraClip as a bridge-to-transplant was confirmed as an effective strategy, allowing elective HTx or eligibility for transplant in one third of patients, and no more need for transplantation in 22.5% of cases.

Keywords: MitraClip; secondary mitral regurgitation; advanced heart failure; heart transplantation; transcatheter mitral valve intervention.

Introduction

The prevalence of advanced heart failure (HF) is increasing worldwide, due to the growing global number of HF patients and the improvement in their treatment and survival¹. Even though the progression in advanced pharmacological and mechanical therapies has partly ameliorated the morbidity and mortality of these patients^{2,3}, prognosis remains poor, with a 1-year mortality ranging from 25 to 75%^{2,4}. Heart transplantation (HTx) remains the only treatment option with effective mid- and long-term results, with a post-transplant 1-year survival of around 90% and a median survival of 12.5 years⁴. However, its accessibility is limited by recipient eligibility and organ donor scarcity^{1,2}. As a consequence, advanced HF patients who are potential candidates for HTx, often need bridging therapies to reduce or reverse worsening and progression of underlying disease until a transplantable organ become available. Previously, 1-year results from the MitraBridge registry reported on the potential role of transcatheter edge-to-edge repair (TEER) with the MitraClip system as a bridge strategy to HTx in 119 patients with advanced HF⁵. Moderate or severe secondary mitral regurgitation (MR) is indeed a common finding in patients with HF⁶, which negatively affects their prognosis increasing the rate of admission for HF and the risk of mortality⁷.

In the MitraBridge study, correction of significant secondary MR by TEER resulted to be a safe and effective procedure in advanced HF patients who were potential candidates or were waiting for HTx: procedural success of TEER was 87.5%, no death occurred at 30 days, and the procedure guaranteeing safe access to or eligibility for transplant in more than 30% of cases⁵. The present report aims to describe clinical outcomes of a larger series of patients with advanced HF post TEER up to 2-year of follow-up.

Methods

Registry design

The MitraBridge is an observational, international, multicenter registry created in 2018 and concluded in November 2021. The registry design and 1-year interim results were previously published⁵. In brief, all consecutive patients with chronic advanced HF (defined as New York Heart Association [NYHA] III or IV and/or left ventricular ejection fraction [LVEF] $\leq 30\%$ and according to the definitions proposed by the Heart Failure Association of the European Society of Cardiology⁸) and concomitant moderate-to-severe or severe secondary MR, who were potential candidates for HTx and treated with MitraClip in the context of a pre-specified bridge strategy, were evaluated for inclusion. By the end of the enrollment period, a total of 23 centers from Europe and Canada (3 more than that previously included⁵) have contributed to the registry. For the purpose of the present analysis, prolonged follow-up data of patients enrolled in the registry were requested and collected from each center whenever available.

The inclusion of patients in the study was approved at each institution by a local ethical committee or per local practice for the collection of prospective data. This study is registered with ClinicalTrials.gov (NCT04293575).

Patients selection

All potential candidates for HTx treated with MitraClip in the context of a pre-specified bridge strategy as per local Heart Team decision, were classified according to one of the following clinical conditions present at the time of the procedure:

1. patients active on an HTx waiting list (*In List group*) with a low likelihood to receive an organ rapidly (e.g., for low priority status) and/or progressive unstable clinical conditions;
2. patients with new unexpected clinical worsening and/or new history of acute HF decompensation, who were otherwise suitable for HTx (according to local Heart Team evaluation) but were still waiting for final clinical decision (*bridge to decision [BTD] group*);

3. patients who could not be yet listed for HTx (*bridge to candidacy* [BTC] group) because of concomitant, potentially reversible clinical contraindications or other reasons preventing eligibility to transplant.

Outcomes

The primary end-point of the present analyses was the 2-year composite adverse events rate of all-cause death, urgent HTx or left ventricular assist device (LVAD) implantation, and first rehospitalization for HF. The secondary end-point was the 2-year rate of first rehospitalization for HF. As exploratory outcome, we considered all HF rehospitalization within 24 months from MitraClip procedure, including recurrent events for patients with more than one hospitalization. Finally, the clinical status of patients at the time of last available follow-up was reported, in order to describe the rates of patients entering (or remaining in) the transplant waiting list, having no more indication to HTx because of significant echocardiographic and/or clinical improvements during the entire observational period, and going for elective HTx. When primary, secondary and exploratory outcomes were assessed, for patients who underwent LVAD implantation or HTx, follow-up data were censored at the time of these events.

Statistical analysis

Results are presented as mean \pm SD for continuous variables normally distributed (tested by the Shapiro-Wilk normality test), as median (25th and 75th percentiles) for continuous variables without normal distribution, and as absolute numbers (percentages) for categorical data. One-way analysis of variance and Student's unpaired t-test were used to compare normally distributed continuous variables. For non-normally distributed continuous variables, the Kruskal-Wallis test and Wilcoxon rank-sum test were used to compare data between 3 or 2 groups, respectively. Chi-square and Fisher exact tests were used to compare categorical variables. Student's paired t-test and Wilcoxon matched-pairs signed-ranks test were used to compare mean changes from baseline to follow-up in normally

distributed and non-normally distributed continuous echocardiographic variables, respectively. Event rates of primary composite and secondary (first rehospitalization for HF) endpoints were estimated using the Kaplan–Meier method; comparisons were performed using the log-rank test. The rate of rehospitalization for HF per patient-year (exploratory outcome) was calculated as the total number of HF hospitalization events divided by total follow-up years. Finally, association between MR severity at follow-up and study endpoints was investigated using univariate and multivariate (adjusting hazard ratio of MR severity for previously identified predictors of primary endpoints: HF hospitalization within previous 6 months, procedural failure, INTERMACS profiles 1-4, left ventricular ejection fraction, NYHA functional class IV⁵) cox regression analyses. The statistical analysis, the Kaplan–Meier mortality curves, and the graphs were performed with the use of Stata version 14 (StataCorp LLC, College Station, TX) and GraphPad Prism software version 6 (GraphPad, Inc, San Diego, CA).

Results

Study population and procedural results

By the end of the enrollment period, further 34 advanced HF patients were screened and included in the MitraBridge registry, obtaining a final study population of 153 patients (median age 59 [53-63] years, 113 [74%] men). As previously reported⁵, before MitraClip procedure, all patients were on guideline-directed medical therapy as tolerated, **Supplementary Table 1**. Nevertheless, HF symptoms were reported in all of them, with 93% of patients being classified in NYHA functional class III or IV. Moreover, at least one hospitalization for HF in the 6 months before the index procedure occurred in 63% of cases. According to the INTEF MACS classification, large part of the study population was in profiles 3 to 6 (profiles 3-4 36%, profiles 5-6 47.5%), **Supplementary Table 1**.

At the time of MitraClip intervention, 38 patients (25%) were on the active HTx waiting list (In List group), 80 patients (52%) were still waiting for a final clinical decision (BTD group), while 35 patients (23%) could not be yet included in the transplant waiting list because of concomitant, potentially reversible contraindications (BTC group). Clinical conditions of patients belonging to the In List and BTC groups were previously described⁵. **Supplementary Table 1** summarizes baseline characteristics of the overall population and of each study group.

As per inclusion study criteria, all patients had secondary MR: the severity of valve regurgitation was moderate-to-severe and severe in 15 (10%) and 138 (90%) cases, respectively. Mean left ventricular ejection fraction (LVEF) was $26.9 \pm 7.7\%$, with 107 patients (70%) having values $\leq 30\%$. Adverse left chamber remodeling was reported in the majority of patients, with a median left ventricular end diastolic volume index of 119.8 (99-150.6) mL/m². At baseline echocardiographic evaluation, elevated systolic pulmonary artery pressure (PAP, ≥ 35 mmHg) was reported in 136 patients (89%), with a median value of 50 (40-60) mmHg, **Supplementary Table 2**. Baseline right heart catheterization data were available for 112 (73%) patients: the hemodynamic evaluation confirmed the severity of left ventricular dysfunction (median cardiac index 1.9 [1.7-2.3] L/min/m²) and the

elevated values of PAP (mean PAP 33 ± 10 mmHg); 87.5% of patients had pulmonary hypertension, with a mean value of pulmonary arterial wedge pressure of 24.6 ± 9.5 mmHg. Combined pre- and post-capillary pulmonary hypertension was reported in 61% of cases, **Supplementary Table 2**.

Procedural success according to the Mitral Valve Academic Research Consortium definition⁹ was achieved in 89.5% of cases, with a higher rate of success for patients belonging to In List (92%) and BTD groups (93.5%) than to BTC group (77%; $p = 0.023$), **Supplementary Table 1**. For three patients (2 from the In List group and 1 from the BTD group) no clip was implanted because of inadequate clip positioning (2 cases) and hemodynamic instability during the procedure (1 case). No deaths occurred during the procedure and within 30 days.

Clinical follow-up status

Overall

The clinical follow-up was available for 145 patients (93.5%), with an overall median follow-up time of 26 (9-52) months; a follow-up time of more than 2 years was available in 77 cases [55.5%, 50 (33-65) months]. All major events stratified according to each study group are reported in a chronological manner in **Figure 1**. After MitraClip procedure, 13 deaths (9.1% of the entire study population with available follow-up) not related to HTx or LVAD occurred, in 9 cases secondary to a clear cardiovascular cause. 9 patients (6.5%) needed urgent LVAD implantation because of MitraClip bridge therapy failure with sudden clinical worsening. On the other hand, according to the progressive nature of their underlying disease, despite an initial hemodynamic stabilization after TEER, 17 patients (11.9%) underwent elective LVAD implantation after a median time of 15 (6-26) months: in 14 cases LVAD was positioned as bridge to HTx strategy; 3 patients received long-term mechanical circulatory support as destination therapy. Of these 26 patients who underwent urgent or elective LVAD implantation, 8 patients (31%) died after a median time of 398.5 (116-796.5) days, while in 6 cases (23.1%) elective HTx was performed after 777 (135-1001) days from LVAD positioning.

While 9 patients (6.5%) needed urgent HTx secondary to sudden clinical worsening despite MitraClip treatment, HTx according to standard listing criteria was successfully performed in 30 patients (21%) after a median time of 15 (5-29) months from the index procedure. Clinical follow-up after transplant was available in 22 of 39 cases (median time 376.6 (110-1022) days): 6 patients died after 11 (1-305) days from HTx because of acute organ rejection or infective complications; the other 16 patients were in good clinical conditions, in the absence of HF symptoms (NYHA functional class I).

Finally, a total of 32 patients (22.5%) no longer had an indication for HTx because of significant clinical improvement, **Supplementary Table 3**.

In List group

Of the 38 patients included into the In list group, follow up data were available in 37 cases (97.4%). Of these, after MitraClip procedure, 2 patients (5.5%) died, one patient (2.7%) needed elective LVAD implantation, 5 subjects (13.5%) received urgent HTx, while in 14 cases (37.8%) HTx according to standard listing criteria was performed. Until the last available follow-up contact, whereas 10 patients (27%) remained in list for HTx, 5 patients (13.5%) were delisted because of improvement of their clinical and echocardiographic conditions.

BTC group

For 34 (97.1%) of 35 patients included into the BTC group follow-up data were available. Of these, during the follow-up period, 4 patients (11.8%) died, 7 patients underwent LVAD implantation (20.6%, in one case urgent LVAD placement was performed), and 5 patients received HTx (14.7%, one urgent HTx). Until the last available follow-up contact, whereas in 4 cases (11.8%) eligibility for transplant was achieved and patients moved to the active HTx waiting list, 12 patients (35.3%) no longer had an indication for HTx because of significant clinical improvement.

BTD group

The clinical follow-up was available for 72 (90%) of the 80 patients included into the BTD group. After MitraClip procedure, 7 patients (9.7%) died, 18 patients underwent LVAD implantation (25%, 10 urgent LVAD placements), 15 patients received HTx (20.8%, 3 urgent HTxs). Until the last available follow-up contact, whereas 5 subjects (6.9%) achieved eligibility for transplant and moved to the active HTx waiting list, in 15 cases (20.8%) an indication for HTx was no longer needed because of significant clinical improvement.

Echocardiographic follow-up

Echocardiographic follow-up data before HTx or LVAD implantation were available in 119 cases (78%), with a median time to the last available echocardiographic control of 391 (211-631) days. A persistent significant improvement in MR severity was observed in most of the study population, with 69% of patients having a MR grade $\leq 2+$, **Supplementary Figure 1**. MitraClip treatment prevented a further deterioration of left ventricular function and dimension, guaranteeing that values of LVEF and left ventricular end diastolic volume remained stable (LVEF baseline $27.4 \pm 7.4\%$ vs follow-up $26.5 \pm 8.7\%$, p-value=0.166; left ventricular end diastolic volume baseline 220 [181.8-278] mL vs follow-up 239 [170.5-272.5] mL, p-value=0.979). A significant amelioration in pulmonary hemodynamics was also reported, with a reduction in systolic PAP from 50 (40-61) mmHg to 43 (33-53) mmHg, p-value<0.001. Finally, no deterioration of right ventricular function occurred (tricuspid annular plane systolic excursion baseline 17.4 ± 4 mm vs follow-up 17.7 ± 4.1 mm, p-value=0.492), **Supplementary Figure 2**. For those patients who no longer had an indication for HTx, at echocardiographic follow-up evaluation (data available for 31 of 32 patients) MR severity $\leq 2+$ was reported in 80.5% of cases; the median values of left ventricular end diastolic volume and systolic PAP changed from 179 (143-229) mL to 170.45 (150-248) mL, p-value=0.665, and from 45 (37.5-53) mmHg to 33 (25-42.5) mmHg, p-value<0.001, respectively. Values of LVEF remained stable (from $31.8 \pm 7.3\%$ to $31.5 \pm 7.5\%$, p-value=0.742).

Clinical outcomes

The 2-year Kaplan-Meier estimates rate of primary composite endpoint (all-cause death, urgent HTx or LVAD implantation, and first rehospitalization for HF) was 53%. Within 24 months from MitraClip treatment, 7 all-cause deaths, 48 first rehospitalizations for HF, 9 urgent HTx, and 7 urgent LVAD implantations occurred, **Table 1, Figure 2A**. The 2-year Kaplan-Meier estimates rate of first rehospitalization for HF (secondary endpoint) was 45%, **Table 1, Figure 2B**. Through 24 months, the total number of HF hospitalization was 81, occurring in 48 patients, with an annualized rate of events of 44% per patient-year, **Figure 3**. At univariate and multivariate cox regression analyses, having a MR severity at follow-up lower than moderate was identified as an independent predictor of freedom from primary and secondary endpoint, **Figure 4**.

Discussion

Considering all patients included in the MitraBridge registry until the end of the enrollment period, and extending the follow-up period, MitraClip treatment was confirmed as an alternative effective “bridge strategy” to HTx in a selected cohort of advanced HF patients with secondary MR. Indeed, the use of MitraClip as a bridge to transplant strategy allowed: 1) a 2-year estimates of freedom from composite adverse events (primary endpoint) of 47%, 2) safe access to HTx in 21% of patients, 3) to maintain or obtain the eligibility for transplant in 13.5% of cases, and 4) to rule out consideration for HTx because of clinical improvement in 22.5% of the study population.

The prevalence of patients with advanced HF continues to rise, with an estimated number in the U.S. adult population ranging from 100.000 to 300.000^{1,10}. At this stage of HF, optimal medical therapy is insufficient to alleviate HF symptoms and prevent worsening of patient’s prognosis, and more advanced therapy are needed. HTx remains the best treatment option for these patients, with a post-transplant 1-year survival of around 90% and a median survival of 12.5 years^{4,11}; nevertheless, its accessibility is limited by recipient eligibility and organ donor scarcity, with a difference between heart requests and organ donor availability of at least an order of magnitude¹². Therefore, to prevent clinical deterioration and reduce waitlist mortality, potential candidates for HTx often need bridging therapies until a transplantable organ become available.

Limited data on the potential role of MitraClip treatment as a bridge to HTx have been previously published¹³⁻¹⁸, and these evidences have been than confirmed by interim results from the larger cohort of patients included in the MitraBridge registry⁵. Secondary MR is indeed a common finding in advanced HF patients⁶, which negatively affects their prognosis^{7,19}; in these advanced stages of the disease, where volume overload and reduced stroke volume dominate the picture leading to persistent congestion and low-flow syndrome¹⁰, a significant regurgitant volume might further increase left ventricular end-diastolic pressure and impair forward stroke volume. The MitraClip treatment, interrupting this vicious circle, might guarantee patients clinical and hemodynamic stabilization, and consequent safe access to HTx²⁰. Extended results from the MitraBridge registry further confirm the

present hypothesis. Up to 2-year from MitraClip procedure, TEER permitted to ameliorate patient's clinical status and mitigate the frequency of HF rehospitalizations: through 24 months the annualized rate of HF hospitalization was 44% per patient-year, which is greater than that observed in the device group of the COAPT trial (35.8%)²¹, but far lower than that reported in the device group of the MitraFR trial (88.3%)²². According to the differences between the three populations, these results highlight the potential role of MitraClip treatment even in a more advanced setting than that considered in the COAPT trial²³, further supporting current guidelines recommendations which give a potential indication to TEER of MR even in patients who do not fulfil the COAPT inclusion criteria but who may benefit from this procedure to improve symptoms and as bridge to transplant⁴.

As observed at echocardiographic follow-up control, TEFR resulted in a significant improvement in pulmonary hemodynamics preventing the development of right ventricular dysfunction. In this advanced setting, severe post-capillary pulmonary hypertension is a common finding which ultimately leads to increased pulmonary vascular resistance and therefore patient's ineligibility for HTx^{18,24}. Moreover, a significant elevation in afterload might deteriorate right ventricular function leading to systemic venous congestion and consequent progressive multi-organ failure²⁵. Correction of mitral regurgitation could reverse this maladaptive process as previously reported in some case reports and limited case series^{10,18,26,28}. Even in the MitraBridge population, a significant reduction in systolic PAP (baseline 50 [40-61] mmHg vs follow-up 43 [33-53] mmHg, p-value<0.001) was observed after MitraClip intervention, guaranteeing the preservation of right ventricular function. In particular, in 4 of 7 patients who could not be listed for HTx before MitraClip procedure because of severe pulmonary hypertension with elevated pulmonary vascular resistance, and for whom hemodynamics follow-up data were available, after 1 year a significant reduction in pulmonary vascular resistance was observed (baseline vs follow-up: patient n 1= 5.81 vs 3.9 WU; patient n 2 = 4.44 vs 1.9 WU; patient n 3 = 15.97 vs 4.1 WU; patient n 4 = 6.49 vs 3 WU). The achievement of these results allowed patients to undergo elective HTx or to become eligible for transplant.

Durable mechanical circulatory support obtained through LVAD implantation represents an effective treatment to improve quality of life and extend survival of advanced HF patients¹². Despite the promising results of new devices²⁸, because of the poor long-term survival and the high frequency of adverse events, LVAD therapy is still restricted to a small portion of high-risk advanced HF patients (INTERMACS 1-3^{29,30}), leaving few therapeutic options for patients in INTERMACS profiles 4-7. In the MitraBridge registry, more than 80% of patients were in INTERMACS profile >3 before the index procedure. According to our results, TEER with the MitraClip system seems to be a suitable treatment strategy for these patients who have few chances to undergo early cardiac replacement therapy.

The present report from the MitraBridge registry is a further proof of concept of the potential role of MitraClip treatment in this complex scenario. Larger prospective data are needed in order to confirm our findings and pave the way at extending indication for TEER even in a more advanced setting, where current criteria of positive response to treatment are not entirely satisfied^{4,20}.

Study limitations

Our study has several limitations that have to be mentioned. First, this is an observational study without a control group. Second, this is a real-world registry reporting the clinical practice in different centers and countries; therefore, echocardiographic and clinical outcomes have been reported by the different sites and investigators without core lab adjudication. Third, as long as we considered MitraClip interventions performed before January 2021, no patient was treated with SGLT-2 inhibitors for HF therapy optimization before the index procedure. Finally, the MitraBridge population includes a specific set of patients with advanced HF and concomitant significant secondary MR, who have been chosen to undergo MitraClip procedure because of the favourable anatomical and clinical characteristics. Therefore, careful patient selection for this treatment strategy is of paramount importance, and the results should be interpreted with some caution.

Conclusions

After two years of follow-up, the use of MitraClip as a bridge to transplant in a larger and selected cohort of advanced HF patients with significant secondary MR who were potential candidates for HTx, was confirmed to be an effective strategy, allowing elective HTx or eligibility for transplant in one third of patients, and no more need for transplantation because of significant clinical improvement in 22.5% of cases.

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Acknowledgements: none.

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Tables

Table n 1. 2-year clinical outcomes.

Outcomes	Overall (n = 153)	In List (n = 38)	BTD (n = 80)	BTC (n = 35)	p value^a
Primary Endpoint	64 (53)	19 (61)	29 (50)	16 (51.5)	0.632
HF rehospitalization ^b	48 (45)	14 (50)	22 (43)	12 (44)	0.749
All-cause death	7 (6.5)	1 (7)	3 (5)	3 (10)	0.536
Urgent LVAD	7 (7)	0 (0)	6 (13)	1 (3)	0.123
Urgent HTx	9 (8)	5 (15.5)	3 (7)	1 (3.5)	0.093

Data are presented as absolute numbers (Kaplan-Meier estimates of events). BTC = bridge to candidacy; BTD = bridge to decision; HF =

heart failure; HTx = heart transplantation; LVAD = left ventricular assist device.

a. p-value referring to log-rank test.

b. First HF rehospitalization

Figure titles and legends

Figure n 1. Timeline reporting relevant events during follow-up stratified according to pre-defined baseline criteria.

Data are presented as absolute numbers (percentages). HTx and LVAD refer to elective heart transplantation and elective LVAD implantation, respectively. Urgent HTx and urgent LVAD refer to urgent heart transplantation and urgent LVAD implantation, respectively.

Delisted identifies those patients who were removed from HTx waiting list. Listed identifies those patients who were included in HTx waiting list.

Median follow-up (25th and 75th percentiles) time: 26 (9-52) months; in 10.5% of cases a follow-up time of more than 2 years was available.

BTC = bridge to candidacy; BTD = bridge to decision; BTT = bridge to transplant; FU = follow-up; HTx = heart transplantation; LVAD = left ventricular assist device.

Figure n 2. Kaplan-Meier curves of freedom from A) primary composite endpoint and from B) secondary endpoint.

Estimates rate of freedom from events with 95% confidence interval are shown.

HF = heart failure; HTx = heart transplantation; LVAD = left ventricular assist device

Figure n 3. Exploratory outcome: annualized rate of HF rehospitalization.

Here reported annualized rate of HF hospitalization occurring in the first year, in the second year and within 2 years from MitraClip treatment. Recurrent events for patients with more than one hospitalization were considered.

BTC = bridge to candidacy; BTD = bridge to decision; HF = heart failure.

Figure n 4. Kaplan-Meier curves of freedom from A) primary and B) secondary endpoint stratified by follow-up mitral regurgitation severity.

Adjusted HR: HR of MR was adjusted for previously identified predictors of primary endpoints: HF hospitalization within previous 6 months, procedural failure, INTERMACS profiles 1-4, left ventricular ejection fraction, NYHA functional class IV⁵.

HR = hazard ratio; MR = mitral regurgitation; CI = confidence interval.

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Highlights

- Advanced heart failure patients often need bridging therapies to heart transplant
- Secondary mitral regurgitation negatively affects their prognosis
- MitraClip used as a bridge to heart transplant strategy
- MitraClip is a safe and effective procedure in this advanced scenario
- It could guarantee safe access to or eligibility for transplant

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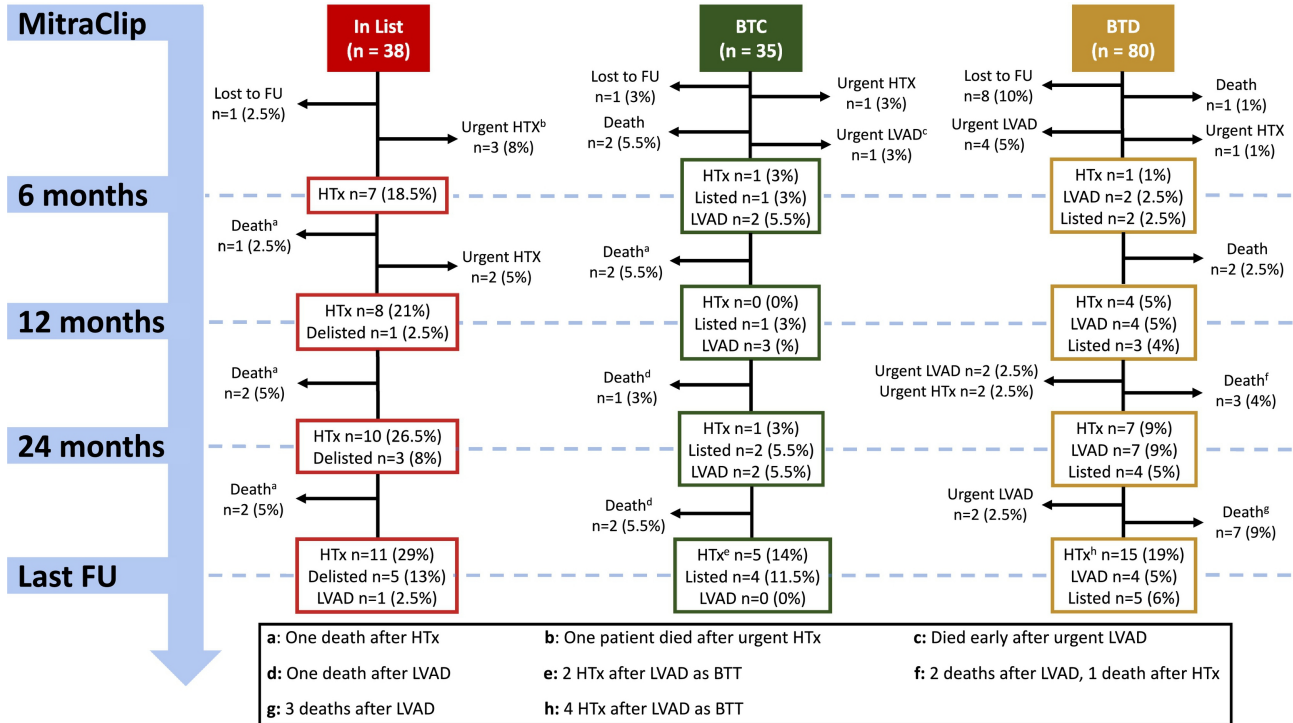


Figure 1

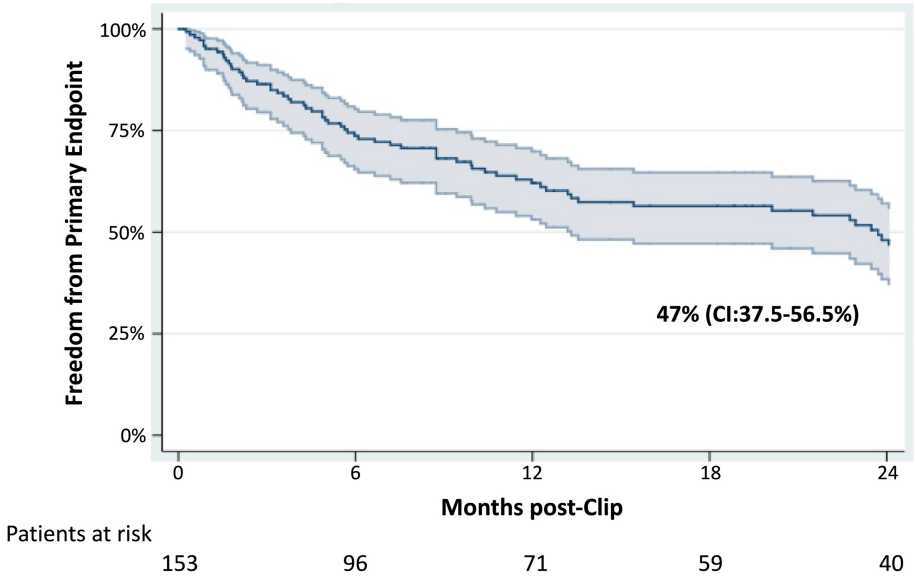
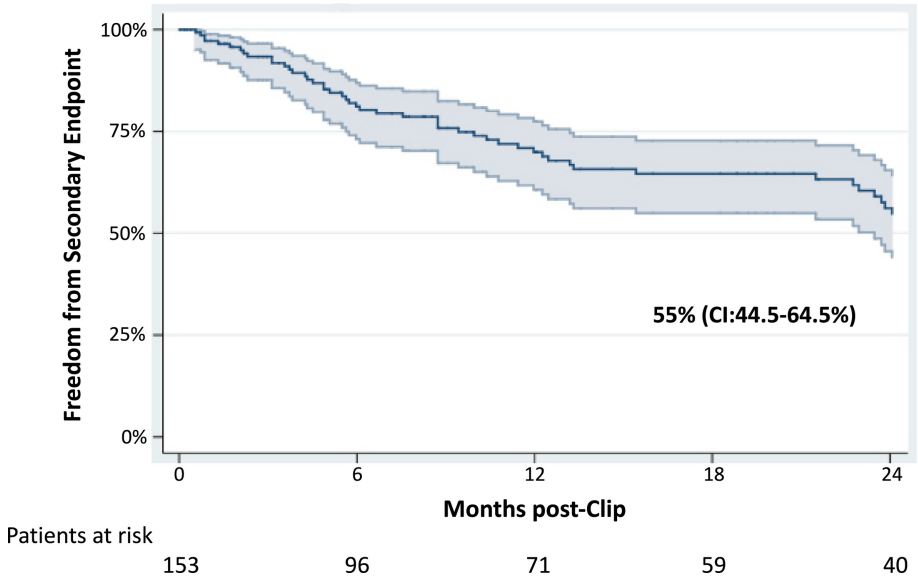
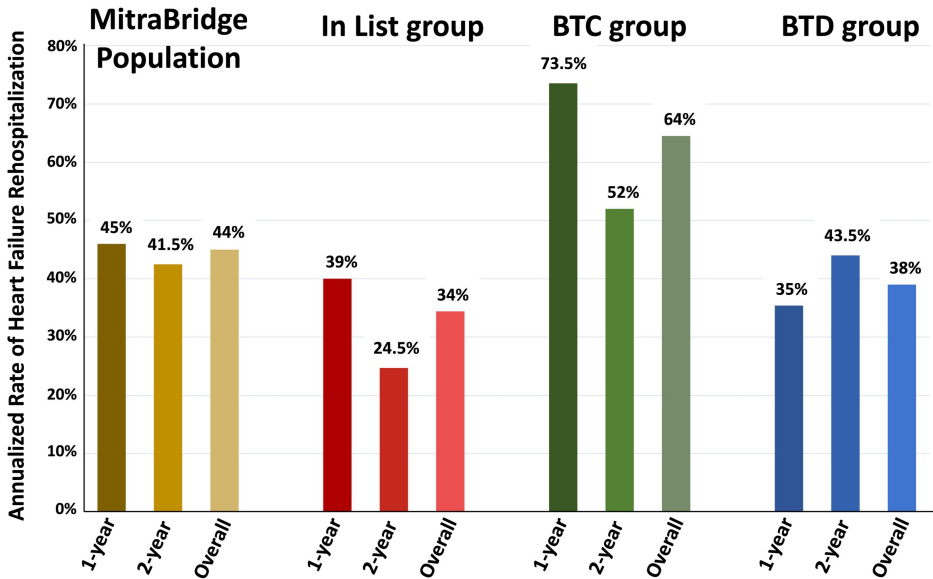
A**B**

Figure 2



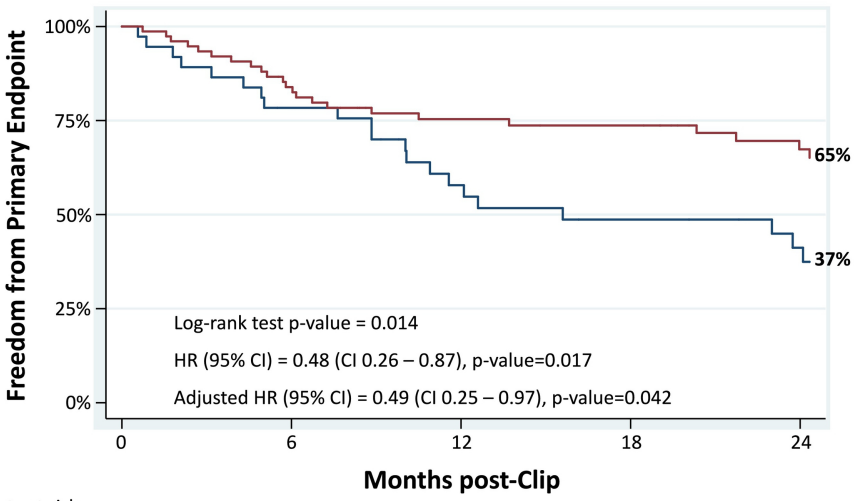
N HF rehospitalization

51 30 81 11 4 15 20 11 31 20 15 35

Patient-years

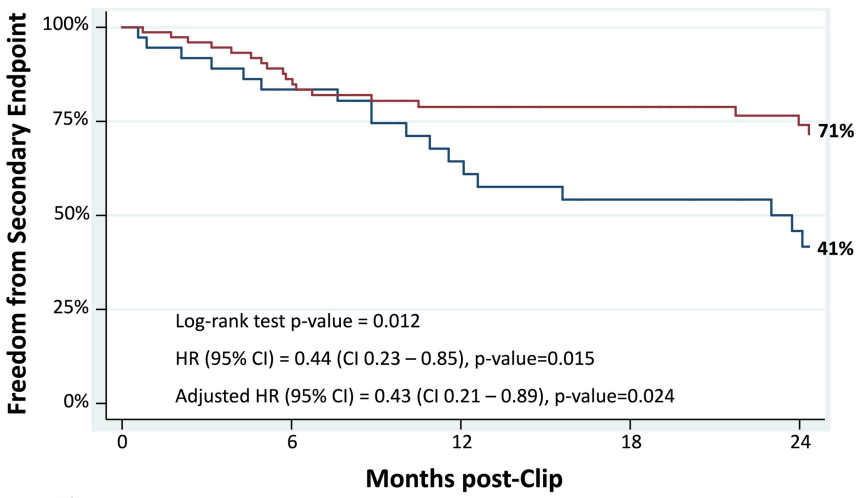
112.7 72 184.6 28.2 16.2 44.5 27.2 21.2 48.5 57.2 34.5 91.6

Figure 3

A

Patients at risk

MR ≤ 2	82	61	48	43	30
MR > 2	37	28	19	15	11

B

Patients at risk

MR ≤ 2	82	61	48	43	30
MR > 2	37	28	19	15	11

Figure 4