Improvement in echocardiographic mitral regurgitation parameters correlates with left ventricular reverse remodeling after percutaneous mitral annuloplasty

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DOI: 10.33963/v.phj.105726

Received:
November 14, 2024

Accepted:
April 8, 2025

Early publication date:
April 14, 2025

ABSTRACT

Background: Carillon annuloplasty reduces functional mitral regurgitation (FMR) and induces left ventricular (LV) reverse remodeling.

Aims: This analysis aims to determine whether the change in MR parameters correlates with the extent of LV reverse remodeling after Carillon annuloplasty.

Material and methods: This retrospective pooled analysis included prospectively collected data of 113 consecutive patients undergoing successful Carillon annuloplasty with complete 1-year echocardiographic follow-up. Patients had grade 2+ to 4+ FMR, LV end-diastolic diameter >5.5 cm, and LV ejection fraction <50%.

Results: At 1 year, significant improvements occurred in all MR severity and LV reverse remodeling parameters. Reductions in LV end-diastolic volume and LV end-systolic volume correlated with improvements in regurgitant volume (RV) (r = 0.27 and r = 0.34) and effective regurgitant orifice area (EROA) (r = 0.27 and r = 0.34), but not vena contracta (VC) width. Change in LVEF was associated with change in RV (r = –0.30), EROA (r = –0.32), and VC width (r = –0.40). Decreased mitral annular area correlated significantly with reductions in RV (r = 0.28), EROA (r = 0.28), and VC width (r = 0.34). The change in LVEF also significantly correlated with the reduction in LV end-systolic volume (r = –0.69), LV end-diastolic volume (r = –0.24), LV end-systolic diameter (r = –0.31), and LV end-diastolic diameter (r = –0.31). Significant correlation was observed between the change in mitral annulus area and change in RV (r = 0.28), EROA (r = 0.28), and VC (r = 0.34).

Conclusions: Carillon annuloplasty induced LV reverse remodeling in patients with FMR, with reduced LV diameters and improved LVEF. The degree of improvement in echocardiographic MR parameters after the Carillon procedure significantly correlated with the extent of LV reverse remodeling.

Key words: annuloplasty, Carillon, functional mitral regurgitation, mitral valve

INTRODUCTION

Secondary or functional mitral regurgitation (FMR) is common among heart failure (HF) patients with enlarged, dilated left ventricles (LV) [1, 2]. Any degree of FMR is associated with a worse prognosis [3]. FMR is generally accepted to be a state in which, despite a structurally normal mitral valve (MV), LV geometry changes can lead to papillary muscle displacement [4] and annulus dilation [2], resulting in MR. Guideline-directed medical therapy (GDMT) remains the first-line treatment approach for all HF patients, including those with FMR [5]. However, improvements in FMR with GDMT are inconsistent, seen in fewer than 50% of medically managed patients. Moreover, surgical approaches have limited prognostic and symptomatic benefit [6–8].

This situation has led to the development of a series of catheter-based, percutaneous

WHAT'S NEW?

Percutaneous mitral annuloplasty with a Carillon device provides an option for the reduction of functional mitral regurgitation and induces left ventricular (LV) reverse remodeling, defined as a reduction in its diameters and improved LV ejection fraction. The study shows, for the first time, that the degree of improvement in echocardiographic mitral regurgitation parameters after the Carillon procedure significantly correlates with the extent of LV reverse remodeling. Reductions in LV diameters and volumes correlated with improvements in regurgitant volume and effective regurgitant orifice area. Increased LV ejection fraction was associated with decreased functional mitral regurgitation parameters and reduced LV diameters and volumes. Decreased mitral annular area correlated significantly with reductions in regurgitant volumes, effective regurgitant orifice area, and vena contracta. The correlations between the change in echocardiographic parameters of functional mitral regurgitation after the Carillon procedure and reverse LV remodeling provide additional proof of the efficacy of this technique.

therapies. Transcatheter edge-to-edge repair is the most widely used [9], but divergent results from the two largest randomized, controlled trials underscore the importance of careful patient selection. Whilst COAPT demonstrated clinical and mortality benefits, MITRA-FR results were resolutely neutral [10]. The reasons that could underpin this discrepancy have been widely discussed with the increasing acceptance that favorable features that predict greater benefit from transcatheter edge-to-edge repair include better LV function, more severe FMR, and less advanced HF [11].

On this background, percutaneous mitral annuloplasty may offer a simple and safe option to reduce MR severity, induce LV reverse remodeling, and improve quality of life [12–14]. It remains unclear whether the mode of action of the device is driven by reductions in MR, subsequent beneficial LV remodeling, or primarily LV remodeling [15, 16]. As a first step to explore this further, this analysis, for the first time, systematically aimed to evaluate whether changes in echocardiographic MR severity measures after Carillon annuloplasty correlated with the extent of LV reverse remodeling in FMR patients, enrolled into previously reported clinical trials [12–14].

MATERIAL AND METHODS

This retrospective analysis pooled data on patients with FMR and HF from the TITAN, TITAN II, and REDUCE-FMR trials evaluating the Carillon Mitral Contour System (Cardiac Dimension Inc, Kirkland, WA, US). The design and eligibility criteria of each study have been previously described. Briefly, TITAN was a prospective, non-randomized study with 5-year follow-up. TITAN II was a prospective, single-arm, multicenter study with 1-year follow-up for non-implanted patients and 2-year follow-up for implanted patients. REDUCE-FMR was a double-blind, randomized, sham-controlled study with 1-year follow-up. For the current analysis, we pooled data for patients from these prior studies, who had both a successful mitral annuloplasty with the Carillon device and complete 1-year echocardiographic follow-up data. The sample size studied was a result of data of patients meeting the requirements out of all 3 trials.

Key eligibility criteria at screening included ischemic or non-ischemic dilated cardiomyopathy despite GDMT with echocardiographic criteria of moderate (TITAN, TITAN II) or at least mild to moderate (REDUCE-FMR) FMR, New York Heart Association (NYHA) class II–IV HF symptoms, 6-minute walk test distance 150 to 450 meters, reduced LV ejection fraction (LVEF) (below 40% in TITAN and 50% in TITAN II and REDUCE-FMR), and LV end-diastolic diameter (LVEDD) >55 mm. Key exclusion criteria were recent revascularization within 30 days, severe MV degenerative pathology, severe mitral annular calcification, or prior MV surgery. Subjects with a coronary sinus device or guideline recommendation for cardiac resynchronization therapy were also excluded due to potential interference with coronary sinus access needed for the Carillon device placement. All patients needed to be stable on optimal GDMT to be enrolled.

An independent core laboratory performed quantitative echocardiographic assessment of MR severity and LV remodeling parameters as per American Society of Echocardiography guidelines [17]. The core laboratory was blinded to treatment allocation, visit interval, and MR grade. The MR echocardiographic parameters included MR grade, effective orifice area, regurgitant volume (RV), and vena contracta (VC) width. LV reverse remodeling parameters included LVEDD and LV systolic diameter (LVESD), LV volumes (LVEDV, LVESV), LVEF, mitral annular area, and left atrial volume. All studies enrolled patients with grade 2+ to 4+ FMR. TITAN and TITAN II used core laboratory pre-screening to exclude subjects with grade 1+ FMR. REDUCE-FMR relied on the local heart team to determine eligibility but used a blinded echocardiographic core laboratory assessment for final MR grade analysis, revealing that few enrolled patients had 1+ grade FMR at baseline. All three trials were monitored by independent bodies, and source files for the analysis, including the follow-up data, were obtained from the official documentation of each trial.

The Carillon indirect mitral annuloplasty procedure has been described previously [18]. Briefly, the device consists of 2 anchors joined by a bridge that plicates the posterior mitral annulus by first deploying the distal anchor, then applying tension to shorten the coronary sinus, and then deploying the proximal anchor just inside the coronary sinus ostium to maintain that cinching. The procedure takes

advantage of the anatomical proximity of the coronary sinus to the mitral annulus for annular reduction. After jugular venous puncture, a 9 F guide catheter is delivered into the distal coronary sinus. The distal anchor of the device is positioned deep in the great cardiac vein approximating the anterolateral commissure. Using the delivery catheter to pull from above and place tension on the coronary sinus, the mitral circumference is shortened. After verifying that the deployed device does not compromise the circumflex coronary artery, tension is maintained and the proximal anchor is deployed in the coronary sinus.

Statistical analysis

Baseline subject characteristics were summarized as the mean (standard deviation) or median (interquartile range) for continuous variables and counts and percentages for categorical data and assessed by Student's t-test and Mann–Whitney test for normally and non-normally distributed, respectively, as well as Wilcoxon test for paired non-normally distributed data. The Pearson correlation coefficient (for normally distributed) or Spearman rank correlation coefficient (for non-normally distributed data) was reported to assess the relationship between changes in echocardiographic parameters over 1-year follow-up. Statistical significance was defined as a two-sided $P < 0.05$. The investigation conforms with the principles outlined in the Declaration of Helsinki, and all subjects gave written informed consent to participate in the study, which was accepted by the local ethics committees of the participating centers.

RESULTS

The dataset included 203 subjects enrolled to mitral annuloplasty with the Carillon device. 139 subjects were treated with mitral annuloplasty while 64 subjects did not receive an implant (non-implanted) due to one or more of the following reasons: patient consent withdrawal, unexpected coronary artery disease requiring revascularization, coronary sinus anatomy not suitable for placement of the CARILLON device, coronary sinus dissection, and/or coronary artery impingement by the device. Of the 139 patients undergoing Carillon annuloplasty in the three pooled studies, 113 had 1-year complete echocardiographic data available for analysis. Mortality over 1 year did not significantly differ between implanted and non-implanted subjects (24 patients in the implanted group and 9 in the non-implanted group; $P = 0.565$). As previously reported, the mean age was 68 (11) years, 75% were male, and most had NYHA II (26%) or III (69%) HF, mainly from ischemic etiology (68%). In the implanted group, the median LVEF at baseline was 30.8 (13.6–49.9) and LVEDD was 6.6 (4.9–8.6) cm (Table 1). Before the procedure, all patients were stable on optimal GDMT, which was modified during the follow-up based on the change in symptoms.

At 1 year after Carillon annuloplasty, significant improvements were observed in functional status (NYHA class, 6-minute walk test distance, Kansas City Cardiomyopathy Questionnaire) and echocardiographic MR and LV reverse remodeling parameters (Figures 1 and 2). Specifically, there were significant reductions in MR severity grade (median decrease of 1 grade), effective regurgitant orifice area (EROA), RV, VC width, and mitral annulus area.

LV reverse remodeling was evident at 1 year, with a statistical decrease in LVEDD (–0.1 [0.5 cm]), LVESD (–0.2 [0.6 cm]), LVEDV (–15.2 [40.5 ml]), and LVESV (–13.7 [37.9 ml]), and with improved LVEF (1.8% [7.7%]). There was no significant change in left atrial volume (p=0.23) (Table 2).

The reductions in LVEDV and LVESV were significantly associated with decreases in RV (r = 0.27 and r = 0.34, respectively) and EROA (r = 0.27 and r = 0.34, respectively) but not VC width (r = 0.20 and r = 0.27, respectively). The decrease in mitral annulus area correlated significantly with reductions in RV (r = 0.28), EROA (r = 0.28), and VC width (r = 0.34). Furthermore, increases in LVEF were associated with decreases in RV (r = –0.30), EROA (r = –0.32), and VC width (r = –0.40), as well as LV reverse remodeling parameters, including LVESV (r = –0.69), LVEDV (r = –0.24), LVESD (r = –0.31), and LVEDD (r = –0.31) (Table 3).

DISCUSSION

This analysis of a cohort of FMR patients treated with the Carillon procedure suggests and reinforces previous findings that indirect mitral annuloplasty improves functional status and leads to LV reverse remodeling. However, this analysis takes a first step in exploring the relationship between change in MR severity and LV reverse remodeling after the Carillon procedure. To our knowledge, such detailed correlative analyses have not been previously reported for percutaneous FMR interventions.

Mitral regurgitation parameters

The current results confirm those of prior studies demonstrating improvement in quantitative echocardiographic MR parameters after Carillon device implantation [12, 14, 16, 19–21]. After 1 year, non-implanted control patients showed no significant MR decreases, and even mitral area increases were noted, suggesting progressive LV dilation. In contrast, implanted subjects had significant reductions across all MR parameters (VC width, RV, EROA) along with decreased mitral annular area (Figure 1). Both VC width and EROA are pivotal indicators of MR severity. Their concurrent reduction with lowered RV highlights the favorable impact of Carillon-mediated annuloplasty on the structure and function of the MV apparatus.

Left ventricular reverse remodeling

LV reverse remodeling induced by neurohormonal antagonists can improve HF prognosis [22, 23]. However, patients with HF and FMR have worse outcomes, with mortality rates up to 50% at 5 years despite GDMT [6]. This highlights the need for interventional procedures like cardiac resynchro-

Table 1. Baseline characteristics of patients

	Non-implanted (n = 64)	Implanted (n = 139)	*P*-value
Baseline	**Mean (SD) or median (IQR)**	**Mean (SD) or median (IQR)**	
Age, years	67.6 (11.2)	67.9 (10.6)	0.73
Males	44 (69%)	105 (75%)	0.31
Weight, kg	77.9 (19.6)	77.2 (18.8)	0.717
Prior myocardial infarction, n (%)	31 (48%)	73 (52%)	0.59
Ischemic etiology, n (%)	39 (61%)	94 (68%)	0.28
History of atrial fibrillation, n (%)	31 (48%)	69 (50%)	0.87
BMI, kg/m^2	26.8 (5.8)	26.4 (5.2)	0.78
6MWT, m	298 (88)	307 (85)	0.51
KCCQ, points	41.9 (5.5–97.9)	48.9 (3.1–97.2)	0.09
NYHA class:			
II	21 (33%)	36 (26%)	0.20
III	43 (67%)	96 (69%)	
IV	0 (0%)	6 (4%)	
MR severity grade:			
1+	10 (16%)	25 (18%)	0.67
2+	17 (27%)	43 (31%)	
3+	27 (43%)	46 (34%)	
4+	8 (13%)	20 (15%)	
LVEF, %	33.1 (9.9–51.8)	30.8 (13.6–49.9)	0.06
LVEDV, ml	198.6 (83.7)	193.3 (62.7)	0.93
LVESV, ml	136.2 (74.9)	135.5 (54.6)	0.51
LVEDD, cm	6.4 (4.5–8.1)	6.6 (4.9–8.6)	0.50
LVESD, cm	5.1 (3.2–7.3)	5.6 (3.4–8.1)	0.08
MAA, MVANA	12.1 (6.2–25.4)	12.5 (4.9–23.1)	0.64
MR EROA (PISA), cm^2	0.27 (0.04–0.7)	0.22 (0.04–0.61)	0.27
MR EROA/LVEDV, cm^2 per 100 ml LVEDV	0.15 (0.09)	0.14 (0.07)	0.42
MR RV (PISA), ml	40.1 (6.3–101.9)	32.4 (5.63–100.2)	0.13
VC, mm	0.50 (0.22–0.86)	0.53 (0.17–0.97)	0.25

Values presented as: n (%) or mean (SD) or median (interquartile range). Student's t-test and Mann–Whitney test for normally and non-normally distributed, respectively

Abbreviations: 6MWT, 6-minute walk test; BMI, body mass index; EROA, effective regurgitant orifice area; IQR, interquartile range; KCCQ, Kansas City Cardiomyopathy Questionnaire; LVEDD, left ventricular end-diastolic diameter; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic diameter; LVESV, left ventricular end-systolic volume; MAA, mitral annulus area; MR RV, mitral regurgitation volume; NYHA, New York Heart Association; SD, standard deviation; VC, vena contracta

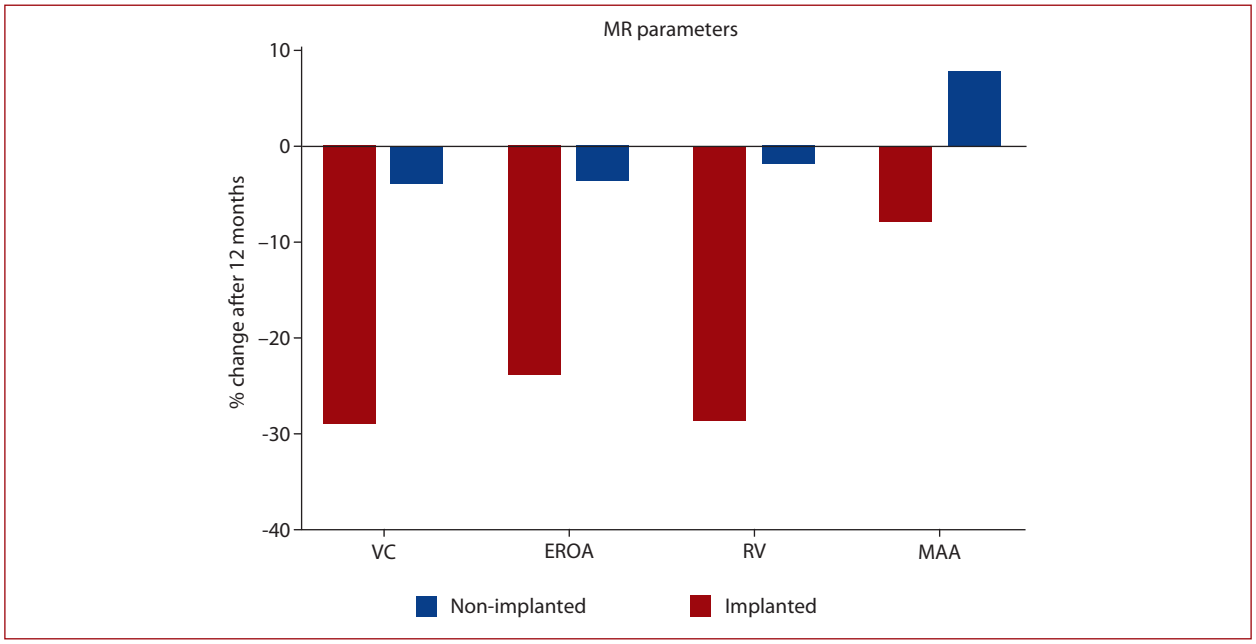


Figure 1. Change in echocardiographic MR parameters over 1-year follow-up between patients treated with Carillon device and non-implanted subjects

Abbreviations: EROA, effective regurgitant orifice area; MAA, mitral annulus area; MR, mitral regurgitation; RV, regurgitant volume; VC, vena contracta

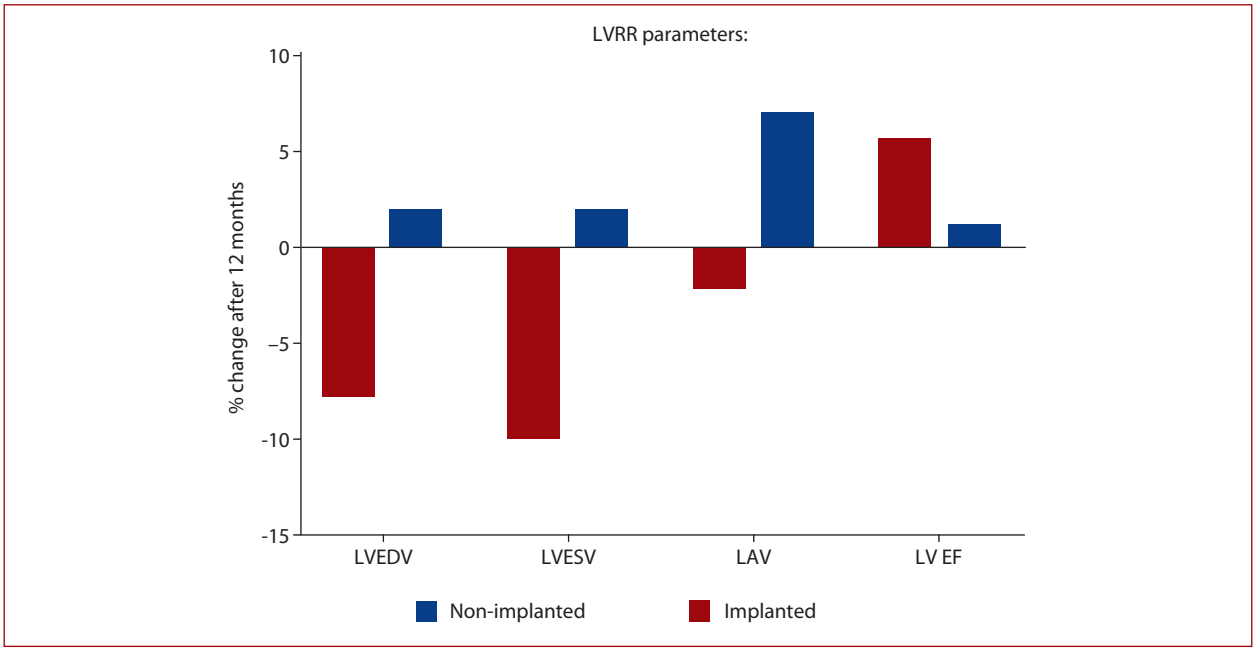


Figure 2. Change in LVRR parameters over 1-year follow-up between patients treated with Carillon device and non-implanted subjects

Abbreviations: LAV, left atrial volume; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; LVESV, left ventricular end-systolic volume; LVRR, left ventricular reverse remodeling

Table 2. Change in functional and echocardiographic parameters 1 year after implantation of the Carillon device

Variable	Carillon implant (n = 113)			Non-implanted controls (n = 64)			Group difference
	Value at 1 year	Change at 1 year	*P*[a]	Value at 1 year	Change at 1 year	*P*[a]	*P*[b]
Functional status							
6MWT	365 (149)	51 (115)	<0.001	339 (121)	22 (65)	0.046	0.06
NYHA[c]	2 (2–3)	–1 (–1 to 0)	<0.001	2 (2–3)	0 (–1 to 0)	0.23	0.04
KCCQ	63.2 (25.4)	11.6 (25.2)	<0.001	56.6 (25.6)	8.1 (21.1)	0.02	0.44
MR parameters							
EROA, cm^2	0.17 (0.13)	–0.06 (0.1)	<0.001	0.26 (0.16)	–0.01 (0.06)	0.48	0.02
RV, ml	25.2 (18.9)	–10.5 (14.9)	<0.001	42.4 (24.4)	–0.8 (17.8)	0.50	0.03
VC, mm	0.41 (0.2)	–0.16 (0.22)	<0.001	0.45 (0.16)	–0.02 (0.12)	0.38	<0.01
MAA, cm^2	11.6 (3.9)	–1.0 (2.7)	<0.001	13.35 (3.5)	1.0 (2.7)	0.04	<0.001
LV reverse remodeling							
LVEDD, cm	6.4 (0.8)	–0.1 (0.5)	0.02	6.4 (0.9)	0.4 (2.9)	0.34	0.08
LVESD, cm	5.4 (0.9)	–0.2 (0.6)	0.03	5.4 (1.0)	0.2 (0.2)	0.73	0.02
LVEDV, ml	180.9 (54.3)	–15.2 (40.5)	0.002	196.4 (78.5)	4.1 (2.9)	0.43	0.55
LVESV, ml	121.7 (46.5)	–13.7 (37.9)	0.009	130.7 (65.3)	2.8 (22.7)	0.24	0.10
LAV, ml	98.1 (41.9)	–2.3 (21.3)	0.23	129.8 (114.1)	8.8 (29.3)	0.12	0.05
LVEF, %	33.4 (8.6)	1.8 (7.7)	0.04	35.6 (8.3)	0.4 (5.9)	0.79	0.37

Student's t-test and Wilcoxon test for normally and non-normally distributed, respectively: [a]*P* for change from baseline, mean (SD). [b]*P* for change in implanted group vs. change in non-implanted controls. [c]Median (interquartile range)

Abbreviations: LAV, left atrial volume; RV, regurgitant volume; other — see Table 1

nization therapy [24] or MV interventions to further promote LV reverse remodeling. It must be emphasized that our patients were on optimized GDMT before enrollment, and none underwent cardiac resynchronization therapy implant during the 1-year follow-up period.

Prior studies have demonstrated that both the MitraClip [25] and Carillon procedures [14, 16, 19] can facilitate beneficial LV reverse remodeling in FMR patients. The REDUCE-FMR trial showed that the Carillon implant significantly reduced RV by 7.1 ml and LVEDV by 10.4 ml, which was at least comparable to the degree of reverse remodeling in the COAPT trial. A prior analysis by Chiarito et al. [26] found that a 30% reduction in RV was associated with subsequent LV reverse remodeling. Our finding of a 29% RV reduction resulting in LV reverse remodeling is consistent with this concept. To our knowledge, this is the first comprehensive analysis demonstrating significant correlations between the degree of improvement in

Table 3. Correlations between 1-year parameter change in implanted and non-implanted patients

Non-implanted patients									
—	RV change	EROA change	VC change	LVEF change	LVEDV change	LVESV change	LVEDD change	LVESD change	MAA change
RV change	—	0.83[c*]	0.12[c]	–0.01[c]	–0.18[c]	–0.08[b]	–0.08[c]	–0.05[c]	0.25[c]
EROA change	0.85[b**]	—	0.17[c]	–0.14[c]	–0.24[c]	–0.22[b]	–0.07[c]	0.01[c]	0.23[c]
VC change	0.38[b**]	0.47[b**]	—	–0.07[c]	0.12[c]	0.12[b]	0.05[c]	0.43[c]	–0.33[c]
LVEF change	–0.30[b*]	–0.32[c**]	–0.40[b**]	—	–0.08[c]	–0.49[b**]	–0.16[c]	–0.29[c]	0.02[c]
LVEDV change	0.27[b*]	0.27[b*]	0.20[b]	–0.24[b*]	—	0.84[b**]	0.47[c**]	0.44[c*]	–0.02[c]
LVESV change	0.34[b**]	0.34[b**]	0.27[b]	–0.69[b**]	0.81[b**]	—	0.33[b]	0.52[b**]	0.11[b]
LVEDD change	0.24[b*]	0.15[b]	0.39[b**]	–0.35[b**]	0.17[b]	0.29[b*]	—	0.36[c*]	0.24[c]
LVESD change	0.12[b]	–0.06[b]	0.24[b]	–0.31[b**]	0.14[b]	0.24[b]	0.65[b**]	—	–0.26[c]
MAA change	0.28[b*]	0.28[c*]	0.34[b**]	–0.13[c]	0.13[b]	0.31[b**]	0.22[b*]	0.13[b]	—
Implanted patients									

[a]Statistically significant correlations in bold; *P <0.05; **P <0.01. [b]Spearman's rank correlation coefficient (not normally distributed data). [c]Pearson's correlation coefficient (normally distributed data)

Abbreviations: see Tables 1 and 2

echocardiographic parameters and LV reverse remodeling after Carillon implantation.

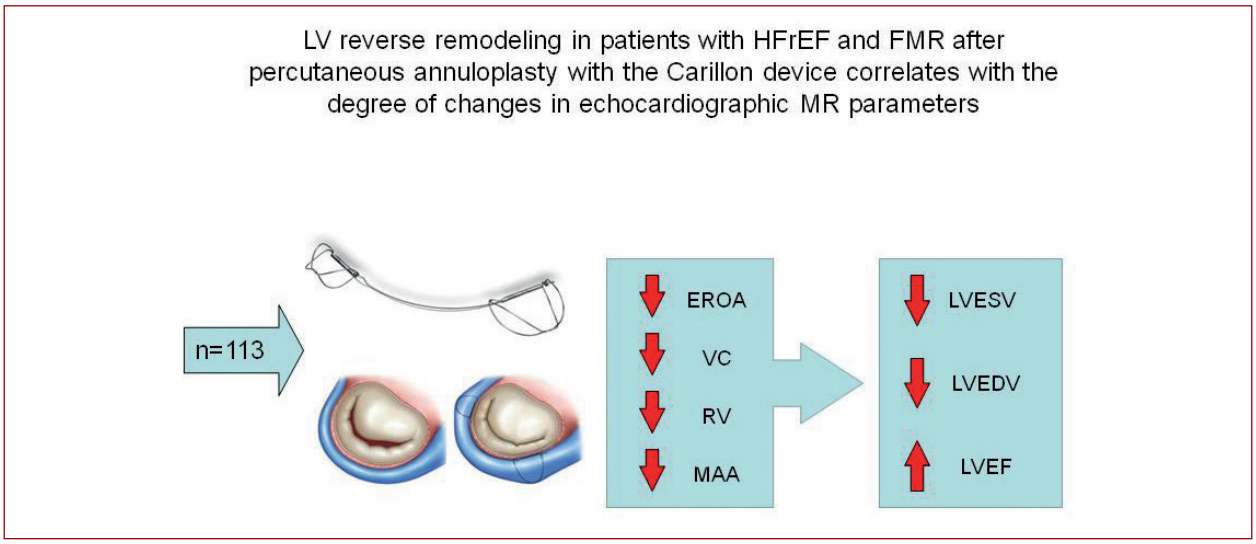
The divergent outcomes of the COAPT and MITRA-FR trials suggest MitraClip benefits may be limited to specific FMR subgroups, emphasizing the importance of careful patient selection. However, "COAPT-like" patients represent only ~5% of real-world FMR cases [19]. This highlights the unmet need to evaluate additional percutaneous mitral repair strategies suitable for broader patient populations. The Carillon device differs substantially from MitraClip in its mechanism and procedural approach. Coronary sinus annuloplasty is technically simpler with a shorter learning curve, making it feasible in most centers without MV repair experience. Rather than directly manipulating the MV leaflets, the Carillon device reshapes the posterior mitral annulus from the outside, without affecting subvalvular structures or limiting future therapies like cardiac resynchronization therapy [27].

Prior studies, including our previous analyses, have demonstrated Carillon's efficacy across a broad spectrum of FMR severities [14, 16], even in patients with only moderate or even mild FMR [21]. Other researchers reported its efficacy in severely dilated LV [28] or when combined with other devices [29]. Moreover, the previous work by Witte et al. [21] in subjects with mild to moderate FMR undergoing the procedure in the early HF stage suggests that it may be beneficial by slowing disease progression. The currently ongoing EMPOWER trial, including patients with mild grade 1+ FMR, will likely help clarify whether Carillon annuloplasty can slow HF progression when applied early for lower-severity FMR.

Grayburn et al. [30] attempted to explain the divergent results of the MITRA-FR and COAPT clinical trials by introducing the concept of MR proportionality based on indexing MR severity to LV size. According to the concept, subjects with proportionate MR (expected relative to LV dilation degree) should respond to medical therapy with neurohormonal antagonists to reduce LV dilation. Those with disproportionate MR (unexpectedly large MR volume relative to LV dilation degree) should respond better to interventional procedures directly targeting the MV (i.e., mitral clipping). We previously performed a pooled post-hoc analysis using the Grayburn proportionality criteria among FMR patients treated with the Carillon device [15]. Interestingly, both proportionate and disproportionate MR subgroups benefited from the Carillon device. Moreover, contrary to MitraClip outcomes, proportionate MR subjects treated with Carillon had better outcomes with LV reverse remodeling. In the current analysis, we included all consecutive patients undergoing Carillon implantation, and significant correlations between MR and LV reverse remodeling parameters persisted. This suggests that the percutaneous catheter annular approach with the Carillon device may provide more consistent LV reverse remodeling across a broad spectrum of FMR patients. Overall, Carillon mitral annuloplasty may interrupt the vicious cycle of LV volume overload, LV dilatation, and subsequent worsening of MR, thus ameliorating HF symptoms and improving quality of life.

Correlations between mitral regurgitation and left ventricular reverse remodeling

Reductions in LVEDV and LVESV were associated with decreases in RV and EROA but not VC width changes. The absence of significant correlations with VC width changes suggests that the absolute reduction in VC may not solely result from changes in LV volumes or dimensions. This may indicate a unique and intricate relationship between MV function, ventricular geometry, and overall cardiac performance. Furthermore, it is important to acknowledge that our VC width measurements were performed by two-dimensional echocardiography, evaluating the cross-sectional area of VC at a single point. While the Carillon procedure potentially influences the VC shape, our single-plane measurement technique has limitations in capturing complex three-dimensional geometrical changes. While implementing a three-dimensional echocardiographic assessment could provide more discernible



Graphical abstract

Abbreviations: FMR, functional mitral regurgitation; HFrEF, heart failure with reduced ejection fraction; other — see Figures 1 and 2

relationships between VC morphological changes and LV reverse remodeling parameters, this imaging modality was not utilized in the present analysis.

Functional status

Improved functional status measured by the Kansas City Cardiomyopathy Questionnaire, NYHA class, or 6-minute walk test distance is usually associated with lower mortality and morbidity in HF patients [31]. Previous studies with the Carillon device demonstrated sustained and clinically meaningful improvements in functional status [12–14, 16, 18], which were corroborated by the current analysis. One year post procedure, we observed significant improvements in the NYHA class (one class median improvement), 6-minute walk test (over 50 meters), and quality of life assessed by the Kansas City Cardiomyopathy Questionnaire (over 11 points). For perspective, the minimal change on this questionnaire that translates into better long-term survival is ≥5 points [32, 33], whereas the average 11-point gain here exceeds improvements from contemporary heart failure therapies, including sacubitril/valsartan [34], sodium-glucose co-transporter 2 inhibitors [35], or cardiac resynchronization therapy implantation [36]. In the COAPT trial with MitraClip, the change in 6-minute walk test distance did not reach statistical significance.

Left ventricular ejection fraction

LVEF has been suggested to reflect systolic function poorly in severe MR [37]. In the paper of Nita et al. [38], no significant LVEF changes were noted after the MitraClip procedure. Even in the subgroup with LV reverse remodeling, only a trend toward LVEF improvement was noted. Assessment of global longitudinal strain might better reflect improvements in LV function in patients after MV repair [39], but such transthoracic echocardiographic analysis was not performed in the Carillon trials. The importance of MR diagnosis seems to be of particular importance in patients who underwent myocardial infarction [40, 41].

We observed a significant increase in LVEF 1 year after the Carillon procedure, which correlated with reductions in quantitative MR echocardiographic parameters, including RV, EROA, and VC. The change in LVEF was also significantly correlated with LV reverse remodeling parameters, including LVESV, LVEDV, LVESD, and LVEDD (graphical abstract). Because we previously reported that patients with "proportionate" FMR demonstrate more pronounced reductions in LV diameters and volumes after the Carillon procedure [15], we speculate that this correlation results from the "proportionate" FMR patients in the cohort studied. However, future analyses are required to confirm this hypothesis.

An unexpected difference in the correlations between changes in LV volumes and diameters in both the implanted group and the observational group was noted (Table 3). The changes in LV volumes were more related to the changes in its diameters in the observational group. With our data we can speculate that the intervention modified the LV shape, affecting the "natural" correlation between changes in LV diameters and volumes.

The first successful Carillon procedure was performed in Poland with a prototype device, as described in *Polish Heart Journal* [42]. Since then, the device underwent several modifications and improvements and later underwent evaluation in multicenter clinical trials [12–16]. After receiving a CE mark, it has become commercially available and reimbursed in several European countries. Very recently, the first commercial cases of Carillon™ device use in Poland, being reimbursed by the National Health System (NFZ), have been performed, allowing this technique to be added to the portfolio of treatment options for FMR patients in everyday clinical practice.

Limitations

This analysis has important limitations. First, a 1-year follow-up duration may fail to fully capture the full extent of progressive reverse remodeling after the Carillon procedure and whether it is sustained. Second, while statistically significant correlations were identified between improvements in FMR and LV remodeling parameters, the strength of the correlation coefficients suggests a significant influence of pathophysiological relationships not fully characterized by these echocardiographic measures alone. In addition, we included patients who completed the follow-up period, and therefore some patients' characteristics, which might affect the results, were not evaluated. Future studies on a large cohort as well as implementation of multivariate analysis may allow identification of predictors of reverse remodeling after the procedure.

CONCLUSION

Our current analysis confirms that percutaneous mitral annuloplasty with the Carillon device in FMR patients results in LV reverse remodeling, defined as decreased LV diameters and volumes and improved EF, which significantly correlated with changes in FMR parameters after Carillon implantation. We believe this is the first dataset indicating a significant correlation between the degree of improvement of echocardiographic FMR parameters and LV reverse remodeling due to percutaneous treatment.

Article information

Acknowledgement: We thank Dr. Larry E. Miller for his professional editorial assistance and Ms. Iza Miechowicz for statistical analyses.

Conflict of interest: PK and RCS — research and travel support from Cardiac Dimensions Inc.; JL, KKW and TS –— research support and proctoring fees from Cardiac Dimensions Inc; RD and AB — nothing to declare.

Funding: The clinical studies being analyzed in the paper were funded by Cardiac Dimensions Inc.

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