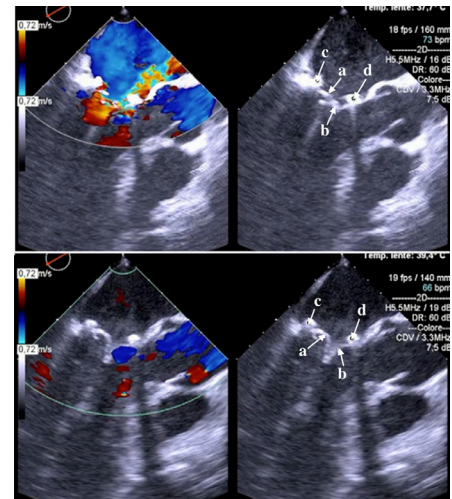


The NeoChord Procedure After Failed Surgical Mitral Valve Repair

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Surgical mitral valve reintervention is associated with significant morbidity and mortality, and repeat repair is not always feasible. We examine the clinical outcomes of the NeoChord procedure after failed conventional mitral valve repair. A total of 312 patients were treated with the NeoChord repair procedure between January 2014 and December 2018 at 5 European centers. Clinical and echocardiographic data were reviewed to identify patients who had a prior surgical mitral valve repair procedure. The primary endpoint (Patient Success) was a composite of placement of at least 2 neochoordae and end-procedure mitral valve regurgitation (MR) \leq mild, freedom from death, stroke, structural or functional procedure failure (MR > moderate), procedure or device-related unplanned procedures, cardiac-related rehospitalization, or worsening NYHA functional class at 1 and 2-year FU. Fifteen (15) patients were identified who required reoperation for failed surgical mitral valve repair. Mean time-to-reoperation was 2.7 years (2.2–6.1). Median intensive care unit stay was 24 hours and median hospitalization time was 7 days (6–8). No in-hospital deaths were observed. At discharge, mitral regurgitation was \leq mild in 13 patients (86.7%). Patient success and freedom from more than mild MR were $92.3 \pm 7.4\%$ and $83.9 \pm 10.4\%$ at 1 and 2-year follow-up respectively. One high-risk patient presented with severe recurrent MR and died during surgical reintervention due to an acute aortic dissection. Selected patients can be successfully treated with the



Preoperative (top) and postoperative (bottom) 2D and 2D color-Doppler-transesophageal echocardiography images in standard long-axis view. In the preoperative figure it is possible to see the eccentric

Abbreviation: MV, mitral valve; MVRe, mitral valve repair; MR, mitral regurgitation; TTE, transthoracic echocardiography; TEE, transesophageal echocardiography; MVARC, mitral valve academic research consortium; FU, follow-up; ASE, American society of echocardiography; ESE, European society of echocardiography; NYHA, New York heart association; PML, posterior mitral leaflet; LVEF, left ventricle ejection fraction; iLVEDV, left ventricle end diastolic volume indexed; ICU, intensive care unit; AF, atrial fibrillation; ViR, valve-in-ring; LVOT, left ventricle outflow tract; LV, left ventricle

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NeoChord procedure after failed surgical mitral valve repair. These results support a wider adoption of the NeoChord procedure as a first-line minimally invasive, alternative therapy to treat failed mitral valve repair.

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INTRODUCTION

Following current guidelines,¹ symptomatic severe mitral valve regurgitation (MR) and asymptomatic moderate MR associated with ventricular dilation require intervention (Class I). Surgical mitral valve repair (MVRe) is the treatment of choice for primary degenerative MR due to prolapse, as it has demonstrated excellent results in the long-term. In expert hands, less than 1% of patients require late reintervention for MR recurrence.^{2–5}

However, in cases of recurrent MR following MVRe, repeat surgical intervention is challenging, and successful resolution of MR is not always achievable^{6–9} and may result in a significantly higher mortality rate compared to first-time MVRe procedures.^{10,11} Percutaneous techniques present a valuable alternative to conventional surgery in terms of improving patient outcomes but are not always applicable.^{12,13} Transventricular, off-pump MVRe with neochord implantation (NeoChord DS1000, NeoChord Inc., St. Louis Park, MN) has demonstrated safe and effective outcomes for MVRe^{14–17} and its use has recently been proposed as a reliable strategy for re-repair in patients with recurrent degenerative MR.¹⁸ Aim of the present study is to present from a multi-center registry the early and 2 years outcomes of patients treated with NeoChord procedure after failed previous surgical MVRe.

METHODS

Data from 5 European Centers, between January 2014 and December 2018, were prospectively collected and analyzed. All adult patients presenting with recurrence of severe MR after a previous surgical MVRe and treated with NeoChord implantation were included in the study. Informed consent was gathered from all patients. All patients underwent preoperative transthoracic and transesophageal echocardiography to establish the grade and mechanism of MR recurrence. The NeoChord procedure was performed as previously described¹⁹ (Central Figure-Fig. 1, Video 1–3). Operative and perioperative outcomes and were assessed according to mitral valve academic research consortium definitions.²⁰ All patients underwent clinical and transthoracic echocardiography follow-up (FU) at discharge, 1, 6, 12 months, and yearly, thereafter. Transthoracic echocardiographic FU was performed independently by each center's investigators according to American society of echocardiography/European society of echocardiography guidelines²¹ and MR was classified as absent/trace, mild, moderate, or severe based on a combination of semi-quantitative and quantitative parameters. The primary endpoint

regurgitant jet, the pre-existent ring (c: posterior portion and d: anterior portion) and the presence of a new prolapse of the posterior mitral leaflet (a). In the postoperative image the ring is still visible while the posterior mitral leaflet now stand on the correct coaptation line as the anterior mitral leaflet (b).

Central Message

NeoChord repair is a safe and effective alternative treatment for recurrent mitral regurgitation after surgical mitral valve repair with low mortality, complication rates and satisfactory early outcomes.

Perspective Statement

Mitral regurgitation can reoccur after surgical mitral valve repair with variable incidence according to the published literature. Surgical reintervention is affected by high mortality and morbidity. Alternative transcatheter repair strategies represent an interesting option to improve outcomes. Safety and efficacy of NeoChord procedure have been already demonstrated confirming NeoChord repair as an alternative, innovative and valuable option available for the treatment of this type of patients.

(Patient Success) was a composite of procedural success (placement of at least 2 neochordae and mild or less MR at the end of the procedure) and freedom from death, stroke, structural or functional failure of the procedure (MR > moderate), unplanned interventions related to the procedure or device, cardiac-related rehospitalization, or worsening New York Heart Association (NYHA) functional class at 1-year and 2-year FU.

Statistical Analysis

Baseline categorical variables were expressed as percentages, while quantitative variables were expressed as medians (first and third quartiles) as appropriate. For the time-to-event analysis Kaplan-Meier methods has been used. SPSS statistical software was used (IBM SPSS Statistics, version 24.0 Armonk, NY).

RESULTS

As shown in [Figure 2](#) that summarize the including process and the most impressive results of our multicenter study, of the 312 patients treated with the NeoChord procedure during the study period, 15 (4.8%) met the inclusion criteria. Median time between the original MVRe and the NeoChord procedure was 2.7 years (2.2–6.1 years). Baseline clinical and echocardiographic characteristics of the study population at the time of reoperation are presented in [Table 1](#). Median age was 61 years (53–72) and 11 (73.3 %) were male. Median EuroSCORE II was 3.2% (2–5.5%). Operative techniques used in the original MVRe procedure are summarized in [Table 2](#). Briefly, an annuloplasty ring was used in all patients, triangular resection was

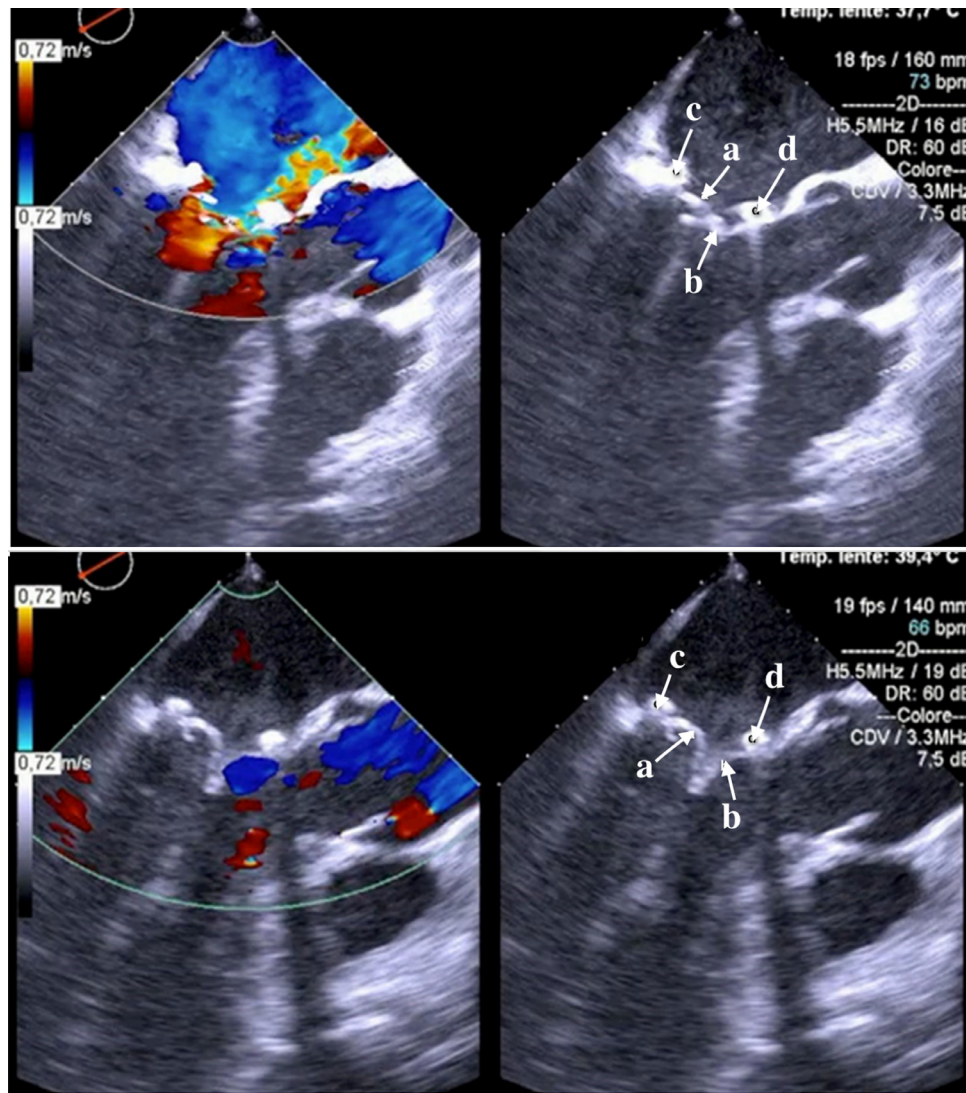
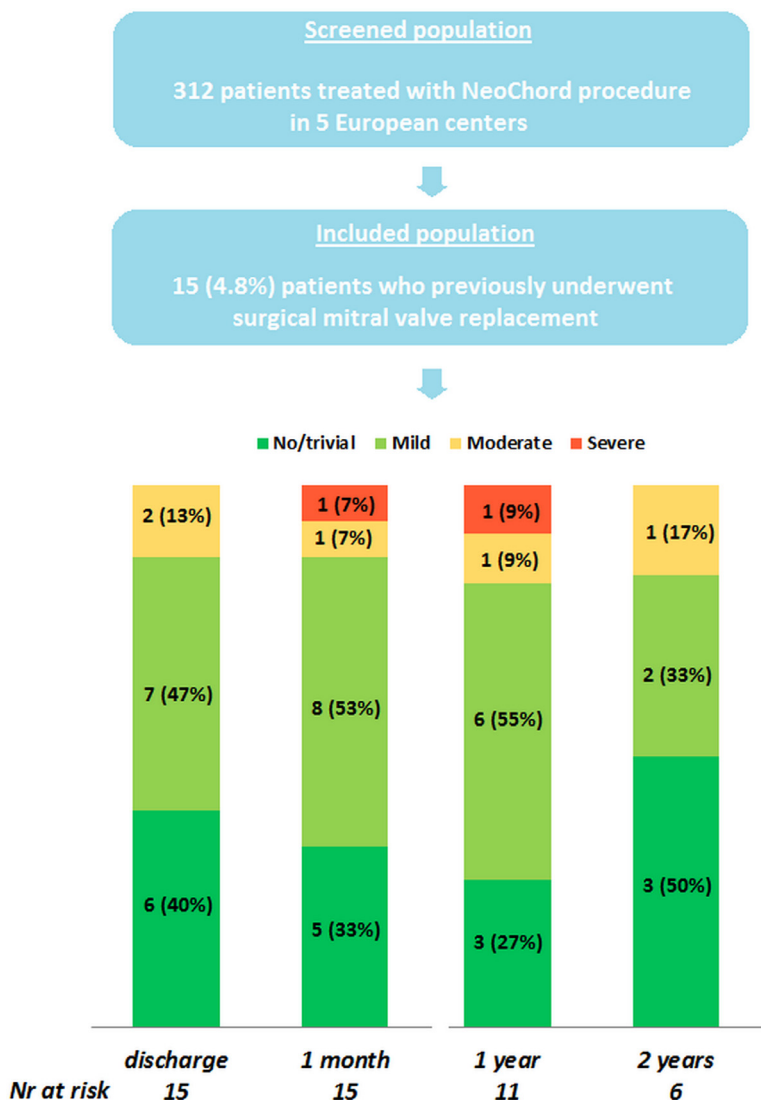


Figure 1. Central Figure showing preoperative (top) and postoperative (bottom) 2D and 2D Color-Doppler-transesophageal echocardiography images in standard long-axis view. In the preoperative figure it is possible to see the eccentric regurgitant jet, the pre-existent ring (C: posterior portion and D: anterior portion) and the presence of a new prolapse of the posterior mitral leaflet (A). In the postoperative image the ring is still visible while the posterior mitral leaflet now stand on the correct coaptation line as the anterior mitral leaflet (B).

performed in 2 patients (13.3%), quadrangular resection with sliding plasty was performed in 1 patient (6.7%), and Gore-Tex artificial chordae implantation was performed in 9 patients (60%). At the time of reoperation all 15 patients presented with severe recurrent MR and were symptomatic with NYHA class II and III in 80% of cases. Re-prolapse or new flail of posterior mitral leaflet (PML) was the leading cause of MR in all patients. In 9 cases (60%), only the P2 scallop was prolapsed while in the remaining 6 cases (40%) multisegment prolapse was observed. Left ventricular ejection fraction (LVEF) was preserved (59.5%, 55–61%) while, on average, a slight left ventricle dilatation was present with a median left ventricle indexed end-diastolic volume of 89 mL/m² (41.7–108.6).

Tables 3 and 4 present the procedural and periprocedural data for the NeoChord MVRe procedure. The median

procedure time was 140 minutes (110–160) and a median of 5 chordae were implanted.^{4,5} Median intraoperative total blood loss was 280 mL (163–328). No intraoperative complications were observed and none of the patients required extracorporeal circulation support or conversion to traditional open-heart surgery. Technical success was achieved in 100% of the cases and all patients left the operating room with a less than moderate MR. Table 5 summarize preoperative anatomical features of the treated patient, NeoChord procedural data and final perioperative result. Median mechanical ventilation time was 5 hours^{3–6} and most patients remained in the intensive care unit for approximately 1 day. Mean hospital length of stay was 7 days^{6–9} and the majority of patients were discharged to home (73.3%). No in-hospital deaths or major complications were



Out of the 312 patients treated with NeoChord procedure in 5 European Centers, 15 were included because receiving the procedure to treat a severe mitral regurgitation recurrence after previous surgical mitral valve repair. NeoChord procedure appeared to be able to assure good early results in this subset of patients.

Figure 2. Selection criteria used for patient inclusion and results from the follow-up periods. Out of 312 patients included in a multi-center registry we identified 15 patients who underwent NeoChord procedure to treat a previous failing surgical mitral valve repair. The bar graph in the bottom shows the number and rate (between commas) of patients presenting a specific grade of recurrent mitral regurgitation (from no/trivial, to moderate and severe) at each of the follow-up time-points (discharge, 1 month, 1 year and 2 years).

observed. Two patients (13.3%) presented with transient conduction disturbances while 5 patients (33.3%) had a new onset of paroxysmal atrial fibrillation that was successfully treated with either pharmacologic or electric cardioversion. None of the patients required surgical revision for bleeding or received blood product transfusions.

At discharge, all patients were asymptomatic/mildly symptomatic in NYHA class I (14, 93.3%) or II (1, 6.7%). Six patients (40%) presented no/trivial MR, 7 (46.7%) mild MR, and 2 patients (13.3%) had moderate MR because of the presence of residual prolapse of P2 scallop. At the end of the procedure median LVEF was 59.5%, (55–60.8).

Table 1. Baseline Clinical and Echocardiographic Features

	Median (I-III Quartile) or N (%)
Age (years)	61 (52.5–72)
Male	11 (73.3%)
Euroscore-II (%)	3.2 (2–5.5)
Arterial hypertension	11 (73.3%)
Chronic obstructive pulmonary disease	2 (13.3%)
Diabetes mellitus type II	0
Associated ischemic cardiomyopathy	1 (6.7%)
Previous percutaneous coronary intervention	0
Previous stroke	1 (6.7%)
Malignancy	1 (6.7%)
Glomerular filtration rate (mL/min)	76.5 (61.8–87.9)
NYHA functional class	
- I	3 (20%)
- II	4 (26.7%)
- III	8 (53.3%)
- IV	0
MR grade	
- Absent/trace	0 (0%)
- Mild	0 (0%)
- Moderate	0 (0%)
- Severe	15 (100%)
- Leaflet prolapse	13 (86.7%)
- Leaflet flail	2 (13.3%)
- LPM disease	15 (100%)
sPAP (mm Hg)	30 (28.5–35.5)
- ≤25	2 (13.3%)
- 26–35	9 (60%)
- 36–45	4 (26.7%)
- >45	0 (0%)
TR	
- Absent	1 (7.7%)
- Mild	10 (76.9%)
- Moderate	2 (15.4%)
LVEF (%)	59.5 (55–60.8)
- ≤30	0 (0%)
- 31–55	6 (40%)
- >55	9 (60%)
iLVEDV (mL/m ²)	89 (41.7–108.6)
- <70	3 (20%)
- 70–100	3 (20%)
- >100	9 (60%)

iLVEDV, left ventricle end diastolic volume indexed; LVEF, left ventricle ejection fraction; MR, mitral regurgitation; sPAP, estimated Pulmonary artery pressure; TR, tricuspid regurgitation.

Median FU time was 1.3 years (0.8–2.3); 11 patients (73.3%) completed 1-year FU and 6 (40%) completed 2-year FU. During FU, 1 cardiovascular death (6.7%) occurred in a high-risk patient (logistic EuroSCORE II 5%, STS PROM 9.2%) with congenital collagenopathy who had undergone 3 previous conventional MVRe procedures prior to the NeoChord procedure. One month following the procedure, the patient presented with new native chords rupture causing severe MR recurrence. The patient also developed moderate-

Table 2. First Mitral Valve Repair Techniques

	N (%)
Annuloplasty ring	15 (100%)
- Closed	12 (80%)
- Open	3 (20%)
Artificial GoreTex chord implantation	9 (60%)
Triangular resection	2 (13.3%)
Quadrangular resection	1 (6.7%)
Edge-to-edge	0

Table 3. Procedural Data for the NeoChord Procedure

	Median (I-III Quartile) or N (%)
Neochordae in place (n)	5 (4-5)
- 2	1 (7.7%)
- 3	8 (61.5%)
- 4	1 (7.7%)
- 5	3 (23.1%)
Operative time (min)	140 (110-160)
Cell-saved blood (mL)	280 (150-335)
ECC/ECMO	0
Intraoperative death	0
Procedure success	15 (100%)

ECC, extracorporeal circulation; ECMO, extracorporeal membrane oxygenator.

Table 4. Perioperative Data

	Median (I-III Quartile) or N (%)
Mechanical ventilation time (hours)	5 (3–6)
ICU stay (days)	1 (1–1)
Total length of stay (days)	7 (6–9)
Discharge	
- Home	11 (73.3%)
- Rehabilitation center	4 (26.7%)
- In hospital death	0
Acute myocardial infarction	0
Transient ischemic attack	0
Stroke	0

ICU: intensive care unit

severe aortic regurgitation with class III NYHA heart failure symptoms and LVEF impairment. During the subsequent surgical mitral and aortic valve replacement, the patient experienced a type B aortic dissection and died within the hospital-stay. No other patients required reintervention for MR recurrence. None of the patients required rehospitalization but 3 (27.3%) patients presented new onset AF, 2 paroxysmal (18.2%) and 1 permanent (9.1%).

At 1-year FU, 3 patients (27.2%) presented with no/trivial MR, 6 patients presented with mild MR (54.6%), 1 patient presented with moderate MR (9.1%), and 1 patient presented with

Table 5. Sum-Up of Patients Anatomical Features, First Intervention Surgical Technique, Procedural Data, and Procedural Result

	First surgery Technique	Mechanism of Failure	Nr of Implanted Neochords	Target Leaflet	Procedural Result
Patient 1	Annuloplasty, Neochors for PML	P2–P3 prolapse	5	PML	No/trivial MR
Patient 2	Annuloplasty	P1–P2 prolapse	4	PML	No/trivial MR
Patient 3	Annuloplasty, Neochors for PML	P2 prolapse	3	PML	Mild MR
Patient 4	Annuloplasty, Quadrangular resection	P2 prolapse	3	PML	No/trivial MR
Patient 5	Annuloplasty, Triangular resection, Neochors for PML	P2–P3 prolapse	3	PML	Mild MR
Patient 6	Annuloplasty	P2 prolapse	2	PML	No/trivial MR
Patient 7	Annuloplasty, Neochors for PML	P2 prolapse	5	PML	Mild MR
Patient 8	Annuloplasty, Neochors for PML	P1–P2 prolapse	3	PML	Mild MR
Patient 9	Annuloplasty, Triangular resection, Neochors for PML	P2 prolapse	3	PML	Mild MR
Patient 10	Annuloplasty, Neochors for PML	P2–P3 prolapse	3	PML	Mild MR
Patient 11	Annuloplasty (band), Neochors for PML	P2 prolapse	3	PML	Mild MR
Patient 12	Annuloplasty (band), Neochors for PML	P2 prolapse	3	PML	No/trivial MR
Patient 13	Annuloplasty (band), P2-P3 cleft closure	P2 prolapse	5	PML	Mild MR
Patient 14	Annuloplasty	P2–P3 prolapse	5	PML	Mild MR
Patient 15	Annuloplasty	P2 prolapse	3	PML	No/trivial MR

MR, mitral regurgitation; PML, posterior mitral leaflet.

severe MR (9.1%). Most of the patients were in NYHA Class I (84.6%). Because of a high surgical risk and the asymptomatic condition, the only patient presenting severe MR at 1-year FU did not undergo redo surgery but the referring surgeons preferred to perform a strict echocardiographic FU and improved the medical therapy. At the 2-year FU interval, MR levels remained stable and demonstrated no change between the 1 and 2 years. Specifically, at 2-years, 3 patients presented with no/trivial MR (50%), 2 patients presented with mild MR (33.3%) and 1 patient presented with moderate MR (16.7%) (Figs. 2 and 3). Five patients (83.3%) were in NYHA Class I, while 1 patient presented in NYHA Class II (16.7%). Patient success and freedom from more than moderate MR were $92.3 \pm 7.4\%$ and $83.9 \pm 10.4\%$ at 1 and 2-year FU respectively (Fig. 4). Freedom from more than mild MR was $92.3 \pm 7.4\%$ and $83.9 \pm 10.4\%$ at 1 and 2-year FU respectively.

DISCUSSION

Compared to first surgical repair, redo MVRe procedure is associated with higher rates of operative mortality and early morbidity.^{11,22} Although, mitral centers of excellence report a low incidence of MR recurrence after conventional MVRe, in

lower volume centers it is estimated to be higher.^{6,7} The introduction of less invasive therapies, such as transcatheter valve-in-ring (ViR) implantation or Mitraclip procedure, have enabled treatment of high risk surgical or inoperable patients with good procedural outcomes. However, transcatheter ViR procedures have been associated with significant technical significant technical issues in patients undergone a previous MVRe, mainly related to the presence of the prosthetic ring, which limited the implantation of the prosthetic valve. In addition, the presence of a rigid annuloplasty ring has been associated with left ventricle outflow tract obstruction due to displacement of the anterior mitral leaflet when performing ViR procedures.²³ On the other hand, use of MitraClip to treat those patients is still under evaluation and only small number of patients have been already treated for MR recurrence after surgical repair. This alternative surely represents a viable options anyway it presents drawbacks connected to patient anatomy. The use of the NeoChord procedure in the treatment of failed surgical MVRe may offer a significant advantage over other catheter-based mitral repair techniques as it is, generally, not limited by the presence of an annuloplasty ring.¹⁸ In fact, in cases of patients with failed complex surgical MVRe, the

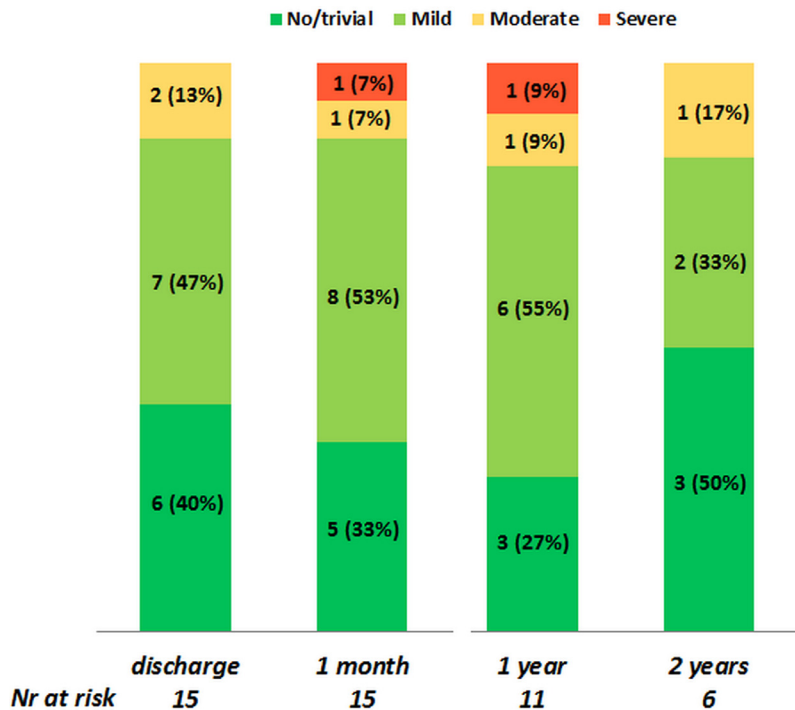


Figure 3. Mitral regurgitation grade at follow-up. The bar graph shows the number and rate (between commas) of patients presenting a specific grade of recurrent mitral regurgitation (from no/trivial, to moderate and severe) at each of the follow-up time-points (discharge, 1 month, 1 year and 2 years).

addition of neochordae to a ring-stabilized, mitral annulus could be the optimal repair strategy to ensure long-term durability and freedom from recurrent MR. Combined percutaneous strategies, recurring to concomitant annuloplasty and neochordae implantation, has already been performed to treat patients with complex valve anatomy, confirming the great advantage that neochords gives to annuloplasty alone.^{24,25} Use of NeoChord repair as the first choice to treat those failing MVRe is obviously a specific decision made by each Center after a global evaluation of patients' characteristics and the anatomy of the mitral valve. The main aim of using NeoChord procedure is to adopt the less invasive but still patient tailored intervention to treat recurrent MR, addressing its specific underlying mechanism.

In the present study, we did not observe any in-hospital mortality or stroke following the NeoChord procedure for failed surgical MVRe. For context, multiple U.S. and European centers have reported rates of mortality and stroke for surgical MVRe ranging from 3.4% to 6.6% and 2.4% to 4.9%, respectively.^{21,25–27} Additionally, mechanical ventilation time, length of intensive care unit stays, and total hospitalization time for the NeoChord procedure was consistent with time reported for first-time surgical MVRe procedures and were significantly shorter than those reported for reintervention with surgical MVRe.^{14,28–31}

When compared to published reports of mitral ViR, the NeoChord procedure demonstrated improvements with in-hospital outcomes. In a large published series of ViR

procedures,¹³ the incidence of in-hospital mortality was reported as 9.9%, while the incidence of early reoperation to treat periprocedural complications, such as severe paravalvular leak or prosthesis embolization, was reported as 17.7%. In this same series of ViR patients, major and life-threatening bleeding events were reported as 3.9% and 6.7%, respectively, whereas no patients in our series required reoperation for bleeding or postoperative transfusion of blood products. With regard to MitraClip procedure, only limited data concerning small populations are currently available.^{32,33} They all confirm the feasibility and the safety of the procedure, underlying the possibility to repeat the clip in case of MR recurrence during FU. In particular, as reported by a Spanish Group of authors, describing their multicenter experience, MitraClip can be an alternative for high-risk patients with failing surgical repairs. They report no periprocedural or FU deaths and recurrence of severe MR in 2 patients out of 6 during FU.³³ One on the major issuer with MitraClip in this subset of patients, as underlined by the authors, is the presence of a large resection of the PML. In this case, the grasping of the leaflet could result tricky or impossible. The possibility of grasping the posterior part of the annulus and clipping it to the anterior leaflet has been suggested but no data exists about its durability. Moreover, in case of small prosthetic rings and low valve areas, the placement of more than 1 clip could drive to a sensible increase in transvalvular gradients. NeoChord procedure, standing in between percutaneous/transeptal procedures and conventional surgery, represent an alternative tool in case of redo MVRe. The widening of

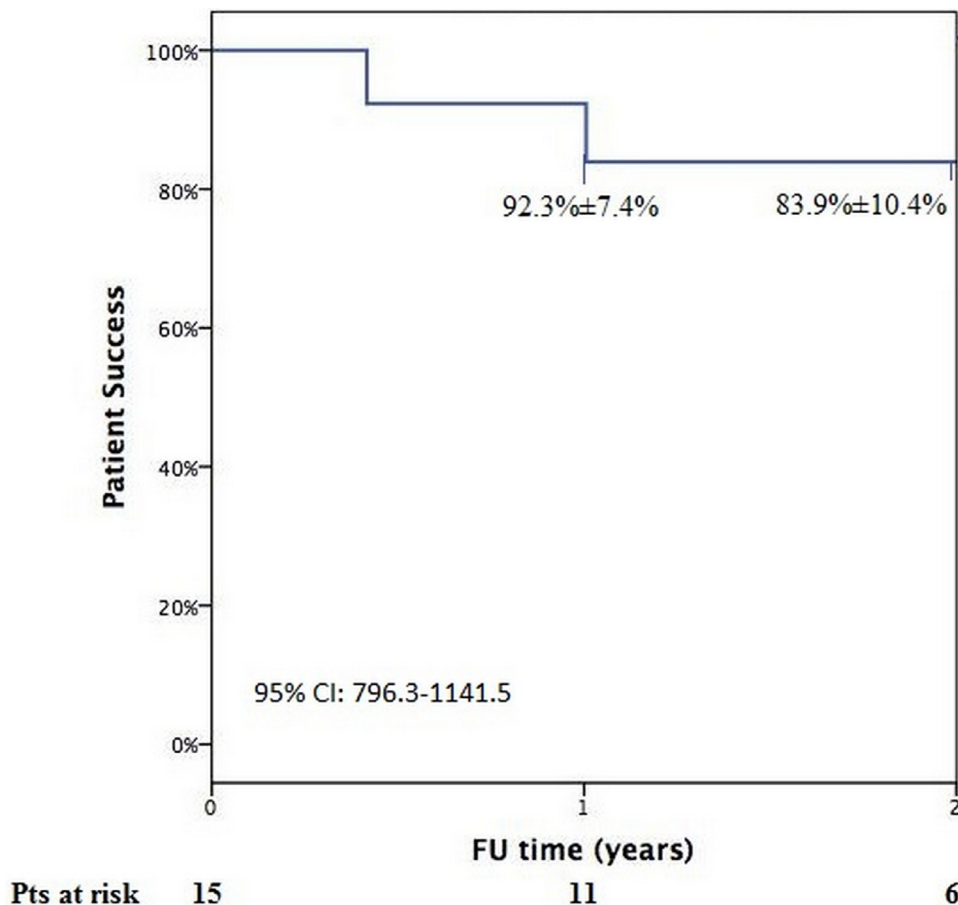


Figure 4. The Kaplan–Meier estimation of treatment success composite endpoint-patient success which includes placement of at least 2 neochordae and mild or less MR at the end of the procedure and freedom from death, stroke, structural or functional failure of the procedure (MR > moderate) (Follow-up (FU) is expressed in years. CI: 95% confidence interval.

the possible treatment options with the inclusion of NeoChord repair, offer the possibility to best address the specific mechanism leading the MR recurrence. The use of this treatment is one of the currently available strategies (Mitraclip, ViV, ViR, Transcatheter Mitral Valve Replacement (TMVR), surgical Redo) to select for a to-treat MR recurrence. We consider this patient centered approach the paradigm to follow to improve outcomes while minimizing invasiveness.

In the present study, Patient Success, was $92.3 \pm 7.4\%$ and $83.9 \pm 10.4\%$ at 1 and 2-year FU. Moreover freedom from more than moderate MR and freedom from more than mild MR were $92.3 \pm 7.4\%$ and $83.9 \pm 10.4\%$ at 1 and 2-year FU respectively, the same as patient success, while we did not observe any rehospitalization, death or NYHA class worsening apart from those relative to the patients who presented severe MR recurrence. Only 1 patient required reintervention with conventional surgery after the 6-month FU window to treat severe MR secondary to native chord rupture from the PML. This patient was considered a high-risk subject with severe collagenopathy that likely affected the durability of NeoChord procedure. The same patient represents the only death reported in our series. In contrast, rate of mortality for

conventional surgical reintervention and ViR are 17% and up to 30%, respectively³⁰ and higher than reported in our series at 7.6%. Clearly, outcomes for reinterventions and ViR also depends on the expertise of the performing Centers, the larger is the number of performed procedures better are the results in terms of MR recurrence and survival. Anyway, NeoChord procedure is clearly another way to treat a challenging population with a reduced surgical risk. In the era of low-risk patients TAVR indication we think that a not-ECC minimally procedure strategy should be taken in account as a first choice and neglected only when not technically feasible. Some authors have also suggested defining NeoChord procedure as a microinvasive approach to mitral valve,^{34,35} enlightening its very low invasiveness deriving from cardiopulmonary bypass (CPB) and aortic cross-clamping avoidance. Even if this definition is still not completely shared by surgical community, it should suggest revising our idea about surgery invasiveness. As mentioned, although repair is mostly preferable, also in the case of recurrent MR after MVRe, very few are the surgeons that, planning a new surgery, will perform a valve re-reconstruction rather than its prosthetic replacement and, nonetheless, very often repair is not durable for anatomical issues. To this

purpose, NeoChord procedure may be an alternative and persuasive strategy, in anatomically suitable cases, toward repair rather than replacement in the case of recurrent MR after MVRe. At the 1-year and 2-year FU windows, greater than 80% of the population who reached those FU time-points (11 out of 15 for the 1 year and 6 out of 15 for the 2 years) had less than moderate MR, similar to what has been reported in literature for first-time NeoChord procedures²⁹ and comparable with recurrent MR rates for surgical reintervention MVRe.³⁰ In addition, early and 2 years Procedural Success and freedom from reintervention or recurrent severe MR in this study was greater than what has been reported for ViR.^{12,23} At 1-year FU only 1 patient was found with severe MR. The decision of not reoperating this patient was mostly driven by his high surgical risk due to comorbidities and because of the light symptoms he presented at the clinical assessment (NYHA I). An appropriate upgrade to the optimal medical therapy allowed avoiding a new intervention that would have been otherwise scarcely tolerated by the patient. The development of moderate MR during FU is an aspect that must be taken in consideration, but only longer studies will be able to say the real evolution and outcome of those patients with moderate MR. Anyway, we do not think that a moderate MR in this subset of challenging patients, should be considered as an absolute failure of the treatment because patients are asymptomatic and in good clinical conditions. Moreover, we all perform a reintervention only in presence of severe MR recurrence and not in case of Moderate MR recurrence that is considered a stage of MV disease in which only to perform a watchful waiting approach.

In this study NeoChord procedure was limited to patients with a degenerative MR who fully satisfied the criteria to be deemed suitable for Neochord procedure^{13,15} and in particular who presented with adequate excess of tissue of the diseased leaflet to achieve effective leaflet coaptation. In patients where the first time MVRe procedure includes a generous leaflet resection, the possibility of performing a Neochord repair is diminished. Therefore, preoperative 3D-transesophageal echocardiography evaluation is necessary to assess feasibility of the NeoChord procedure. Careful patient selection and accurate assessment of the patient's anatomy is key to achieving good results. In particular, our work-up includes an Angio-CT scan with 3D reconstructions to assess anatomical and leaflet morphology, as well as, to identify the optimal LV entry site.^{24,31} NeoChord procedure should consequently be taken in consideration as a valuable option only in those cases where valve features satisfy the anatomical criteria necessary to assure a good procedural result as previously reported.^{13,15} Repair should always be the surgeon goal also in the setting of a redo mitral valve surgery. Because an effective repair may be not always achievable with traditional surgery, we suggest NeoChord procedure as another possible strategy to offer the patients the best treatment.

Early results showed an acceptable morbidity and mortality in particular if we consider the limited experience with this new surgical approach. Although our study involved multiple

centers, our enrolled population is quite small, at this stage and larger study population and more FU data will be needed to obtain a more powerful and consistent analysis. No comparison can be made with other, long standing techniques, such as with conventional surgical reintervention. Nevertheless, our preliminary results are encouraging and support the application of NeoChord as one of possible strategies to be adopted in this challenging clinical scenario. We are also aware that only a small part of the population reached the 2-year FU time-point at the moment of the analysis anyway we decided to report those still preliminary data because they represent the only available experience in this field. A critical interpretation of our 2-years results is obviously necessary but we preferred to report few data instead of no data at all. In conclusion, the NeoChord procedure, when used for the correct patients, was demonstrated to be a safe and effective alternative to treat recurrent MR after conventional MVRe thanks to low mortality, low operative/postoperative complication rates, and reduced hospitalization times. Based on these preliminary findings, NeoChord procedure could be proposed as one of the available strategies to treat recurring MR when standard redo surgery is not feasible or when proposing a minimally invasive alternative.

SUPPLEMENTARY MATERIAL

Scanning this QR code will take you to the article title page to access supplementary information.



REFERENCES

1. Nishimura RA, Otto CM, Bonow RO, et al: 2017 AHA/ACC Focused Update of the 2014 AHA/ACC guideline for the management of patients with valvular heart disease: A report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. 20:e1159–e1195, 2017
2. MacHaalany J, Sénéchal M, O'Connor K, et al: Early and late mortality after repair or replacement in mitral valve prolapse and functional ischemic mitral regurgitation: A systematic review and meta-analysis of observational studies. *Int J Cardiol*. 173:499–505, 2014
3. Suri RM, Vanoverschelde JL, Grigioni F, et al: Association between early surgical intervention vs watchful waiting and outcomes for mitral regurgitation due to flail mitral valve leaflets. *JAMA* 310:609–616, 2013
4. Castillo JG, Anyanwu AC, Fuster V, et al: A near 100% repair rate for mitral valve prolapse is achievable in a reference center: Implications for future guidelines. *J Thorac Cardiovasc Surg* 144:308–312, 2012
5. David TE, Armstrong S, Ivanov J: Chordal replacement with polytetrafluoroethylene sutures for mitral valve repair: A 25-year experience. *J Thorac Cardiovasc Surg* 145:1563–1569, 2013
6. Chan V, Elmistekawy E, Ruel M, et al: How does mitral valve repair fail in patients with prolapse?- Insights from longitudinal echocardiographic follow-up. *Ann Thorac Surg* 102:1459–1465, 2016

7. Spoon JN, Nkomo VT, Suri RM, et al: Mechanisms of mitral valve dysfunction following mitral valve repair for degenerative disease. *JACC Cardiovasc Imaging* 8:1223–1227, 2015
8. Suri RM, Schaff HV, Dearani JA, et al: Recurrent mitral regurgitation after repair: Should the mitral valve be rerepaired? *J Thorac Cardiovasc Surg* 132:1390–1397, 2006
9. Zegdi R, Sleilaty G, Latrémoille C, et al: Reoperation for failure of mitral valve repair in degenerative disease: A single-center experience. *Ann Thorac Surg* 86:1480–1484, 2008
10. Onorati F, Perrotti A, Reichart D, et al: Surgical factors and complications affecting hospital outcome in redo mitral surgery: Insights from a multi-centre experience. *Eur J Cardiothorac Surg* 49:e127–e133, 2016
11. Kwedar K, McNeely C, Zajarias A, et al: Outcomes of early mitral valve reoperation in the medicare population. *Ann Thorac Surg* 104:1516–1521, 2017
12. Eleid MF, Cabalka AK, Williams MR, et al: Percutaneous transvenous transseptal transcatheter valve implantation in failed bioprosthetic mitral valves, ring annuloplasty, and severe mitral annular calcification. *JACC Cardiovasc Interv* 9:1161–1174, 2016
13. Yoon S-H, Whisenant BK, Bleiziffer S, et al: Outcomes of transcatheter mitral valve replacement for degenerated bioprostheses, failed annuloplasty rings, and mitral annular calcification. *Eur Heart J* 40:441–451, 2019
14. Colli A, Manzan E, Zucchetta F, et al: Transapical off-pump mitral valve repair with Neochord implantation: Early clinical results. *Int J Cardiol* 204:23–28, 2016
15. Colli A, Manzan E, Besola L, et al: One-year outcomes after transapical echocardiography-guided mitral valve repair. *Circulation* 138:843–845, 2018
16. Colli A, Besola L, Bizzotto E, et al: Mechanisms of recurrent regurgitation after transapical off-pump mitral valve repair with neochord implantation. *Eur J Cardiothorac Surg*. 25, 2019. <https://doi.org/10.1093/ejcts/ezz048>. pii: ezz048
17. Seeburger J, Rinaldi M, Nielsen SL, et al: Off-pump transapical implantation of artificial neo-chordae to correct mitral regurgitation: the TACT Trial (Transapical Artificial Chordae Tendinae) proof of concept. *J Am Coll Cardiol* 63:914–919, 2014
18. Colli A, Besola L, Gerosa G: Transapical off-pump neochord implantation for mitral regurgitation recurrence. *Rev Esp Cardiol (Engl Ed)* 69:515, 2016
19. Colli A, Zucchetta F, Torregrossa G, et al: Transapical off-pump mitral valve repair with Neochord Implantation (TOP-MINI): Step-by-step guide. *Ann Cardiothorac Surg* 4:295–297, 2015
20. Stone GW, Adams DH, Abraham WT, et al: Mitral Valve Academic Research Consortium (MVARC). Clinical trial design principles and endpoint definitions for transcatheter mitral valve repair and replacement: Part 2: Endpoint definitions. *J Am Coll Cardiol* 66:308–321, 2015
21. Zoghbi WA, Adams D, Bonow RO, et al: Recommendations for noninvasive evaluation of native valvular regurgitation: A Report from the American Society of Echocardiography Developed in Collaboration with the Society for Cardiovascular Magnetic Resonance. *J Am Soc Echocardiogr* 30:303–371, 2017
22. Mehaffey HJ, Hawkins RB, Schubert S, et al: Contemporary outcomes in reoperative mitral valve surgery. *Heart* 104:652–656, 2018
23. Eleid MF, Whisenant BK, Cabalka AK, et al: Early outcomes of percutaneous transvenous transseptal transcatheter valve implantation in failed bioprosthetic mitral valves, ring annuloplasty and severe mitral annular calcification. *JACC Cardiovasc Interv*. 10:1932–1942, 2017
24. von Bardeleben RS, Colli A, Schulz E, et al: First in human transcatheter COMBO mitral valve repair with direct ring annuloplasty and neochord leaflet implantation to treat degenerative mitral regurgitation: Feasibility of the simultaneous toolbox concept guided by 3D echo and computed tomography fusion imaging. *Eur Heart J* 39:1314–1315, 2018
25. Colli A, Beiras-Fernández A, Ruf T, et al: Transcatheter mitral valve repair: Single stage combo approach. *Rev Esp Cardiol (Engl Ed)* 2019. <https://doi.org/10.1016/j.rec.2019.04.003>
26. D'Agostino RS, Jacobs JP, Badhwar V, et al: The Society of Thoracic Surgeons Adult Cardiac Surgery Database: 2017 update on outcomes and quality. *Ann Thorac Surg* 103:18–24, 2017
27. Gammie JS, Zhao Y, Peterson ED, et al: Less-invasive mitral valve operations: Trends and outcomes from The Society of Thoracic Surgeons Adult Cardiac Surgery Database. *Ann Thorac Surg* 90:1401–1408, 2010
28. Colli A, Manzan E, Aidietis A, et al: An early European experience with transapical off-pump mitral valve repair with NeoChord implantation. *Eur J Cardiothorac Surg* 54:460–466, 2018
29. Kilic A, Acker MA, Gleason TG, et al: Clinical outcomes of mitral valve reoperations in the United States: An analysis of The Society of Thoracic Surgeons National Database. *Ann Thorac Surg* 107:754–759, 2019
30. Aphram G, De Kerchove L, Mastrobuoni S, et al: Re-repair of the failed mitral valve: Insights into aetiology and surgical management. *Eur J Cardiothorac Surg* 54:774–780, 2018
31. Colli A, Zucchetta F, Kliger C, et al: CT for the transapical off-pump mitral valve repair with neochord implantation procedure. *JACC Cardiovasc Imaging* 10:1397–1400, 2017
32. Lim DS, Kunjummen BJ, Smalling R: Mitral valve repair with the MitraClip device after prior surgical mitral annuloplasty. *Catheter Cardiovasc Interv* 76:455–459, 2010
33. Estévez-Loureiro R, Arzamendi D, Carrasco-Chinchilla F, et al: Spanish working group on the MitraClip. Usefulness of MitraClip for the treatment of mitral regurgitation secondary to failed surgical annuloplasty. *Rev Esp Cardiol (Engl Ed)* 69:446–448, 2016
34. D'Onofrio A, Gerosa G: Shifting a paradigm of cardiac surgery: From minimally invasive to micro-invasive. *J Heart Valve Dis* 24:528–530, 2015
35. D'Onofrio A, Gerosa G: Technique versus technology and the (r)evolution of cardiac surgery: A professional journey from classical surgery to embracing intervention. *Eur J Cardiothorac Surg* 52:835–837, 2017