Effects of a Cloud-based Synchronous Telehealth Program on Valvular Regurgitation Regression: Retrospective Study

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Abstract

Background: Telemedicine has been associated with better cardiovascular outcomes, but its effects on the regression of mitral regurgitation(MR) and tricuspid regurgitation(TR) remain unknown.

Objective: To evaluate whether telemedicine could facilitate the regression of MR and TR compared to usual care and whether it was associated with better survival.

Methods: This retrospective cohort study enrolled consecutive patients with isolated MR or TR of at least moderate severity and with a follow-up transthoracic echocardiograms (TTE) at least 3 months apart from 2010 through 2020, with follow-up through December, 2022. Patients receiving telehealth services for at least two weeks within 90 days of baseline TTE were categorized as the telehealth-group; the remainder constituted the non-telehealth group. Daily biometric data including blood pressure, pulse rate, blood glucose, electrocardiogram, and oxygen saturation, were transmitted to a cloud-based platform for timely monitoring in telemedicine participants. Experienced case managers contacted patients regularly and initiated immediate action for concerning measurements.

Results: The MR cohorts consisted of 264 patients (mean age, 67 years), including 97 regressors and 74 telehealth-participants. Telehealth participation (HR 2.20; 95% CI 1.35-3.58; P=0.001) was robustly associated with MR regression, which was linked to reverse cardiac remodeling, represented by left ventricular ejection fraction (LVEF), and LV and LA dimensions (all P?0.02). Determinants of ACD were age, LVEF, percutaneous coronary intervention, and MR-regressors (all P?0.02). The TR cohort consisted of 245 patients(mean age, 68 years), including 87 regressors and 61 telehealth participants. Telehealth was one of the univariable determinants of TR regression, while beta-blocker use and baseline TR remained strong predictors of TR regression in multivariable analysis (both P?0.048).

Conclusions: Patients in the telehealth group were 2.2 times more likely to experience MR regression. Moreover, MR regressors had better survival and reverse cardiac remodeling compared to non-regressors. These findings may have important implications for future guidelines.

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Abstracts

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Keywords: mitral regurgitation; tricuspid regurgitation; telehealth; telemedicine; cardiac remodeling

Introduction

Valvular heart disease (VHD), which poses a substantial medical burden and is reported to be under-diagnosed, has affected 11% of people aged more than 65 years old[1,2]. Of these, mitral regurgitation (MR) is one of the most common VHD in several population-based studies; it precipitates atrial fibrillation, left-sided heart failure (HF), and reduces life expectancy[3-6]. Tricuspid regurgitation (TR), another common VHD, often develops secondary to left-sided heart disease or pulmonary hypertension, increasing the risk of all-cause death (ACD)[7,8]. Timely intervention before irreversible cardiac remodeling could prevent detrimental outcomes[9-11], highlighting the importance of early detection and close monitoring.

The demands for telemedicine have surged in the post-COVID-19 era, and a plethora of studies have demonstrated its benefits in reducing mortality and HF hospitalization for patients with chronic cardiovascular(CV) diseases[12-16]. However, the associations between tele-monitoring and VHD remained largely unknown[17]. Previously, we had reported for the first time that patients receiving telehealth service, who had higher comorbidity burdens than the control group, showed similar progression rates for MR and TR, suggesting that telemedicine might somewhat halt the worsening of MR or TR [18]. Nevertheless, the effect of tele-monitoring on the regression of ≥moderate MR or TR remains obscure.

In this context, our study aimed to: (1) compare the profiles of regressors and non-regressors in MR and TR; (2) identify factors influencing MR/TR regression, including telemedicine versus standard care; and (3) assess the determinants of survival.

Methods

Study Population

We retrospectively enrolled patients admitted to the cardiology ward in National Taiwan University Hospital (NTUH) between 2010 and 2020. The inclusion criteria were as follows: (1) patients with at least two transthoracic echocardiograms (TTEs) performed at least three months apart; (2) baseline

TTE indicating moderate, moderate-severe, or severe MR or TR; and (3) absence of moderate or greater aortic stenosis, aortic regurgitation, or mitral stenosis on baseline TTE; and (4) no prior mitral or tricuspid valve surgeries **(Supplemental Figure 1)**.

We divided our cohort into two groups: (1) the telehealth group, consisting of patients who received telehealth services for at least two weeks within 90 days of the baseline TTE (patients who received telehealth after their last TTE were excluded to avoid confounding); and (2) the control group, consisting of patients who did not participate in the telehealth program at any point during the follow-up period. This study was approved by our Institutional Review Board and was conducted by the Taiwan ELEctroHEALTH study group (TELEHEALTH study group).

Telehealth Services

Since 2010, Telehealth Center of NTUH has been pioneering the use of remote care specifically for patients with CV disease[18-20]. We invited patients admitted to CV ward at NTUH to participate in our telehealth program; these patients usually presented with conditions such as arrhythmias, acute myocardial infarction (AMI), coronary artery disease (CAD), congestive HF, or a history of surgical or congenital heart defects. Prior to initiating telehealth services, a comprehensive eligibility assessment was conducted. This included a face-to-face training session for both the patient and their primary caregiver. The session focused on proper operation of sensors, including manometers, oximeters, glucometers, and electrocardiography devices. Notably, detailed instructions were given on proper home blood pressure (BP) measurement techniques, following established guidelines and using commercially available BP monitors.

Participating patients recorded their biometric data daily, including BP, pulse rate, finger-stick blood glucose, single-lead electrocardiogram, and oxygen saturation. All collected data was securely transmitted to a cloud-based database. This centralized platform allowed case managers and physicians to remotely monitor our patients. Upon identifying any concerning measurements, defined as data exceeding or falling below established thresholds or exhibiting other abnormalities, case managers would initiate immediate action. This involved direct contact with patients to verify their well-being, investigate potential issues, and offer guidance on dose adjustments. Case managers, who had attained at least level 2 out of 4 in our center (**Supplemental Table 1**), contacted patients and caregivers every 2-3 days to monitor their overall condition, and more frequently if unstable conditions were present. During the same period (2010-2020), we enrolled control group patients who were admitted to the CV ward, received only standard care, and did not participate in the telehealth program.

Clinical Data

Baseline demographics, BP, prescribed medications, echocardiographic parameters, and past histories of percutaneous coronary interventions (PCI) were collected. Baseline BP was defined as BP measured within 1 month of baseline TTE. The Charlson Comorbidity Index (CCI) was calculated, excluding data on HIV infection status to comply with confidentiality regulations mandated by the HIV Infection Control and Patient Rights Protection Act.

Endpoints

The *primary* endpoint was defined as MR/TR regression from ≥moderate to < moderate degree. The follow-up period was from baseline TTE to the last TTE. The *secondary* endpoint was ACD. The follow-up duration was from baseline TTE to the date of ACD or the last follow-up, which ended on December 31, 2022. The date and cause of death were obtained from both electronic records and research data from the National Health Insurance, a government-run, single-payer plan covering over 99% of the population in Taiwan [21].

Transthoracic echocardiograms

In patients with multiple exams, we used the earliest qualifying TTE as baseline for analysis (**Supplemental Figure 1**). Trained sonographers performed the TTEs using commercially available equipment. Chamber quantification, including left ventricular ejection fraction (LVEF), left atrial (LA) dimension, LV end-diastolic dimension (LVEDD), and LV end-systolic dimension (LVESD), was done based on guideline recommendations[22]. The severity of MR and TR was quantified comprehensively using semi-quantitative and quantitative methods[23]. To assess MR/TR regression, we reviewed all available TTEs. In patients receiving surgery or transcatheter intervention on mitral or tricuspid valve, the pre-surgical TTEs were used as the last TTE. To ensure that the severity of MR and TR was correctly graded, 20 random cases were selected for re-evaluation. The intraclass correlation coefficient(ICC) was calculated, which was 0.85 for both MR and TR. In cases of conflicting severity interpretations, two experienced imagers (LTY, CCH) discussed to reach a final decision.

Statistical Analysis

Continuous variables, expressed as mean (standard deviation [SD]) or median (interquartile range [IQR]) according to data distribution, were compared using Student's t tests. Categorical data, presented as count and percentages, were compared using chi-squared tests and/or Fisher's exact test. The primary endpoint of MR or TR regression was analyzed using the Cox-proportional hazard model, where variables with clinical relevance plus univariate $P < 0.05$ were chosen for multivariable analyses. PCI was treated as a time-dependent variable in the multivariable model. Adjusted cumulative incidence for MR/TR regression and survival were presented using the Kaplan-Meier curves. All statistical analyses were performed using commercially available software (JMP 17 and SAS 9.4, SAS Institute Inc., Cary, North Carolina, R version 4.1.2, R foundation, Vienna, Austria). A two-sided P <0.05 was considered statistically significant.

Results

Baseline characteristics between MR regressors and non-regressors

The final MR-cohort consisted of 264 patients with moderate or greater isolated MR(**Table 1)**. At a median follow-up of 5.0 (IQR: 2.3-7.3) years, there were 97 regressors and 167 non-regressors. As compared with non-regressors, regressors were younger, more likely to participate in the telehealth program, had smaller LA dimension, and less severe baseline MR (all $P \leq 0.0048$); both groups had similar mechanisms of MR and medications used (P≥0.06). At last TTE, as expected, regressors had smaller LA/LV dimensions, less severe TR, and better LVEF (all P≤0.005; **Table 1, Figure 1**). At a median of 6.8 (IQR: 2.3-10.2) years, 62 patients underwent PCI; regressors had 1.69-fold likelihood of having PCI (age- and sex-adjusted hazard ratio [HR], 1.69; 95% confidence interval [CI], 1.02-2.80, P=0.04) as compared with non-regressors.

Table 1. Baseline characteristics of mitral regurgitation regressors vs. non-regressors and telehealth vs. non-telehealth groups (N=264)

	Regressors (N=97)	**Non-regressors (N=167)**	***P***	**Telehealth (N=74)**	**Non-telehealth (N=190)**	***P***
Age, year	64±14	69±13	*.002*	64±14	68±13	*.031*
Male	41(42)	82(49)	.28	41(55)	100(53)	.68
SBP, mmHg	130±23	133±25	.22	128±23	133±25	.13
DBP, mmHg	76±14	76±16	.97	76±14	189±16	.85
Telehealth	39(40)	35(20)	*.0009*	—	—	—
AFib at TTE	18(19)	46(28)	.09	16(6)	58(21)	.53
CCI	1.26±1.44	1.20±1.44	.72	1.22±1.17	1.22±1.53	.98
Hypertension	30(31)	56(34)	.66	26(35)	60(32)	.58
Diabetes mellitus	25(25)	49(29)	.53	19(26)	55(29)	.59
MI	9(9)	17(10)	.81	9(12)	17(9)	.43
Heart failure	31(31)	50(29)	.73	29(39)	52(27)	.06
Malignancy	6(6)	9(5)	.78	5(7)	10(5)	.64
Statin	32(33)	51(31)	.67	29(39)	54(28)	.09
Antiplatelet	63(65)	94(56)	.16	49(66)	108(57)	.16
Anticoagulant	35(36)	42(25)	.06	31(42)	46(24)	*.005*
ACEi and ARB	65(67)	111(66)	.92	47(64)	112(59)	.49
Beta blocker	68(70)	105(63)	.23	59(80)	115(60)	*.0018*
CCB	37(38)	62(37)	.86	24(32)	75(40)	.28
Diuretics	59(61)	117(70)	.13	52(70)	124(65)	.43
Baseline echocardiographic parameters						
LVEF, %	53±18	55±16	.50	50±1	56±16	*.015*
LA dimension, cm	4.3±0.7	4.6±0.7	*.0002*	4.3±0.7	4.6±0.7	*.002*
LVEDD, mm	51±10	54±9	.08	53±9	53±9	.86
LVESD, mm	37±12	38±11	.62	40±13	37±11	.14
Mechanisms of MR[a]			.09			.05
FMR	85(89)	134(81)		66(90)	153(81)	
Primary MR	11(11)	32(19)		7(10)	36(19)	
Baseline MR			*.0048*			*.0009*
Moderate	84(86)	116(69)		67(91)	133(70)	
Moderate-severe	12(12)	45(26)		7(9)	50(26)	
Severe	1(1)	6(3)		0(0)	7(4)	
Baseline TR			.09			.89
None	1(1)	0(0)		0(0)	1(<1)	
Trivial	1(1)	1(<1)		1(<1)	1(1)	
Mild	39(40)	50(30)		28(38)	61(32)	
Mild-moderate	14(14)	26(16)		12(16)	28(15)	
Moderate	37(38)	68(41)		27(36)	78(41)	
Moderate-severe	5(5)	17(10)		5(7)	17(9)	
Severe	0(0)	5(3)		1(<1)	4(2)	
Echocardiographic parameters at last TTE						

LVEF, %	60±13	55±18	*.005*	54±17	57±16	.19
LA dimension, mm	4.1±0.7	4.9±0.9	*<.0001*	4.3±0.8	4.7±1.0	*.003*
LVEDD, mm	49±8	54±10	*<.0001*	53±10	52±9	.52
LVESD, mm	34±9	39±12	*.0002*	38±12	36±11	.24
TR≥ moderate	19(20)	108(65)	*<.0001*	26(35)	101(53)	*.008*
PCI after baseline	29(30)	33(20)	.06	20(27)	42(22)	.40

MR regressors: patients with MR regression to less than moderate severity in the last TTE. Non-regressors: patients with MR severity equal to or more than moderate in the last TTE. AFib, Atrial fibrillation; TTE, transthoracic echocardiography; ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCI, Charlson comorbidity index; CCB, calcium channel blocker; DBP, diastolic blood pressure; FMR, functional mitral regurgitation; LA, left atrial; LVEF, left ventricular ejection fraction; LVEDD, LV end-diastolic dimension; LVESD, LV end-systolic dimension; MI, myocardial infarction; MR, mitral regurgitation; PCI, percutaneous coronary intervention; SBP, systolic blood pressure; TR, tricuspid regurgitation.

[a]In 2 patients, the MR mechanisms were unknown.

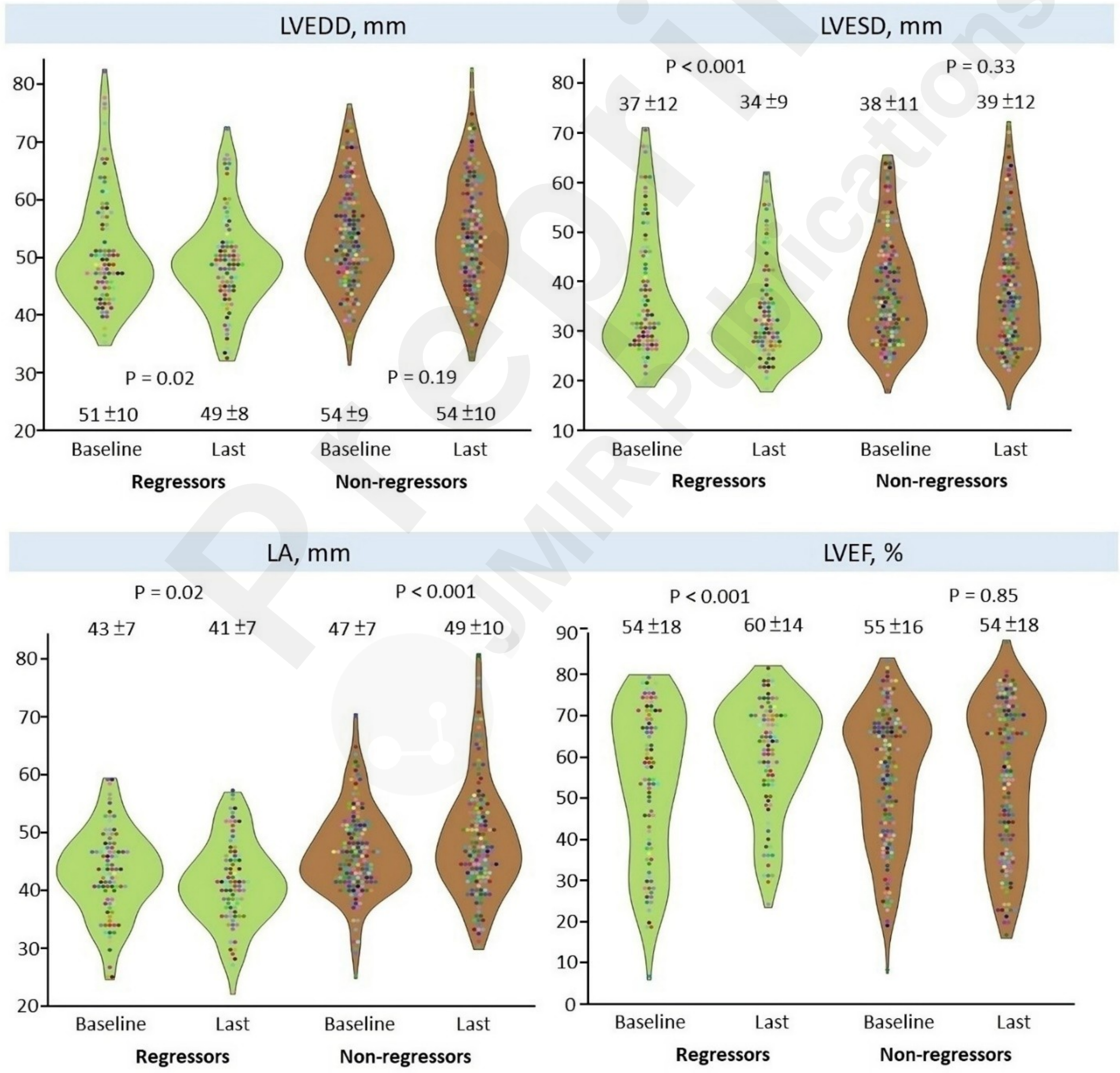

Figure 1. Left heart parameters between regressors and non-regressors. Patients with MR regression to <moderate had smaller LV and LA size as well as improved LVEF compared with non-regressors.

Telehealth versus non-telehealth patients in the MR cohort

Compared to the non-telehealth group, telehealth patients were younger, had smaller LA dimensions, fewer cases of ≥moderate-severe MR, and lower baseline LVEF; this was reflected in their higher likelihood of being treated with anticoagulants and beta blockers(all *P*≤0.043)(**Table 1**). At last TTE, telehealth participants had smaller LA dimensions (*P*=0.003), less ≥moderate TR (*P*=0.008) yet similar LVEF and LV dimensions (all *P*≥0.19) (**Table 1).** The time elapsed from baseline TTE to last TTE in the telehealth and non-telehealth group (4.6±2.8 years versus 5.3±3.1 years; *P*=0.09) was similar. At a median follow-up of 6.8 (IQR: 2.3-10.2) years, telehealth group had 1.79-fold likelihood of having PCI (age- and sex-adjusted hazard ratio, 1.79; 95% CI, 1.28-2.50, *P*=0.0007) as compared with non-telehealth participants.

Primary endpoint: MR regression to <moderate degree

In univariable analysis, smaller baseline LA dimensions, lower LVEF, less severe baseline MR/TR, performance of PCI, prescription of beta-blockers, and the telehealth service were associated with MR regression(all *P*≤0.05; **Table 2**). Comparison of patients with or without beta blocker use was shown in **Supplemental Table 2**. Those who used beta-blockers were older, had higher systolic BP, more prevalent hypertension, and greater use of concomitant renin-angiotensin system inhibitors and antiplatelet agents; they also had lower LVEF and larger LA size compared to non-users (all P≤0.047). Multivariable analysis adjusted for MR mechanisms and abovementioned parameters, including time-dependent PCI, revealed that telehealth group was the only determinant for MR regression(*P*=0.001; **Table 2**). Adjusted Kaplan-Meier curves revealed that the telehealth group had higher 8-year incidence of MR-regression to <moderate (67±7% vs 37±10%; *P*<0.001; **Figure 2).** The incidence of MR-regression to <moderate was 11.4 (95% CI, 8.1-15.6) per 100-person years in the telehealth group and 5.8(95% CI, 4.4-7.5) per 100-person years in non-telehealth group. In a

subgroup analysis including only those with baseline moderate MR, the telehealth group remained independently associated with MR regression to <moderate (HR 2.56, 95% CI 1.56–4.21; *P*<0.001) (N=200; **Supplemental Table 3**).

Table 2. Univariable and multivariable determinants for mitral regurgitation regression to less than moderate (N=97).

	Univariable analysis		**Multivariable analysis**	
	HR (95% CI)	*P*	HR (95% CI)	*P*
Telehealth vs. non-telehealth	2.67 (1.72-4.12)	*<.0001*	2.20(1.35-3.58)	*.001*
Age, year	0.99 (0.98-1.00)	.46	0.99(0.98-1.01)	.94
Male	1.14 (0.76-1.71)	.51	1.08(0.69-1.68)	.72
SBP, mmHg	1.00(0.99-1.01)	.88		
DBP, mmHg	0.99(0.98-1.01)	.97		
CCI	1.07 (0.93-1.21)	.30		
AFib at TTE	0.71(0.42-1.19)	.18		
ACEi and ARB	0.93 (0.60-1.42)	.74		
Diuretics	1.18 (0.78-1.78)	.41		
Statin	1.19 (0.77-1.82)	.42		
Antiplatelets	1.14 (0.75-1.74)	.51		
Beta blocker	1.53 (0.99-2.37)	*.049*	1.32(0.81-2.15)	.26
CCB	1.11 (0.73-1.68)	.61		
Baseline LA dimension, cm	0.73 (0.55-0.97)	*.03*	0.78(0.57-1.07)	.13
Baseline LVEF, %	0.98 (0.97-0.99)	*.04*	0.99(0.97-1.00)	.25
Baseline LVEDD, mm	0.98 (0.96-1.01)	.36		
Baseline LVESD, mm	1.00 (0.98-1.02)	.47		
TRPG	1.00 (0.98-1.02)	.53		
Baseline MR severity (Ref: moderate)				
Moderate-severe	0.51(0.27-0.93)	*.029*	0.63(0.31-1.25)	.18
Severe	0.24(0.03-1.84)	.17	0.40(0.05-3.25)	.39
Primary MR vs FMR	0.78(0.41-1.47)	.42	1.34(0.67-2.68)	.40
Baseline TR< moderate	1.50(0.99-2.27)	.05	1.28(0.83-2.00)	.25
Time-dependent PCI	1.75(1.13-2.71)	*.012*	1.23(0.76-1.99)	.38

TRPG: tricuspid regurgitation peak gradient. See Table 1 for other abbreviations.

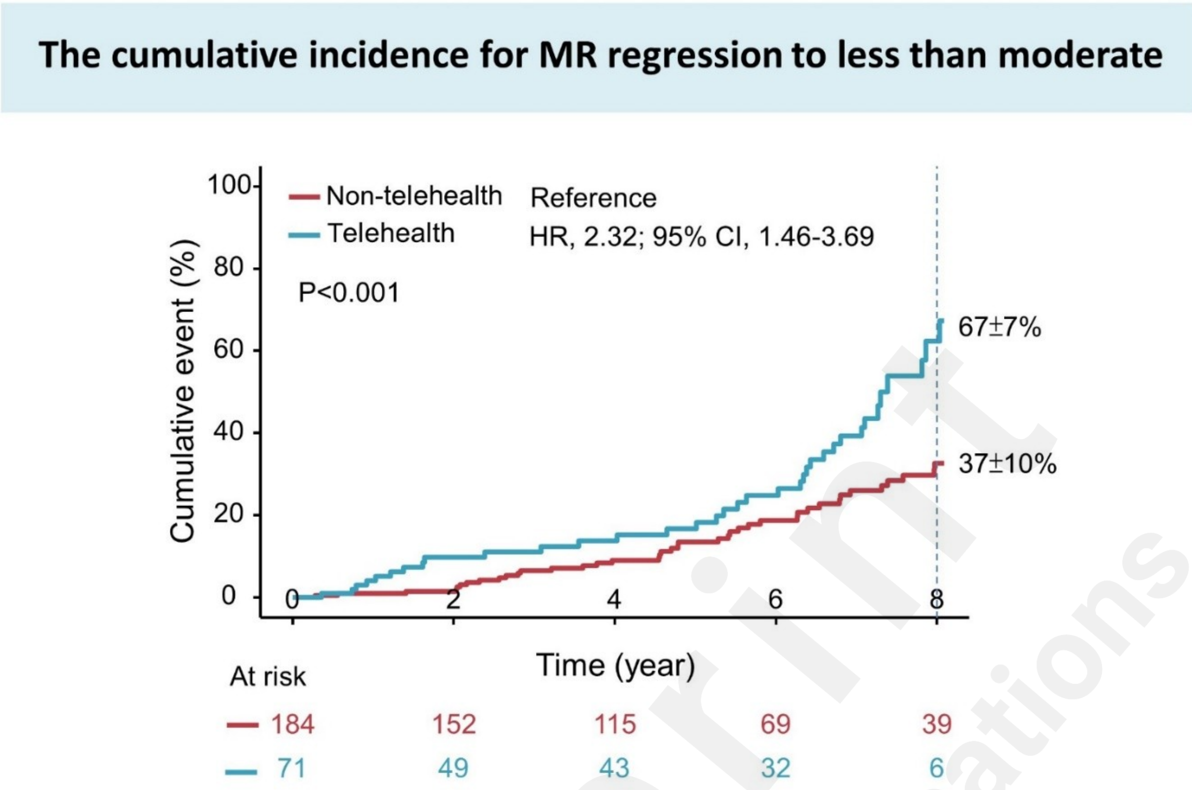

Figure 2. The cumulative incidence for MR regression and survival. Kaplan-Meier curves adjusted for age, sex, LVEF, LA size, and baseline MR/TR severity revealed that the telehealth group had higher 8-year incidence of MR-regression to <moderate.

Secondary endpoint: determinants for ACD

As of Dec. 31st, 2022, the follow-up rate for ACD was 100%. Over a median follow-up of 8.5 years (IQR: 4.8-10.7), 134 (51%) deaths occurred, with a 10-year survival rate of 51±3%. Univariable determinants for ACD were older age, lower diastolic BP, use of diuretics and calcium channel blocker(CCB), higher CCI, larger baseline LA size, reduced LVEF, performance of PCI, and regression of MR to <moderate (all $P \leq 0.034$; **Table 3**). Age-adjusted multivariable determinants for ACD-free survival were MR-regressors (HR 0.61, 95% CI: 0.41-0.92, P=0.02), better LVEF (HR per 1%, 0.97, 95% CI: 0.96-0.98, P< 0.001), and performance of PCI (HR 0.82, 95% CI: 0.77-0.88, P<0.001) (**Table 3**). Adjusted Kaplan-Meier curves showed that regressors had better 10-year survival as compared with non-regressors(P=0.047) (**Figure 3**). After adjusting for the same covariates, telehealth group tended to have better 10-year survival than non-telehealth group (P=0.09) (**Figure 4**).

Table 3. Univariable and multivariable determinants for all-cause death(N=134) in the mitral regurgitation cohort

	Univariable analysis		Multivariable analysis	
	HR (95% CI)	*P*	HR (95% CI)	*P*
Regressors vs non-regressors	0.60(0.41-0.88)	*.007*	0.61(0.41-0.92)	*.02*
Age, year	1.05(1.03-1.06)	*<.0001*	1.05(1.03-1.07)	*<.001*
Male	0.96(0.68-1.35)	.82	0.86(0.60-1.24)	.43
SBP, mmHg	1.00(0.99-1.01)	.19		
DBP, mmHg	0.98(0.97-0.99)	*.017*	0.99(0.98-1.01)	.80
Telehealth vs. non-telehealth	0.73(0.48-1.11)	.14		
CCI	1.18(1.06-1.30)	*.002*	1.11(0.99-1.25)	.06
AFib at TTE	1.04(0.70-1.54)	.84		
ACEi and ARB	1.21(0.83-1.76)	.29		
Diuretics	1.78(1.20-2.63)	*.002*	0.99(0.64-1.52)	.96
Statin	0.98(0.68-1.42)	.94		
Antiplatelets	1.26(0.88-1.79)	.18		
Beta blocker	1.18(0.82-1.70)	.35		
CCB	1.44(1.03-2.03)	*.034*	1.03(0.71-1.50)	.85
Baseline LA dimension, cm	1.26(1.02-1.57)	*.032*	1.18(0.91-1.54)	.20
Baseline LVEF, %	0.98(0.97-0.99)	*.017*	0.97(0.96-0.98)	*.0003*
Baseline LVEDD, mm	1.01(0.99-1.03)	.22		
Baseline LVESD, mm	1.01(0.99-1.02)	.06		
TRPG	1.01(0.99-1.02)	.05		
Baseline MR severity (Ref: moderate)				
Moderate-severe	0.84(0.55-1.28)	.42	0.89(0.55-1.45)	.66
Severe	0.88(0.32-2.41)	.81	1.15(0.35-3.73)	.81
Primary MR vs FMR	0.72(0.44-1.17)	.17		
Baseline TR < moderate	0.98(0.70-1.38)	.93	1.24(0.86-1.80)	.23
Time-dependent PCI	0.81(0.77-0.86)	*<.001*	0.82(0.77-0.88)	*<.001*

See Table 1 for abbreviations.

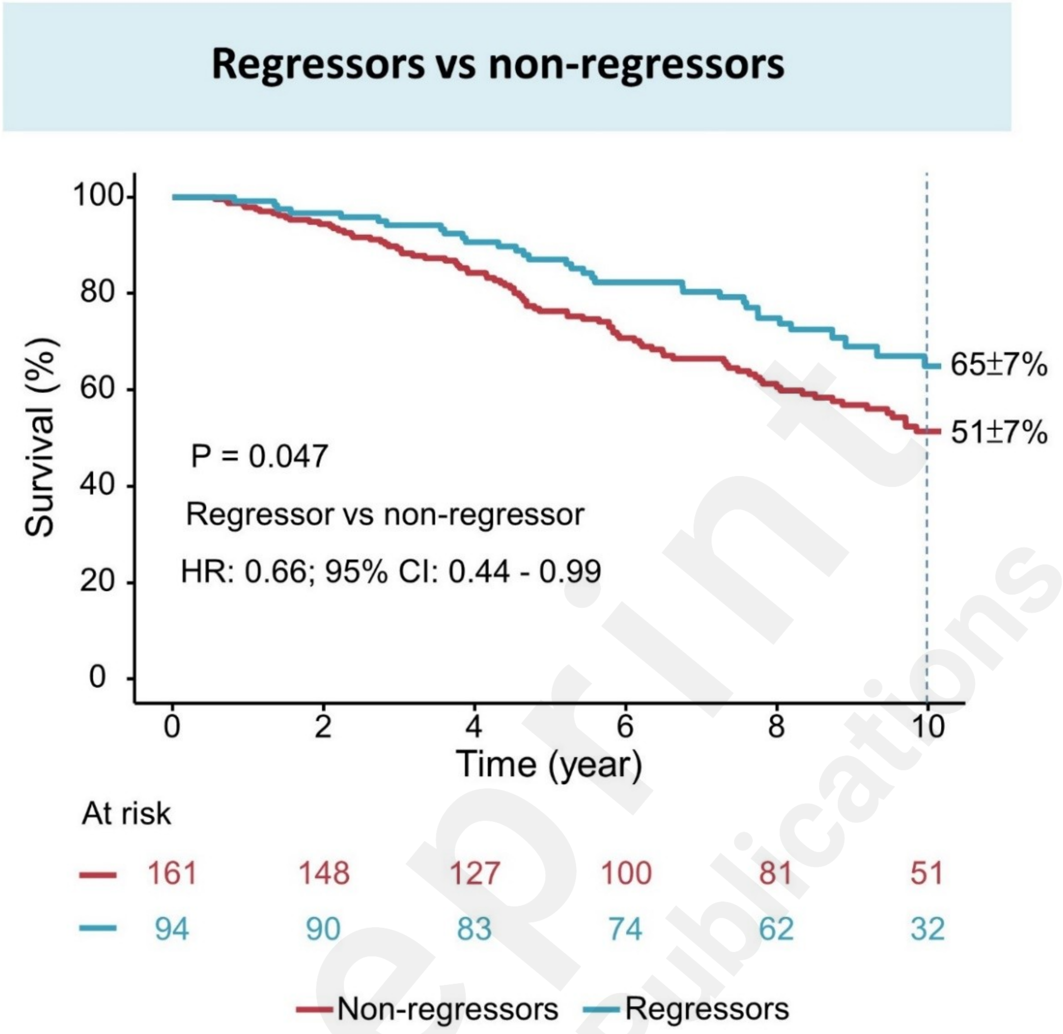

Figure 3. The survival curves between regressors and non-regressors. Kaplan-Meier curves adjusted for the same covariates revealed that regressors had better 10-year survival as compared with non-regressors.

Baseline characteristics between TR regressors and non-regressors

In the TR cohort, which included 245 patients with ≥moderate TR at baseline, there were 87 regressors and 158 non-regressors, with a median follow-up of 4.99 (IQR: 2.57–7.25) years (**Supplemental Table 4**). Compared to non-regressors, regressors were younger, had smaller baseline LA dimensions, less severe TR, and were more likely to receive telehealth services (all $P \leq 0.05$). At last TTE, regressors had higher LVEF, smaller LA dimension, LVESD, and less severe MR(all $P \leq 0.05$).

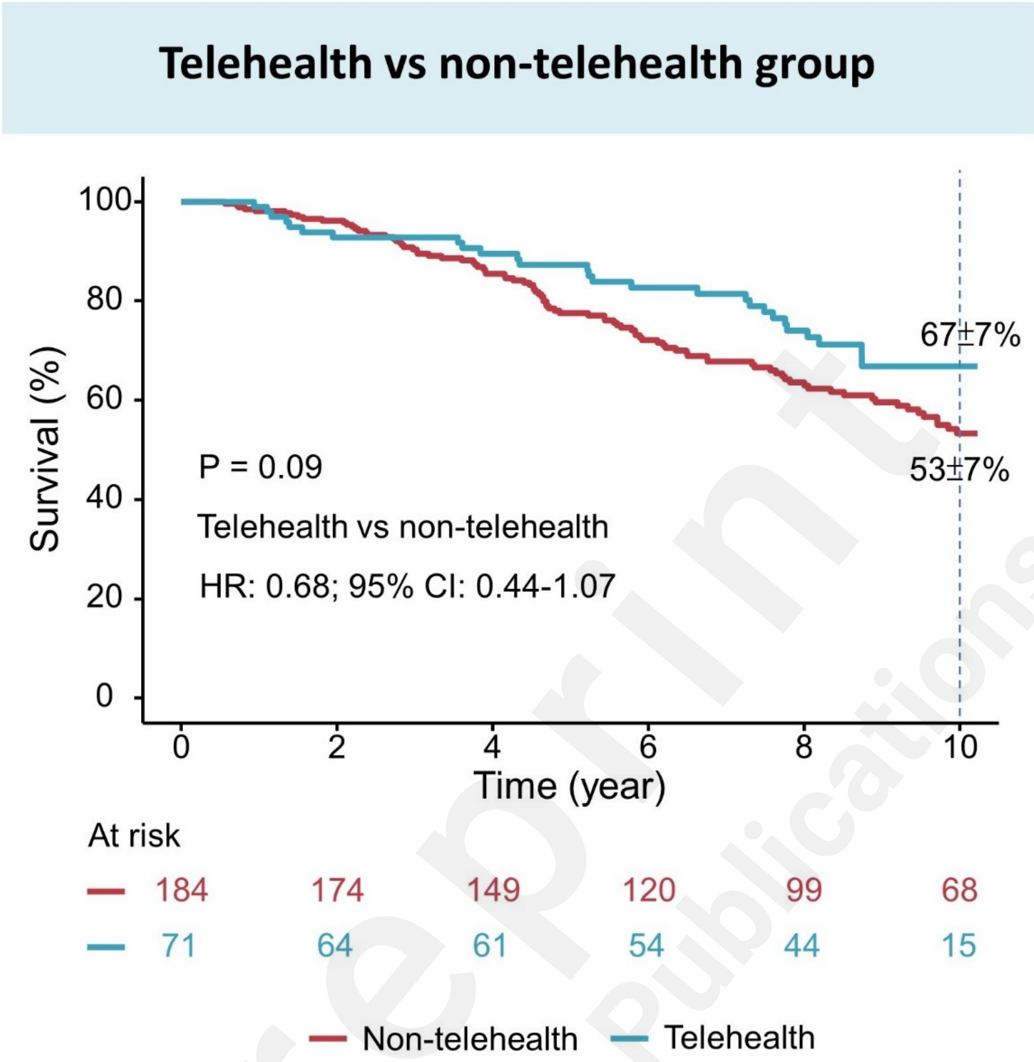

Figure 4. The survival curves between telehealth and non-telehealth group. telehealth group tended to have better 10-year survival than the non-telehealth group via adjusted Kaplan-Meier curves.

Baseline characteristics between telehealth and non-telehealth patients in the TR cohort

Compared to the non-telehealth group (**Supplemental Table 4**), telehealth patients were younger, had lower LVEF and smaller LA dimensions (all $P \leq 0.027$), with similar baseline MR/TR severity. At the final TTE, the telehealth group had a smaller LA dimension ($P<0.0003$).

Determinants of TR regression to <moderate degree

Univariable predictors of TR regression were prescription of beta-blocker, smaller LA dimension, less severe baseline TR, performance of PCI and the telehealth group (all $P \leq 0.05$**; Supplemental Table 5**). In multivariable analysis, beta-blocker use and more severe baseline TR were robust markers of TR-regression(all *P*≤0.048); telehealth participation was not a multivariable determinant(*P*=0.33) (**Supplemental Table 5**).

Determinants of ACD in TR cohort

At a median follow-up of 8.6 (IQR: 5.2-11.0) years, 113(46%) ACD occurred, with a 10-year survival rate of 54±3%. Univariable determinants for ACD in TR cohort was shown in **Supplemental Table 6**; the telehealth group was associated with better survival (HR, 0.5; *P*=0.005). However, in multivariable analysis, only younger age and better LVEF were associated with ACD (**Supplemental Table 6**; *P*≤0.004).

Discussion

To the best of our knowledge, this is the first study to investigate the impact of telemedicine on the regression of MR or TR. Our principal findings were: (1) MR- and TR-regressors were younger, more likely to be in the telehealth program, use more beta blockers, had smaller LA, reflected by less severe baseline MR or TR, and as expected, had better chamber reverse remodeling at last TTE. Interestingly, MR-regressors had less severe TR at last TTE; likewise, TR-regressors also had less severe MR at last TTE; (2) enrollment in the telehealth program was a robust indicator for MR regression in the entire cohort and in patients with baseline moderate MR; however, its effect on TR regression was less pronounced; (3) the incidence of MR-regression to <moderate (MR-regressors) was 11.4 (95% CI, 8.1-15.6) per 100-person years in the telehealth group; (4) besides younger age, better LVEF, and the performance of PCI, MR-regressors independently linked to better survival; (5) TR regression was associated with the prescription of beta-blockers and with less severe TR at baseline; and (6) in the TR cohort, independent determinants of ACD included older age and reduced LVEF; TR regression was not linked to ACD.

Benefits of telehealth and the unmet need

Telehealth has emerged as a promising healthcare model with the potential to improve outcomes over a variety of disciplines, including chronic CV diseases. It has been shown to reduce HF hospitalization and mortality[14-16], and when operated by a nurse practitioner, it was non-inferior to cardiologist-led standard care in patients with AMI[24]. Indeed, our study found that, although patients in both the MR and TR cohorts showed overall reduced survival (10-year survival rate of 51-54%)—a trend previously noted in patients with functional MR[25], functional TR[26], and heart failure with preserved LVEF[27]—telehealth intervention emerged as the sole determinant of MR regression; notably, MR regression served as a strong marker for improved survival (**Table 2, 3**). Additionally, telehealth has demonstrated better cost-effectiveness when considering the reduction in subsequent hospitalizations[20]. However, data on the impact of telemedicine on VHD remain scarce, with most studies focusing on patients undergoing transcatheter aortic valve replacement for aortic stenosis[17] [28], and only one study reporting associations with MR and TR progression[18].

Factors associated with regression of MR or TR

In our MR-cohort (**Table 1**), we found that univariable determinants of MR regression included telehealth participation, beta blocker use, lower LVEF, smaller LA dimension, less severe baseline MR/TR, as well as the performance of PCI; MR-regressors also had improved LVEF and further reductions in LV and LA sizes. These findings were supported by several studies. Campwala et al. found that in patients undergoing coronary artery bypass grafting, post-surgical MR-regression was associated with reductions in LV dimensions, improved LVEF, and use of beta-blockers [29]. Likewise, Bartko et al. found that larger LA size and concomitant TR were associated with MR progression[30]. These observations are unsurprising, as coronary revascularization is associated with reverse cardiac remodeling, which improves MR through enhanced coaptation of the mitral leaflets[10]. On the other hand, the use of beta-blockers, incorporated as part of the guideline-directed medical therapy in HF with reduced LVEF, was associated with MR regression, possibly due to myocardial protection and promotion of reverse cardiac remodeling[29]. In the final multivariable analysis, however, only "telecare" was linked to MR-regression (**Table 2**). Potential mechanisms for this association will be discussed later.

Univariable determinants of TR regression in this study included telehealth participation, beta-blocker use, smaller LA dimensions, less severe baseline TR, and performance of PCI. Given the similarities between these factors and those observed in MR regression, we hypothesized that LV and LA reverse remodeling likely plays a pivotal role in TR regression as well. The persistent significance of beta-blocker use in the multivariable analysis suggests that left heart function may play an even more crucial role in influencing TR regression than previously anticipated.

The role of telehealth in MR/TR regression

Our study did not demonstrate a direct causal effect of telehealth on MR and TR regression in patients with moderate or greater MR and TR. However, our analysis did reveal an independent association between telehealth and MR regression. Our comparison of MR and TR regressors and non-regressors revealed similar medication prescriptions, yet regressors were more likely to have received telecare interventions at baseline. We therefore believe that telehealth interventions may play a supportive "booster" or "catalyst" role for established treatments, potentially by improving access to care, optimizing risk-factor management, enhancing medication adherence[31-33],[34], facilitating timely dose titration of guideline-directed medical therapy for HF, providing early warning of abnormal events, or improving patient awareness through frequent communication with experienced nurse practitioners (**Supplemental Table 1**)[14,33]. In other words, telehealth programs may offer patients several direct and indirect benefits related to existing medical care, thereby facilitating reverse cardiac remodeling[35] and MR regression. Combined with our previous study, which found that telehealth could potentially slow the progression of MR and TR, this suggests that telehealth intervention plays a significant yet not fully understood role in MR and TR regression (**Figure 5**).

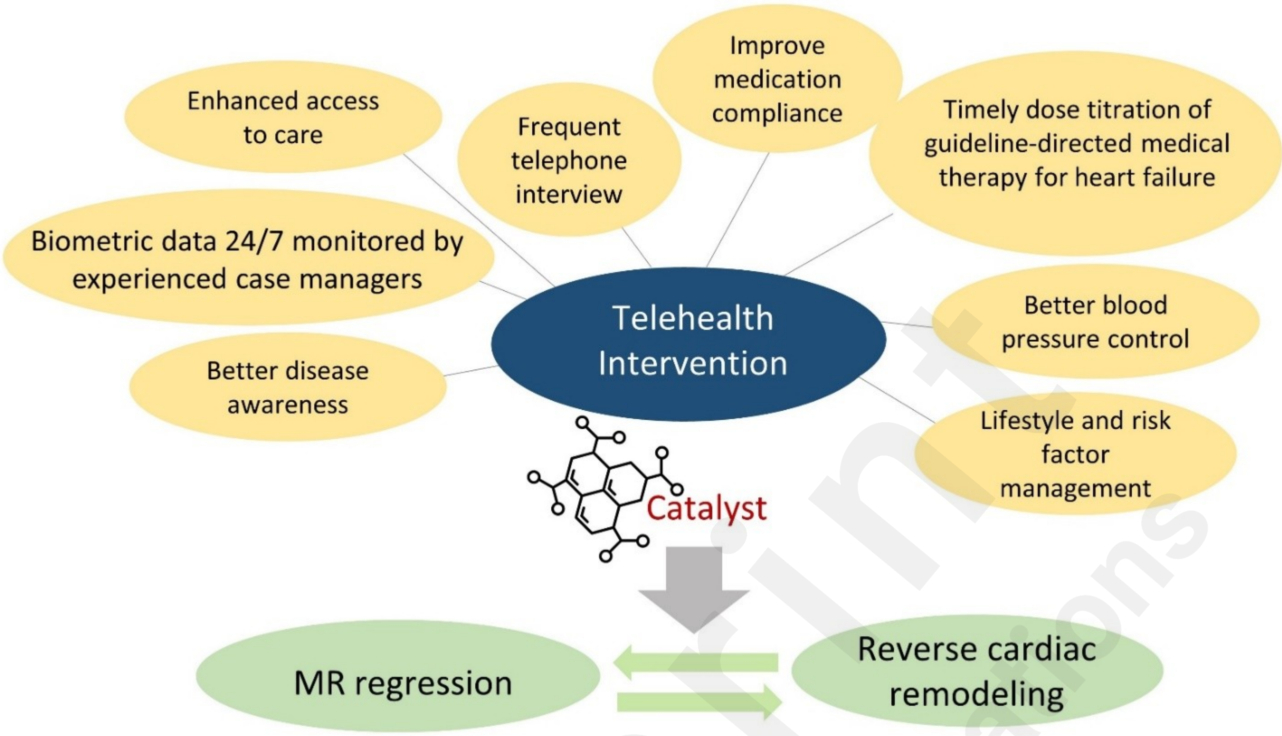

Figure 5. Hypothesis of telehealth intervention. Potential mechanisms by which telehealth affected reverse cardiac remodeling and MR regression.

The telehealth services offered by our hospital included a range of functions encompassing biometric monitoring, routine care, and timely interventions for abnormal events. Due to the lack of data in our study, we were unable to determine which facets of our telehealth services contributed most to MR and TR regression, or whether the effect was due to a combination of all services. Further studies are needed to explore this topic.

Clinical implications

Our investigation distinguishes itself from these contemporary studies into telehealth interventions by being, to our knowledge, the first to examine the impact of telemedicine on MR or TR regression. The latest guideline for the management of lower extremity peripheral artery disease(PAD)[36] recommends the use of telemedicine in patient care, drawing from a recent study conducted by us, which found that PAD patients in our telehealth program exhibited lower risk of ischemic stroke compared to usual care[19]. Guidelines for the management of valvular and structural heart diseases developed during the COVID-19 pandemic also recommended the use of telemedicine to monitor patients with severe MR[37]. Therefore, it appears that telehealth services are gaining traction as supplementary treatment for CV diseases, owing to their beneficial effects on patient outcomes. Based on the results of our study, we would recommend inclusion of telemedicine in future guidelines for management of VHD patients, particularly regarding patients with significant MR or TR.

Limitations

This research has several limitations. As a retrospective study from a tertiary referral center, it inherently carries the risk of selection bias. Additionally, quantitative measurements for assessing MR and TR severity were incomplete. Limited access to data on dosage adjustments and patient medication adherence also posed constraints. Regarding cardiac reverse remodeling parameters, data on LV volume and LV global longitudinal strain were lacking. Furthermore, we acknowledge the potential for selection bias among telehealth patients due to disparities in digital literacy and access, which are complex and multifaceted.

Conclusions

This study is the first to report associations between telehealth services and MR or TR regression. Patients in the telehealth group were 2.2 times more likely to experience MR regression. Additionally, MR regressors demonstrated better survival and reverse cardiac remodeling compared to non-regressors. These findings support integrating telemedicine into the management of moderate or greater MR, which may have important implications for future guidelines.

Acknowledgements

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Conflicts of interest

None declared.

Abbreviations

VHD: valvular heart disease

MR: mitral regurgitation

HF: heart failure

TR: tricuspid regurgitation

ACD: all-cause death

CV: cardiovascular

NTUH: National Taiwan University Hospital

TTE: transthoracic echocardiogram

AMI: acute myocardial infarction

CAD: coronary artery disease

BP: blood pressure

PCI: percutaneous coronary interventions

CCI: Charlson Comorbidity Index

LVEF: left ventricular ejection fraction

LA: left atrial

LVEDD: left ventricular end-diastolic dimension

LVESD: left ventricular end-systolic dimension

ICC: intraclass correlation coefficient

SD: standard deviation

IQR: interquartile range

HR: hazard ratio

CI: confidence interval

PAD: peripheral artery disease

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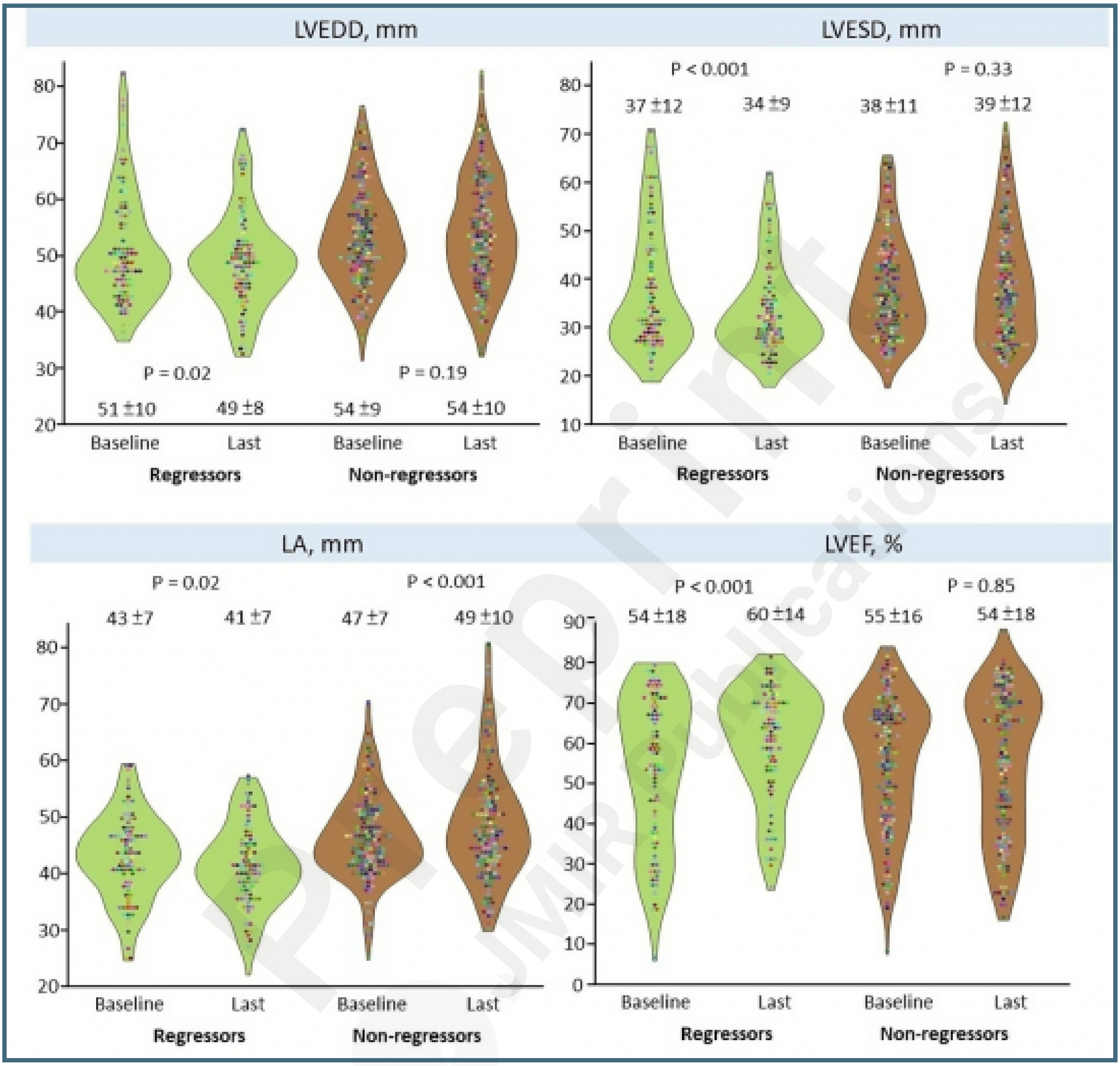
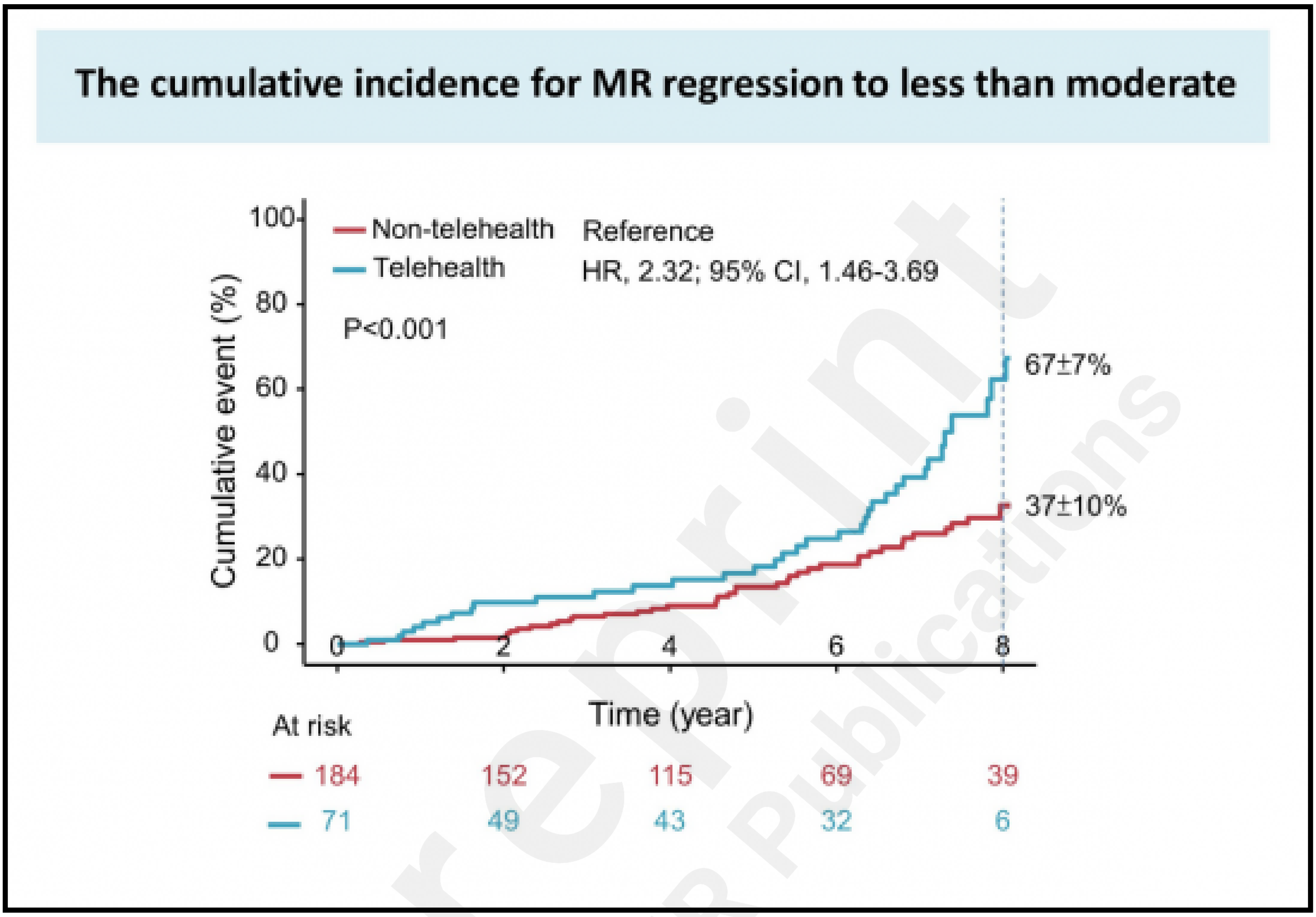
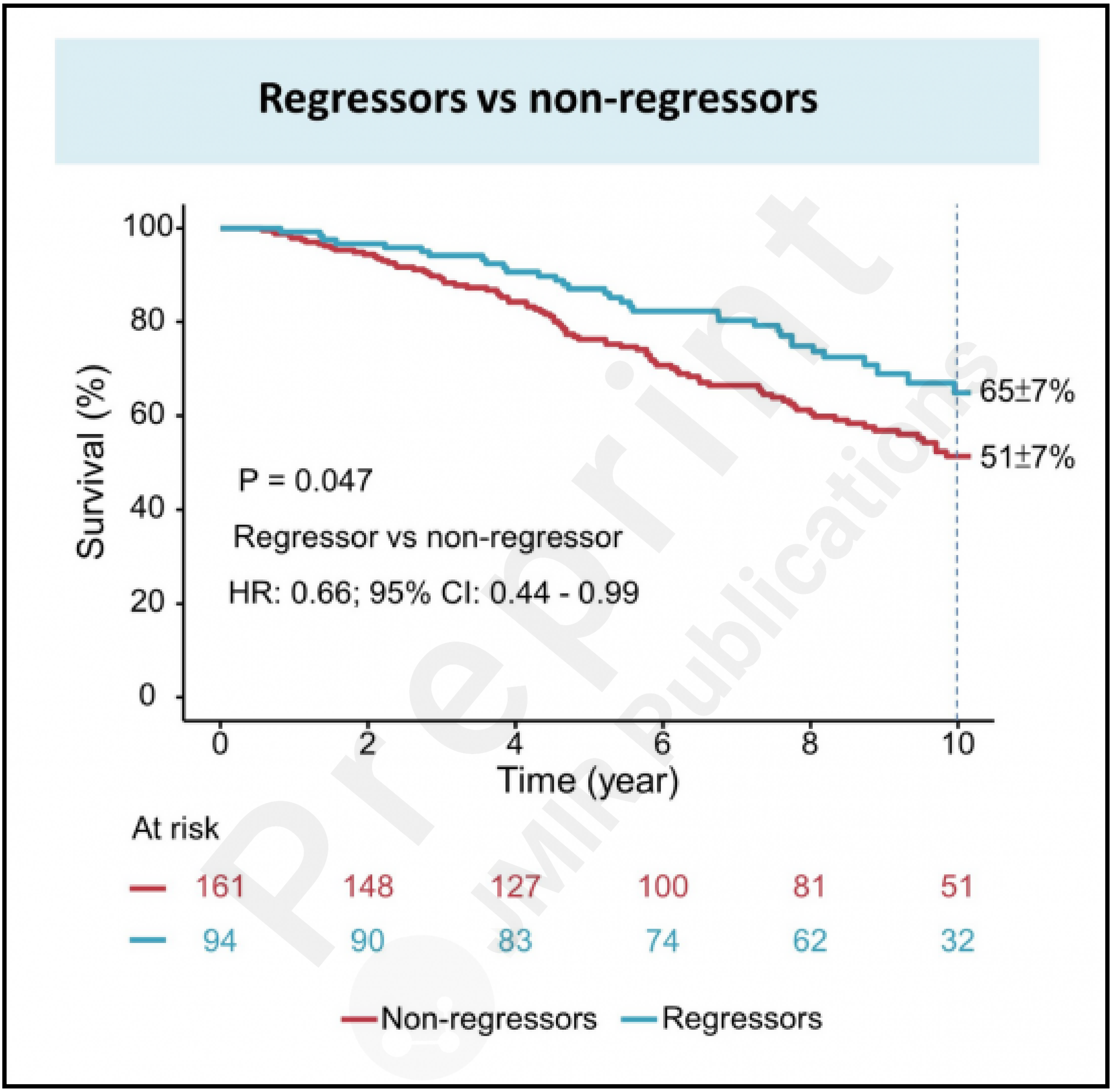
Supplementary Files

Figures

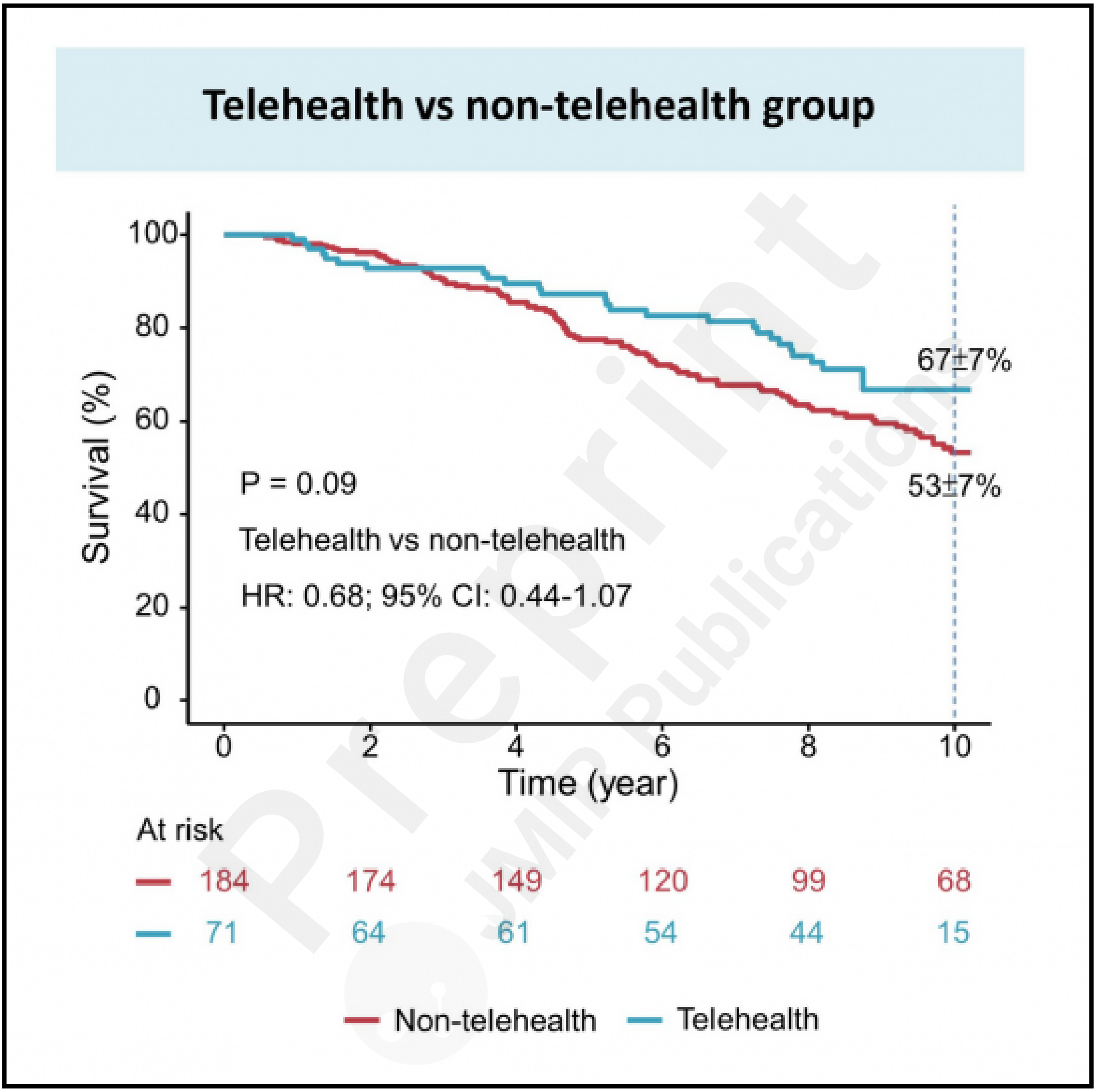

LVEDD, mm
P = 0.02
P = 0.19
51 ±10
49 ±8
54 ±9
54 ±10
Baseline
Last
Baseline
Last
Regressors
Non-regressors
LVESD, mm
P < 0.001
P = 0.33
37 ±12
34 ±9
38 ±11
39 ±12
Baseline
Last
Baseline
Last
Regressors
Non-regressors
LA, mm
P = 0.02
P < 0.001
43 ±7
41 ±7
47 ±7
49 ±10
Baseline
Last
Baseline
Last
Regressors
Non-regressors
LVEF, %
P < 0.001
P = 0.85
54 ±18
60 ±14
55 ±16
54 ±18
Baseline
Last
Baseline
Last
Regressors
Non-regressors


The cumulative incidence for MR regression to less than moderate
Non-telehealth
Telehealth
Reference
HR, 2.32; 95% CI, 1.46-3.69
P<0.001
67±7%
37±10%
Cumulative event (%)
100
80
60
40
20
0
0
2
4
6
8
Time (year)
At risk
184 152 115 69 39
71 49 43 32 6

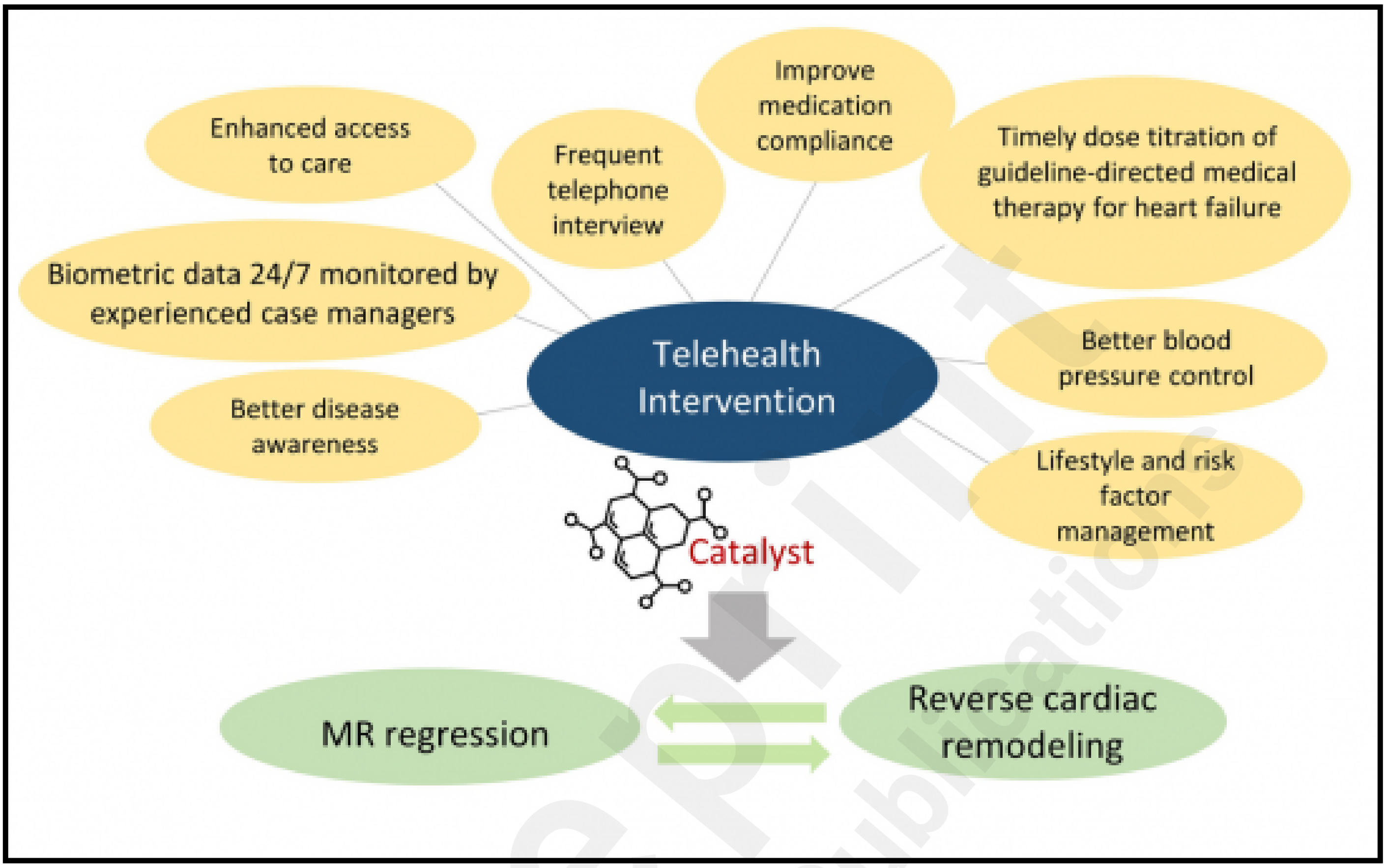
The survival curves between regressors and non-regressors. Kaplan-Meier curves adjusted for the same covariates revealed that regressors had better 10-year survival as compared with non-regressors.



The survival curves between telehealth and non-telehealth group. telehealth group tended to have better 10-year survival than the non-telehealth group via adjusted Kaplan-Meier curves.



Hypothesis of telehealth intervention. Potential mechanisms by which telehealth affected reverse cardiac remodeling and MR regression.



Multimedia Appendixes

Flowchart, nurse level classification, and additional tables of MR and TR cohorts.

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