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ORIGINAL RESEARCH ARTICLE

Association of transcatheter direct mitral annuloplasty with acute anatomic, haemodynamic, and clinical outcomes in severe mitral valve regurgitation

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Abstract

Aims Several approaches for transcatheter mitral valve repair for functional mitral valve regurgitation are established. Interventional direct annuloplasty is a novel trans-venous, trans-septal approach. While feasibility was proven recently, knowledge on its influence on cardiac dimensions, pressures, biomarkers, and clinical outcomes is sparse.

Methods and results Patients consecutively treated with direct annuloplasty-only procedures between December 2015 and April 2018 were included in this monocentric analysis. Echocardiographic measurements, biomarker levels, clinical status [New York Heart Association (NYHA) class and 6 min walk test] were assessed at baseline, at discharge, and at a 30 day follow-up. Overall, 18 patients (in mean 77.0 ± 7.4 years, 44.4% women) with initially all high-grade mitral valve regurgitation (MR) were included in this study. Procedural success rate was high (94.4%) without severe complications. Direct annuloplasty resulted in MR-reduction (post-procedural-MR mild or no/trace: 72.2%) and the proportion of patients with severe dyspnoea (NYHA III/IV) was reduced (88.9% vs. 50%, $P = 0.008$). Clinical results were associated with a relevant diminution of left atrial volumes (-16.5%, $P < 0.001$) and cardiac pressures [left atrial pressure (-32.3%, $P = 0.019$) and systolic pulmonary arterial pressure (PAP, -15.8%, $P = 0.025$)]. Patients with lower baseline levels of PAP ($P = 0.022$) as well as elevated highly sensitive troponin ($P = 0.034$) were more likely to archive clinical benefit (improvement in NYHA class $\geq$1 grade) after 1 month, which could not be correlated with the grade of MR-reduction.

Conclusions Transcatheter mitral valve repair by direct annuloplasty results in a relevant reduction of intracardiac pressures, left atrial volumes, dyspnoea, and MR. Lower PAP and higher troponin values at baseline could be associated to dyspnoea reduction.

Keywords Mitral valve disease; Mitral valve repair; Transcatheter direct annuloplasty; Multidisciplinary heart team; Heart failure

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Introduction

Severe mitral valve regurgitation (MR) has an age-dependent prevalence of 1–2% overall and over 10% in the population older than 75 years, ranking slightly behind aortic valve stenosis in industrialized countries.[1] While a pathology of the leaflets is the key player for the development of primary MR, an underlying cardiac disease resulting in a pathologic remodelling of the mitral annulus represents the pathomechanism in functional MR (FMR). A classification for MR has been introduced and later slightly modified by Carpentier[2] emphasizing the central role of a ventricular pathology leading to annular dilatation (Carpentier Class I) or restricted leaflet motion (Carpentier IIIb) for the

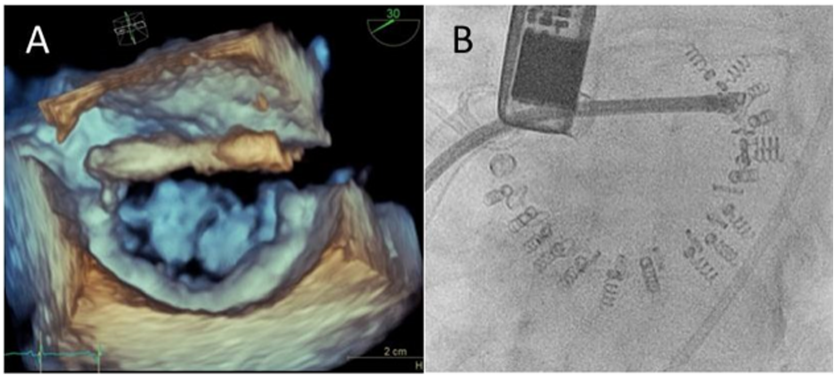
development of FMR. A surgical annuloplasty methodology was developed to reverse annular pathology; a beneficial effect on outcome for FMR, however, was not proven up to now,[3,4] and FMR represents an independent predictor for a poor prognosis of underlying heart failure.[5,6] Several interventional devices for transcatheter mitral valve repair (TMVR) have been developed and introduced over the last years. In 2013, Cardioband® (Edwards Lifesciences, Irvine, CA, USA), a transcatheter direct annuloplasty device, was first implanted in a human subject,[7] and approval by the European CE-mark was granted in 2015. TMVR is performed by a trans-venous, trans-septal implantation of a flexible Dacron band mounted on a steerable catheter system. Twelve to 17 metal anchors are deployed around the posterior annulus guided by fluoroscopic and echocardiographic imaging followed by a dynamic reduction of the band aiming on remodelling the annulus (*Figure 1*). A feasibility trial for these devices reported on a relevant reduction of MR-severity as well as a high successful implantation rate of 93.6%[8]; a clinical benefit could be demonstrated for a follow-up of up to 1 year.[9,10] Diminution of the annular diameters seems to mediate this effect directly.[11] A trend on a reduction of systolic pulmonary arterial pressure (PAP) was reported. Evidence for a significant lowering effect on left atrial pressure (LAP) and PAP is still lacking.

Thus, the objectives of the present study were (i) to investigate the impact of transcatheter direct annuloplasty on clinical and echocardiographic parameters at discharge and after 30 day follow-up, (ii) to compare patients with dyspnoea reduction (NYHA class reduction ≥1) after implantation (baseline versus 30 day follow-up), and (iii) to identify predictors of dyspnoea reduction.

Methods

From December 2015 to September 2018, 25 patients were treated with TMVR by transcatheter direct annuloplasty in our centre. Of these, seven underwent a simultaneous combined therapy with edge-to-edge repair (Abbott MitraClip®) or chordal reconstruction (NeoChord® DS 1000) and were not included in this retrospective analysis. All subjects were adult individuals (≥18 years) with symptomatic high-grade MR despite optimal medical treatment including cardiac resynchronization therapy—if applicable—and estimated to be at high-risk for valve surgery by an interdisciplinary board, as assessed by scoring systems (e.g. Logistic Euro Score) and other individual factors of frailty and co-morbidities. Individual decision for interventional direct annuloplasty as choice for TMVR was taken at the team's discretion respecting pathomechanism of MR and assessment of anatomical suitability for direct annuloplasty as well as other available forms of TMVR and approved by specialists of the manufacturing company. Anatomical feasibility was evaluated (and confirmed by experts of the manufacturing company) by a protocol of transesophageal echocardiography (TEE) and computed tomography (CT, for specifications of CT protocol in detail, see reference[12]), which were also used for planning the procedure (e.g. planning fluoroscopic angulations, optimal height of trans-septal puncture and anchor implantation zones, and selection of the size of the device). Implantations were guided by fluoroscopy and three-dimensional TEE (*Figure 1*) performed by experienced interventional echocardiographers using a predefined echocardiography protocol implementing real-time multiplanar reconstruction.[13] At the end of the procedure, at discharge and at 30 day clinical follow-up visit, severity of MR, left atrial volume, and the right-ventricular-

Figure 1 Implantation of transcatheter direct annuloplasty. Echocardiographic and fluoroscopic aspect of a transcatheter direct annuloplasty procedure: three-dimensional echocardiographic image during transcatheter direct annuloplasty before dynamic reduction of the band with implantation catheter still *in situ* (A), fluoroscopic image during dynamic reduction of the band (B).



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right-atrial regurgitation gradient to estimate PAP was again assessed by the standards of contemporary recommendations and guidelines.[14-17] Further specifications of the transcatheter direct annuloplasty system as well as the detailed description on the technical part of its trans-venous implantation have been explicated in detail elsewhere.[7] All procedures were performed under general anaesthesia.

Study outcomes

Primary efficacy endpoints of the retrospective analysis included

1 Technical success, as defined by the Mitral Valve Academic Research Consortium[18]: ability to deploy the device as intended, for example, by advancing the steering device in the anchoring positions, implanting the anchors, dynamic contraction of the device, and successful retrieval of the delivery catheter without peri-procedural mortality or need of emergency surgery or intervention.
2 Effect on MR post-procedural and at discharge in comparison to baseline; assessment comprised four standard semi-quantitative echocardiographic grades of regurgitation based on EACVI/ESC recommendations (0: no or trace, 1: mild, 2: medium; 3: severe MR).[15,17]
3 Peri-procedural reduction of the anterior-posterior and medio-lateral diameters of the mitral annulus (determined by TEE), invasive measurement of the pressure in the left atrium including v-wave, measured directly after septal puncture before implantation as well as a second measurement performed at the end of the procedure before removing the trans-septal sheath.
4 Effect on PAP and left atrial volume: determined by assessment of the systolic right-ventricular-right-atrial gradient on tricuspid valve regurgitation plus estimated central venous pressure as well as left atrial volume, derived from biplane measurement, at baseline, at discharge, and at 30 day follow-up by transthoracic echocardiography.
5 Peri-procedural trends in biomarkers for myocardial injury (high-sensitive troponin I), renal function (creatinine), and heart failure [brain natriuretic peptide (BNP)] at baseline, at the first post-procedural day, and at 30 day follow-up, as well as physical capability assessed by 6 min walk test distance at baseline and at 1 month.
6 Dyspnoea reduction (NYHA class reduction $\geq$1) at baseline versus 30 day follow-up.

Ethical aspect

Because the study involved an anonymized, retrospective analysis of diagnostic standard data, ethics approval was not required according to German law.

Statistical analysis

Continuous variables are presented as mean ± standard deviation or as median and interquartile range, and categorical variables are expressed as percentages. Continuous variables found not to follow a normal distribution when tested with the modified Kolmogorov–Smirnov test (Lilliefors test) and Shapiro–Wilk test were compared using the Wilcoxon matched-pairs signed rank test (for comparison of parameters in the course of the three time-points: pre-procedural, post-procedural during hospitalization, and at 30 day follow-up) or the Wilcoxon–Mann–Whitney test for comparison between two groups. Normally distributed continuous variables were compared using the Student's *t*-test and categorical variables with Fisher's exact or χ^2 test, as appropriate. We compared pre-procedural versus post-procedural values of clinical, echocardiographic, and laboratory parameters during hospitalization and up to 30 day follow-up. In addition, we compared patients with and without NYHA class reduction $\geq$1 after the procedure (baseline versus 30 day follow-up). Univariate and multivariate logistic regression analyses (adjusted for patients' age) were performed in order to identify predictors of NYHA class reduction $\geq$1. Odds ratios (OR) are given with the corresponding 95% confidence intervals (CIs). Receiver operating characteristics (ROC) curves were calculated for predictors of NYHA class reduction $\geq$1, and the area under the curve was presented with the corresponding 95% CI. Optimized cut-offs were calculated based on ROC analyses using Youden index quantification. Sensitivity, specificity, negative predictive value, and positive predictive value were computed for parameters, which were accompanied by significant prognostic performance. *P* values $<$0.05 (two-sided) were considered to be statistically significant. Statistical analysis was conducted using SPSS software version 24 (IBM SPSS Statistics for Windows, Version 24.0, Armonk, NY, USA).

Results

Patients' baseline characteristics

Overall, 18 patients (mean 77.0 ± 7.4 years, 44.4% women) with all severe MR at baseline (mean EROA 30.4 ± 8.9 mm^2, mean regurgitation volume 45.8 ± 11.8 mL) were included in the study. Leading aetiology was FMR (94% of the patients, mostly by dilatation of the mitral ring/Carpentier Class I); 88.9% of the patients reported severe dyspnoea of functional NYHA class III/IV before interventional treatment. Atrial fibrillation and coronary artery disease were the most frequent co-morbidities (*Table 1*). Left ventricular ejection fraction was reduced in mean (34.9 ± 14.8%), left ventricular end-diastolic dimensions were mostly enlarged compared with a healthy population[16] (volume in mean

Table 1 Baseline characteristics (absolute values or median and interquartile range/mean value ± standard deviation, $n = 18$)

Variable	All patients ($n = 18$)	Patients with NYHA class reduction ≥1 pre-procedure versus 30 day post-procedure ($n = 7$)	Patients with NYHA class reduction <1 pre-procedure versus 30 day post-procedure ($n = 7$)	*P*-value
Age at procedure (years)	77.0 ± 7.4	79.0 ± 4.5	73.7 ± 9.5	0.215
Female gender	8 (44.4%)	3 (42.9%)	4 (57.1%)	0.593
Body mass index (kg/m^2)	28.0 ± 5.2	27.9 ± 6.8	27.4 ± 4.1	0.878
Weight (kg)	83.5 ± 14.5	84.3 ± 20.5	80.6 ± 4.8	0.655
Height (cm)	173.2 ± 11.0	174.1 ± 14.2	172.4 ± 11.0	0.805
Functional mitral regurgitation	17 (94.0%)	7 (100.0%)	7 (100.0%)	
Anchors used for Cardioband® procedure	15 (15/16)	15 (15/17)	15 (15/16)	0.285
Technical success	17 (94.4%)	7 (100%)	7 (100%)	1.000
NYHA class III or IV	16 (88.9%)	7 (100.0%)	7 (100.0%)	
Logistic EuroScore I (%)	23.1 ± 12.7	24.5 ± 11.1	16.7 ± 10.2	0.199
COPD	6 (33.3%)	2 (28.6%)	1 (14.3%)	1.000
Atrial fibrillation	16 (88.9%)	7 (100.0%)	5 (71.4%)	0.462
Coronary artery disease	7 (40.0%)	3 (42.9%)	1 (14.3%)	0.559
Prior coronary artery bypass grafting	3 (16.7%)	1 (14.3%)	0 (0.0%)	1.000
Renal impairment[a]	6 (33.3%)	2 (28.6%)	1 (14.3%)	1.000
Diabetes mellitus	6 (33.3%)	3 (42.9%)	1 (14.3%)	0.559
BNP at baseline (pg/mL)	794.0 ± 776.3	821.1 ± 723.4	505.3 ± 311.3	0.319
hs-troponin I at baseline (pg/mL)	23.3 ± 35.2	16.6 ± 7.8	8.3 ± 4.4	0.034*
Creatinine at baseline (mg/dL)	1.5 ± 0.6	1.3 ± 0.3	1.3 ± 0.2	0.709

[a]Renal impairment was defined as creatinine-baseline-level >1.5 mg/dL.
*$P < 0.05$.

183.3 ± 70.3 mL, indexed volume in mean 93.6 ± 37.7 mL/m^2; left ventricular end-diastolic dimension in mean 6.3 ± 1.1 cm) and the PAP (mean 44.4 ± 8.8 mmHg) elevated. Average indexed left atrial volume was 76.0 ± 22.9 mL/m² at baseline (*Table 2*). Devices used were Cardioband® sizes C to F, implanted with 15 anchors in median (14 to 17).

Technical success rate and effect on mitral regurgitation and other parameters during follow-up

We observed a technical success rate of 94.4%; in one patient, the final dynamic reduction of the band became impossible due to peri-interventional rooting out of several anchors at an advanced stage of the procedure. Thus, the procedure was completed by fixation of the loose end of the band in the septal part of the mitral ring to avoid potential complications by a pendulating device. As the subject was neither eligible for other TVMR devices nor surgical valve replacement, this patient was continued on optimal medical therapy.

Mortality during a follow-up period of 30 days after intervention was low (5.6%), and no severe cardiac related adverse events (e.g. peri-cardial tamponade, injury of adjacent structures, necessity to convert to surgical therapy, relevant bleeding, and relevant cardiac rhythm disturbances) were observed; one patient died during hospitalization for sepsis due to pneumonia.

Overall, transcatheter direct annuloplasty resulted in a significant reduction of MR directly after the procedure and at 30 days follow-up (*Figure 2* and *Table 2*). While all patients showed severe MR at baseline, the rate of mild or no/trace MR was 72.2% after implantation. After 30 days, MR was more pronounced compared with the degree of MR directly after TMVR, but the overall reduction compared with baseline was still significant with no or minimal up to medium MR in most patients (85.7%). Furthermore, the proportion of patients with severe dyspnoea (NYHA III/IV) was significantly reduced from 88.9% to 50% ($P = 0.008$). The clinical improvement (measured by NYHA class) was not associated with the extent of reduction of MR-grade [linear regression β −0.24 (95% CI −1.035–0.444), $P = 0.401$]. A pre-interventional to post-interventional reduction of LAP and v-wave was measured after the procedure. The LAP decreased in mean by 32.3% and left atrial v-waves by 31.7%, respectively. In line, PAP was also diminished by 16% peri-procedurally. This effect was even more pronounced after 30 days (*Figure 3A–C* and *Table 2*). Yet no statistically significant improvement of right-ventricular systolic function as assessed by TAPSE (tricuspid annular plane systolic excursion) could be documented: at baseline, TAPSE was measured 16 mm [13/18] in median with slight increment at discharge [17 mm (15/20), $P = 0.063$ compared with baseline] and 30 day follow-up [17 mm (15/18.5), $P = 0.254$ compared with baseline]. The procedure led to a significant reduction of the mitral annulus diameters and left atrial volume pre-interventional to post-interventional (*Figure 3D,E*). The first day after the Cardioband® procedure, we measured a significant increase in high-sensitive troponin levels, which normalized back to baseline within 30 days. In contrast, BNP-levels remained elevated without relevant alteration (*Figure 3H–J*). With respect to the 6 min walking test, there

Table 2 Echocardiographic, haemodynamic, and clinical changes as well as biomarkers at baseline, discharge[a] and 30 day follow-up after transcatheter direct annulopasty

Variable	Value baseline (1)	Value discharge[a] (2)	Value 30 day follow-up (3)	*P*-value 1–2	*P*-value 1–3	*P*-value 2–3
Mean systolic left atrial pressure (mmHg)	22.3 ± 5.6	15.1 ± 3.4[a]	—	0.019[*] $n = 16$	—	—
v-wave (mmHg)	35.7 ± 12.7	24.4 ± 6.2[a]	—	0.014[*] $n = 15$	—	—
Anterior-posterior annular diameter (cm)	4.0 ± 0.5	3.3 ± 0.3[a]	—	0.002[**] $n = 18$	—	—
Medio-lateral annular diameter (cm)	4.5 ± 0.4	3.6 ± 0.4[a]	—	<0.001[**] $n = 18$	—	—
MR-grade mean	3.0 ± 0.0	1.11 ± 0.83	1.75 ± 0.83	<0.001[**] (0.001[**]) $n = 18$	<0.001[**] (0.001[**]) $n = 14$	0.007[**] (0.017[*]) $n = 14$
Systolic pulmonary arterial pressure (mmHg)	44.4 ± 8.8	37.4 ± 7.2	32.8 ± 15.0	0.003[*] (0.042[*]) $n = 18$	0.025[*] (0.028[*]) $n = 13$	0.197 (0.195) $n = 13$
Left atrial volume (mL)	150.1 ± 56.8 ml	128.8 ± 40.8	125.3 ± 64.1	<0.001[**] (0.002[**]) $n = 18$	<0.001[**] (0.002[**]) $n = 12$	0.506 (0.271) $n = 12$
LA volume indexed (per BSA) (mL/m^2)	76.0 ± 22.9	64.9 ± 15.9	62.7 ± 24.9	<0.001[**] (0.002[**]) $n = 18$	<0.001[**] (0.002[**]) $n = 12$	0.396 (0.239) $n = 12$
BNP (pg/mL)	794.0 ± 776.3	954.1 ± 1017.4	758.5 ± 580.0	0.525 (0.600) $n = 18$	0.484 (0.196) $n = 13$	0.627 (0.753) $n = 13$
hs-troponin I (pg/mL)	23.3 ± 35.2	3453.7 ± 2963.4	23.1 ± 21.7	<0.001[**] (0.001[**]) $n = 18$	0.03[*] (0.002[*]) $n = 13$	<0.001[**] (0.001[**]) $n = 13$
Creatinine (mg/dL)	1.51 ± 0.62	1.40 ± 0.59	1.43 ± 0.37	<0.001[**] (0.026[*]) $n = 18$	0.057 (0.706) $n = 14$	0.350 $n = 14$
6 min walk test (m/6 min)	334.1 ± 127.9	Not determined	380.1 ± 95.1 m	—	0.135 (0.091) ($n = 7$)	—

[a]Values for "Discharge" for left atrial pressure, v-wave, and mitral ring diameters derived directly after the procedure by invasive measurement or transesophageal echocardiography.
[*]$P < 0.05$.
[**]$P < 0.01$ (in brackets: *P* value when tested with Whitney signed rank test).

was a trend to a larger distance [in mean +26% (±SD) or 76 m ± SD in absolute values in comparison with baseline] (*Figure 3K*).

Impact of device implantation on New York Heart Association class ≥1 at 30 day follow-up

We stratified the study subjects into patients with and without NYHA class reduction ≥1 at 30 day follow-up. NYHA class at 30 day follow-up was available in 14 patients. Seven patients reported a NYHA class reduction ≥1 after the procedure. Both groups were of comparable age and comorbidities, and all patients had reported severe dyspnoea (NYHA class III/IV) at baseline (*Table 1*). Most echocardiographic parameters were similar between the groups including left ventricular dimensions and EROA (for details, see Supporting Information, *Table S1*), although PAP at baseline was higher in patients without NYHA-reduction ≥1 in comparison with those with clinical benefit ($P = 0.022$). The level of high-sensitive troponin I at baseline was higher in patients with than those without NYHA-reduction ≥1 (*Table 1*). BNP levels did not differ significantly.

Predictors of New York Heart Association class reduction ≥1 at 30 day follow-up

In a logistic regression model, lower PAP ($P = 0.063$) and a higher high-sensitive troponin level at baseline ($P = 0.072$) were both predictive of NYHA class reduction ≥1 after interventions yet not reaching significance. Both parameters showed a good prognostic performance (area under the curve) in the ROC analysis (for details, results for other parametersv in monovariate and multivariate regression models, and ROC analysis, see Supporting Information, *Tables S2* and *S3*).

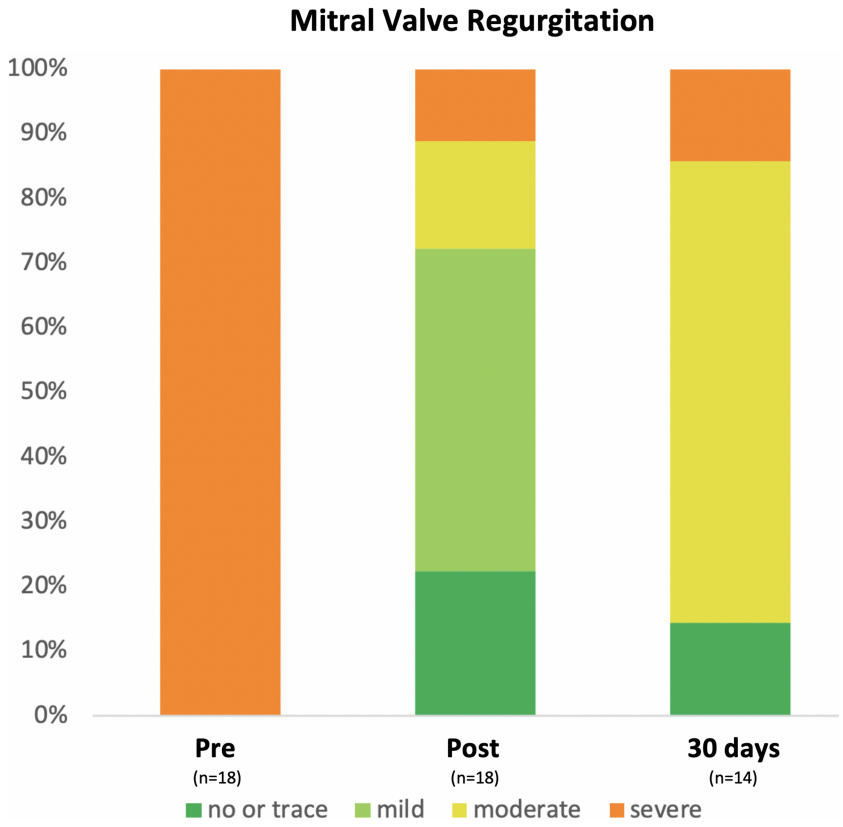
Discussion

Transcatheter mitral valve repair by direct annuloplasty is a novel approach for the treatment of symptomatic MR in selected patients. In analogy the feasibility trial,[8–11] trans-venous implantation of the device was proven to be feasible, safe, and effective with a low 30 day mortality of 5.6%.

The key study findings can be summarized as follows:

i TMVR by direct annuloplasty significantly reduced MR.
ii The procedure demonstrated a high technical success rate (94.4%) without severe cardiac related adverse events.
iii The intervention resulted in a marked reduction of severe dyspnoea (NYHA III/IV).

Figure 2 Peri-interventional reduction of MR. Distribution of mitral valve regurgitation (assessment in Grades 0: no or trace regurgitation, 1: mild, 2: moderate, 3: severe regurgitation, according to EACVI/ESC-Recommendation[15,17]) before and after transcatheter direct annuloplasty (N = 18) as well as at 1 month follow-up (n = 14).

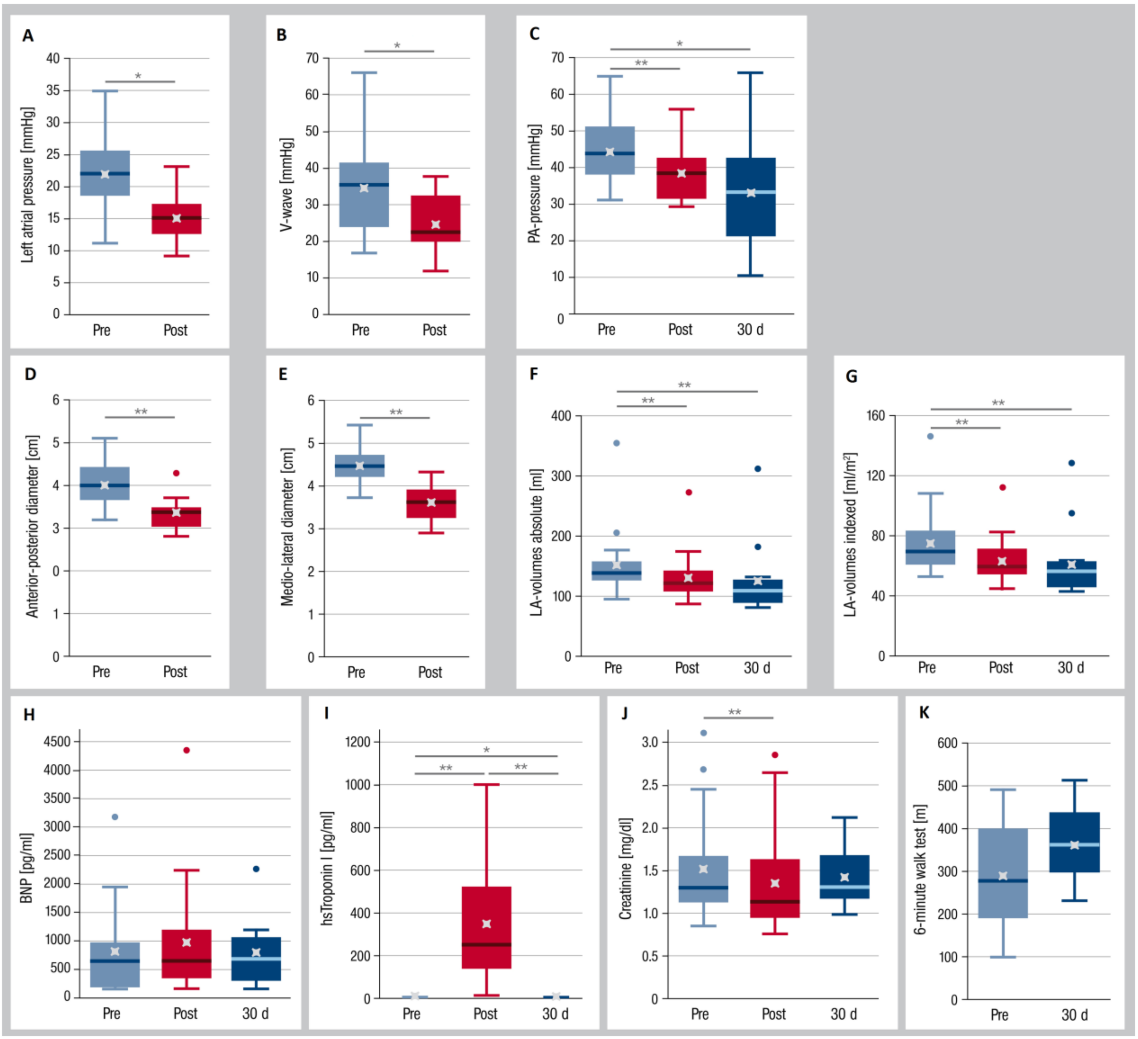


iv Mitral annular diameters, atrial pressures, and LA volume were significantly reduced by device implantation.
v Lower pre-interventional PAP was a predictor of NYHA class reduction ≥1.

The present study generates further evidence that transcatheter direct annuloplasty is capable of a significant reduction of MR, in accordance with already published data.[8–11] Regarding the baseline characteristics of subjects included, patients receiving the device tended to be older (in mean 77.0 vs. 71.8 years) and were more likely female (44.4% vs. 16.1%), were less likely to have coronary artery bypass grafting (16.7% vs. 41%), diabetes mellitus (33.3% vs. 45%), or renal impairment (33.3% vs. 93%) compared with the first in human trial.[9] The prevalence of atrial fibrillation (88.9% vs. 77%) and the computed logistic Euro Score I (23.1 ± 12.7% vs. 18.1 ± 11.9%) were similar in both studies. The technical success rate in the present cohort was high (94.4%). Up to now, knowledge on potential predictors of peri-procedural failure of direct annuloplasty implantations is still lacking. The reasons for the rooting out of anchors that lead to implantation failure in one patient could not be completely elaborated so far and might be due to a limited implantation experience at that early timepoint of the first implantations as well as potential anatomical reasons (subject was the only in the cohort with PMR as pathomechanism). Additionally, and after, the implantation protocol was adjusted by the manufacturer during the study phase in order to avoid complications that have been reported by other study groups.

The interventional annuloplasty reduced substantially the MR accompanied by a substantial decrease in dyspnoea, although the degree of MR-reduction could not be statistically correlated to a decline in NYHA class. With the present studies, we established a significant reduction of mitral annular diameters, atrial pressures, and LA-volume by TMVR. In contrast to previously published results, PAP and LAP as well as its v-wave were all found to be significantly reduced. LAP is influenced by a variety of factors including left ventricular function and mitral valve disease, and the extent of the v-wave is a surrogate marker of MR, left atrial compliance, and left ventricular preload. A decline of LAP and v-wave has been observed previously after edge-to-edge TMVR.[19] In PMR patients who underwent interventional edge-to-therapy, a correlation between clinical improvement (as measured by 6 min walking distance) and the extend of v-wave reduction of LAP was reported.[20] While our study

Figure 3 Effects of TMVR by direct annuloplasty. (A) Reduction of left arterial pressure measured invasively after trans-septal puncture and at the end of the procedure before removing the trans-septal sheath. (B) Diminution of v-wave height during the procedure (measured invasively). (C) Decrease of pulmonary arterial pressure at baseline, at discharge ($n = 17$), and at 1 month follow-up ($n = 12$). (D, E) Anterior-posterior and medio-lateral annulus diameter at baseline and after direct annuloplasty. (F, G) Significant peri-interventional reduction of absolute as well as indexed (per body surface area) left atrial volumes (pre-interventional versus post-interventional, $n = 17$) and statistically non-significant trend for further volume reduction at 1-month follow-up ($n = 11$). (H–J) Peri-interventional and short-term development of blood markers BNP, hs-troponin I, and creatinine: whereas no relevant change in BNP values can be observed, hs-troponin I shows a marked peri-interventional increase as well as a complete recovery after 30 days (also significantly lower than baseline level); mean creatinine level is not relevantly influenced after 30 days. (K) Trend (statistically not significant) for improvement in 6 min walk test (in mean by 68 m absolutely or 23.8%, respectively; $n = 10$). Asterisk: statistical significance level. $^{*}P < 0.05$, $^{**}P < 0.01$.



demonstrates an improvement in NYHA class, it failed to prove a significant increase in the 6 min walking distance presumably due to the relatively small patient cohort.

The extent of the peri-interventional reduction of the mitral annulus diameters was larger than reported previously,[10] and we measured a significant and persistent reduction of atrial volumes by the procedure.

We could not document statistically significant changes in BNP and creatinine. As to be expected, high-sensitivity troponin was measured significantly elevated post-intervention to mostly relatively moderate extents and normalized at the 30 day follow-up to slightly lower levels than before treatment. As no patient showed new wall motion abnormalities or other clinical signs of acute coronary syndrome, control coronary angiography was not performed in any case due to a lacking suspicion of coronary obstruction by the device. The subgroup of patients with initially high PAP showed less clinical benefit in terms of dyspnoea reduction (NYHA class reduction ≥ 1). In contrast, higher baseline levels of high-sensitive troponin compatible with increased myocardial stress before implant were found to correlate well with the observed net clinical benefit (NYHA class reduction).

Limitations

Some limitations of our study merit consideration: first of all, the design is a monocentric retrospective analysis. Additionally, patients' eligibility was determined by assessment of the screening results by our centre and specialists of the manufacturer and not by a corelab; thus, a relevant selection bias cannot be excluded. Finally, our study cohort is only medium-sized with limited follow-up; thus, statistical results have to be interpreted with caution, and not all correlations might gain statistical significance.

Conclusions

Transcatheter mitral valve repair by direct annuloplasty is a safe and feasible procedure in patients being at high-risk for surgical treatment. Implantations of the device resulted in a significant clinical benefit such as a reduction in NYHA class. The present study also established a significant reduction of LAP, left atrial v-wave, and PAP by remodelling of the mitral annulus, resulting in a reduction of MR and accordingly left atrial volume. An elevated PAP could be identified as potential predictor for less clinical post-procedural benefit. Larger and randomized studies are needed to better identify which patients are suited optimally for this distinct device and will profit most from the procedure as part of a multimodal heart failure therapy. Because the need for TMVR in patients with heart failure will increase in the future, direct annuloplasty may represent an additional valuable and feasible therapeutic option.

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Conflict of interest

M.G., K.K., E.S., A.R.T., T.F.R., T.G., and T.M. declare no conflict of interest. F.K. reports having received consultancy and lecture honoraria from Abbott Vascular, Cardiac Implants, and Edwards Lifesciences. A.B.-F. reports having received lecture honoraria from Edwards and consultancy from Abbott Vascular. E.S. reports lecture honoraria from Edwards Lifesciences and Medtronic. R.S.v.B. reports having received consultancy and lecture honoraria from Abbott Vascular, Cardiac Dimensions, Edwards Lifesciences, GE Health Systems, and Philips Healthcare.

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Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1. periprocedural echocardiographic, hemodynamic and clinical parameters stratified for NYHA reduction (mean value +/− standard deviation, N = 18).
Table S2. Predictors of NYHA-reduction ≥1 from pre-procedural to post procedural visit at 30-day follow-up.
Table S3. ROC analysis for predictors of NYHA-reduction ≥1 from pre-procedural to post procedural visit at 30-day follow-up.

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