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# Change in mitral regurgitation severity impacts survival after transcatheter aortic valve replacement☆

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ABSTRACT

*Background:* The impact of a change in mitral regurgitation (MR) following TAVR is unknown. We studied the impact of baseline MR and early post-procedural change in MR on survival following TAVR.
*Methods:* The SWEDEHEART registry included all TAVRs performed in Sweden. Patients were dichotomized into no/mild and moderate/severe MR groups. Vital status, echocardiographic data at baseline and within 7 days after TAVR were analyzed.
*Results:* 1712 patients were included. 1404 (82%) had no/mild MR and 308 (18%) had moderate/severe MR. Baseline moderate/severe MR conferred a higher mortality rate at 5-year follow-up (adjusted HR 1.29, CI 1.01–1.65, p = 0.04). Using persistent ≤mild MR as the reference, when moderate/severe MR persisted or if MR worsened from ≤mild at baseline to moderate/severe after TAVR, higher 5-year mortality rates were seen (adjusted HR 1.66, CI 1.17–2.34, p = 0.04; adjusted HR 1.97, CI 1.29–3.00, p = 0.002, respectively). If baseline moderate/severe MR improved to ≤mild after TAVR no excess mortality was seen (HR 1.09, CI 0.75–1.58, p = 0.67). Paravalvular aortic regurgitation (PVL) was inversely associated with MR improvement after TAVR (OR 0.4, 95%: CI 0.17–0.94; p = 0.034). Atrial fibrillation (OR 2.1, 95% CI: 1.27–3.39, p = 0.004), self-expanding valve (OR 3.8, 95% CI: 2.08–7.14, p < 0.0001), and PVL (4.3, 95% CI 2.32–7.78. p < 0.0001) were associated with MR worsening.
*Conclusions:* Moderate/severe baseline MR in patients undergoing TAVR is associated with a mortality increase during 5 years of follow-up. This risk is offset if MR improves to ≤mild, whereas worsening of MR after TAVR is associated with a 2-fold mortality increase.



## 1. Introduction

Aortic stenosis and mitral regurgitation (MR) are the most common valve diseases in Europe and the United States [1,2]. Approximately a fifth of patients who undergo transcatheter aortic valve replacement (TAVR) to treat aortic stenosis also have concomitant moderate or severe MR [3].

Recent meta-analyses show that baseline MR increases 30-day and 1-year mortality after TAVR [4–6], but less is known about the prognostic impact of baseline MR beyond the first post-procedural year. Furthermore, although residual MR has been shown to confer an increased mortality rate after TAVR [5], the clinical effect of MR reduction or MR worsening is not known. We therefore assessed the long-term impact of pre-TAVR MR, and MR change from baseline to first available post-procedural echocardiogram in TAVR recipients in the Swedish TAVR Registry.

### 2. Methods

Between the 1st of January 2008 and 31st of April 2015, 1739 patients underwent TAVR for treatment of symptomatic severe aortic stenosis at eight Swedish centers. The

☆ All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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balloon-expandable Cribier-Edwards, Edwards SAPIEN, SAPIEN XT or Sapien 3 (Edwards Lifesciences, Irvine, California) was used in 735 cases (43%); the self-expandable Medtronic CoreValve (Medtronic, Minneapolis, Minnesota) in 886 (52%); and the Boston Lotus Valve (Boston Scientific, Marlborough, Massachusetts) was used in 75 cases (4%). Patients were excluded from analysis if data on MR severity were missing at baseline or if a patient had undergone a mitral valve procedure of any kind, leaving a final study population of 1712 patients.

All procedures were performed after patient consent and Heart Team evaluation according to institutional standards of each participating center. The Regional Ethical Review Board in Stockholm approved the registry data for this study, in conformity to the ethical guidelines of the 1975 Declaration of Helsinki.

### 2.1. Data collection and definitions

Demographic and procedural data were entered into an electronic database platform of the SWEDEHEART Registry after each TAVR procedure. Clinical and echocardiography data were prospectively entered into the same database at baseline, hospital discharge, and at follow up visits. Record linkage through the National Civil Registry ensured full data capture for mortality. Baseline transthoracic echocardiography was performed before TAVR, and a pre-discharge echocardiogram was performed within a week of TAVR. MR severity was graded as none/trivial, mild, moderate, or severe according to the European Society of Cardiology/American College of Cardiology/American Heart Association [7,8] recommendations. For clinical purposes, a decrease from moderate/severe to ≤mild MR was considered as improved MR; and an increase from ≤mild to moderate/severe MR was considered as worsened MR. Left ventricular ejection fraction (LVEF) was calculated using the biplane Simpson's method or by visual assessment, and was graded as normal (LVEF > 50%); mildly reduced (LVEF 40–49%); moderately reduced (LVEF 30–39%) or severely reduced (LVEF < 30%). Aortic valve area (AVA) was calculated according to the continuity equation. Pulmonary artery pressure was estimated by Doppler echocardiography and pulmonary hypertension was defined as pulmonary artery systolic pressure (PASP) >60 mm Hg. Recent myocardial infarction was defined according to international guideline definitions [9] within three months of TAVR. Mitral regurgitation mechanism, whether functional or organic, was retrospectively assessed according to American Society of Echocardiography valvular regurgitation guidelines [10].

### 2.2. Statistical analysis

Continuous variables are expressed as mean ± standard deviation or as median and interquartile range, in cases of skewed distributions. Categorical variables are expressed as frequencies and percentages. Inter-group differences for continuous variables between two groups were tested using the Wilcoxon rank sum test and *t*-test, and the Kruskal-Wallis test was used for three groups. In cases in which the samples were paired, the Wilcoxon signed rank or paired *t*-test was used. Categorical variables were compared using the chi-square test. Survival rates at 5 years were estimated and graphed using the Kaplan-Meier method. Cox regression models were used to estimate hazard ratios (HR) and 95% confidence intervals (CI) to compare the patients with moderate or severe MR with those with mild or less MR at baseline, and at 7 days after TAVR, respectively, for all-cause mortality. The following potential confounders were included in the adjusted analyses as they were associated ($p < 0.10$) with moderate/severe MR: age, sex, body mass index, recent myocardial infarction, diabetes, chronic obstructive pulmonary disease, claudication, atrial fibrillation, NYHA class, aortic valve area, LVEF. Hypertension was included as a covariate due to clinical relevance. AVA was used to adjust for aortic stenosis severity at baseline. Survival curves for 5-year all-cause mortality were compared with a log-rank test according to MR severity. Univariate and multivariate logistic regression models including age, sex, atrial fibrillation, valve prosthesis type (balloon or self expanding device), LVEF dichotomized as normal or impaired (<50%), paravalvular aortic leak (PVL) (dichotomized as ≤mild or ≥moderate), and mitral regurgitation mechanism (functional or organic) were used to identify predictors for MR improvement and MR worsening after TAVR, respectively. Analyses were conducted using STATA version 13.1 (StataCorp LP, College Station, Texas) and tested using 2-sided tests at a significance level of 0.05.

## 3. Results

A total of 1712 consecutive patients were included in the analysis. At baseline MR was mild or less in 1404 patients (82%), and moderate or severe in 308 patients (18%). Of those with moderate or severe MR, 148 (48%) had organic MR and 158 (52%) had functional MR, data was missing for two subjects. As shown in Table 1, moderate or severe MR was associated with female sex, older age, lower BMI, lower incidence of recent MI, atrial fibrillation, higher degree of NYHA class, lower LVEF, lower AVA and a higher prevalence of pulmonary artery hypertension.

### 3.1. Procedural outcomes and survival

Access route, prosthesis size and type, and use of general anesthesia were similar regardless of MR severity. Rates of early post-procedural pacemaker implantation and stroke were also similar (Table 1). Mortality from any cause at 30 days was 5.4% in patients with mild or less MR, and 8,5% in patients with moderate to severe MR. After adjustment no difference in mortality rate was found at 30 days (unadjusted HR: 1.61; 95% CI: 1.03 to 2.52; p = 0.036; adjusted HR: 1.51; 95% CI: 0.94 to 2.44; p = 0.091). Mortality rates during 1-year (unadjusted HR: 1.48; 95% CI: 1.10 to 1.99; p = 0.01; and adjusted HR: 1.42; 95% CI: 1.03 to 1.97; p = 0.03) and 5-year follow-up (unadjusted HR: 1.33; 95% CI: 1.07 to 1.65; p = 0.01; and adjusted HR: 1.29; 95% CI: 1.01 to 1.65; p = 0.04) were higher in those with moderate or severe MR at baseline compared to those with mild or less baseline MR (Fig. 1).

**Table 1**
Clinical and procedural characteristics at baseline, and 30-day outcomes of the population according to the degree of mitral regurgitation at baseline.

| | No/mild MR n = 1404 | Moderate/severe MR n = 308 | p-Value |
|---|---|---|---|
| Female | 679 (48%) | 177 (58%) | 0.004 |
| Age (years) | 81.3 ± 7.6 | 82.3 ± 6.1 | 0.03 |
| BMI | 26.5 ± 5 | 25.3 ± 5 | <0.001 |
| Previous PCI | 414 (30%) | 79 (26%) | 0.18 |
| Previous stroke | 206 (15%) | 48 (16%) | 0.68 |
| Recent MI | 88 (6.3%) | 10 (3.2%) | 0.04 |
| Diabetes | 324 (23%) | 56 (18%) | 0.06 |
| Hypertension | 1012 (72%) | 210 (68%) | 0.17 |
| COPD | 296 (21%) | 50 (16%) | 0.05 |
| Atrial fibrillation | 460 (33%) | 157 (51%) | <0.001 |
| NYHA Class III or IV | 1289 (92%) | 297 (96%) | 0.001 |
| LVEF >50% | 878 (63%) | 131 (43%) | <0.001 |
| LVEF 40–49% | 241 (17%) | 57 (18%) | <0.001 |
| LVEF 30–39% | 185 (13%) | 69 (22%) | <0.001 |
| LVEF <30% | 100 (7%) | 51 (17%) | <0.001 |
| Creatinine (μmol/l) | 94 (76–116) | 97 (79–121) | 0.3 |
| AVA ($cm^2$) | 0.65 ± 0.19 | 0.61 ± 0.22 | <0.001 |
| Claudication | 294 (21%) | 50 (16%) | 0.06 |
| PASP >60 mm Hg | 57 (4%) | 32 (10%) | <0.001 |
| Access route | | | 0.6 |
| Transfemoral | 1111 (79%) | 252 (82%) | |
| Transapical | 242 (17%) | 48 (16%) | |
| Subclavian | 30 (2%) | 6 (2%) | |
| Direct aortic | 21 (1.5%) | 2 (<1%) | |
| Prosthesis type | | | 0.8 |
| Medtronic CoreValve | 727 (52%) | 159 (52%) | |
| Edwards Sapien 3/XT | 605 (43%) | 130 (42%) | |
| Boston Scientific Lotus | 58 (4%) | 17 (5.5%) | |
| Other prostheses[a] | 14 (1%) | 1 (<1%) | |
| Prosthesis size (mm) | | | 0.7 |
| 23 | 231 (17%) | 60 (20%) | |
| 26 | 517 (37%) | 111 (36%) | |
| 29 | 486 (35%) | 101 (33%) | |
| 31 | 117 (8%) | 23 (8%) | |
| Other sizes[b] | 53 (3%) | 13 (3%) | |
| General anesthesia | 685 (49%) | 148 (48%) | 0.8 |
| Paravalvular aortic leak[c] | 95 (7%) | 27 (9%) | 0.17 |
| New major stroke | 34 (2.4%) | 5 (1.6%) | 0.4 |
| New pacemaker | 166 (12.7%) | 39 (13.5%) | 0.7 |
| Mortality | 75 (5.4%) | 26 (8.5%) | 0.03 |

Values are n (%), mean ± standard deviation, or median (25th–75th interquartile range), depending on variable distribution. The frequencies of stroke and death refer to within 30 days of TAVR. The frequency of new pacemaker refers to new permanent pacemaker implant during index hospital admission.
AVA = aortic valve area, BMI = body mass index, COPD = chronic obstructive pulmonary disease, LVEF = left ventricular ejection fraction, MI = myocardial infarction, NYHA = New York Heart Association, PASP = pulmonary artery systolic pressure, PCI = percutaneous coronary intervention.
[a] St Jude Portico n = 13, JenaValve n = 1.
[b] Boston Scientific Lotus n = 53, St Jude Portico n = 13.
[c] Denotes moderate or severe paravalvular aortic regurgitation.

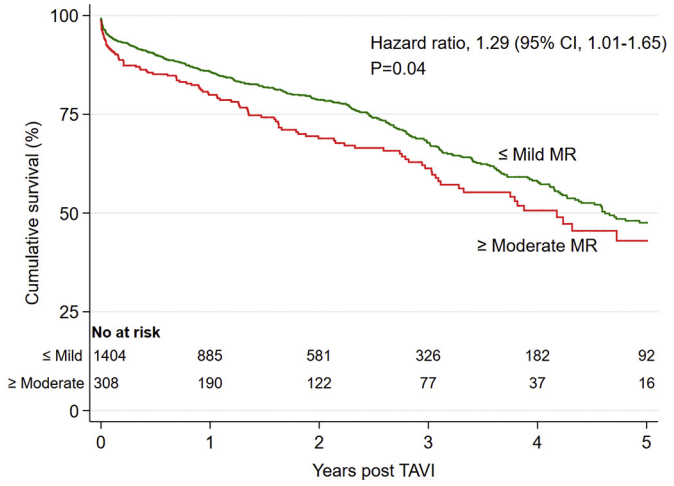


**Fig. 1.** Mortality after TAVR according to mitral regurgitation at baseline. Kaplan-Meier curves for 5-year all-cause mortality in patients with ≤mild or ≥moderate mitral regurgitation (MR) at baseline undergoing TAVR.

### 3.2. MR severity and change

A follow-up transthoracic echocardiogram within a week after TAVR was available in 1536 (90%) patients: 1263 with ≤mild MR at baseline and 273 with moderate/severe MR at baseline; whereas 59 (3.4%) were dead; and 117 (6.8%) were alive but lacked data on MR severity. Of 287 cases with moderate/severe baseline MR 145 (50.5%) improved to ≤mild, 128 (44.6%) remained moderate/severe, and 14 (4.9%) died before a follow up echocardiogram was registered. In the group with ≤mild MR (n = 1302) at baseline 1200 (92%) remained ≤mild after TAVR, whereas 68 (5.2%) worsened to moderate/severe, and 34 (2.6%) died.

In the univariate logistic regression analysis absence of ≥moderate paravalvular aortic regurgitation increased the probability of MR improvement after TAVR (OR 2.47, 95% CI: 1.07–5.72; p = 0.034), whereas absence of atrial fibrillation, valve prosthesis type, LVEF, and functional MR mechanism did not. Among those with no or mild baseline MR, atrial fibrillation (OR 2.07, CI 1.27–3.38, p = 0.004), self-expandable valve (OR 3.80, CI 2.06–7.02. p < 0.0001), and ≥moderate paravalvular aortic leak (OR 4.25, CI 2.32–7.78, p < 0.0001) increased the probability of worsening MR after TAVR. These associations remained significant after adjustment in a multivariate regression analysis (see Table 2).

### 3.3. Prognostic impact of pre- to post-procedural MR change

The association between MR change from baseline to discharge echocardiogram within 7 days of TAVR, and mortality was assessed at 30 days, 1 year and 5 years. Compared with patients with persisting ≤mild MR, only those with worsening MR after TAVR had a higher mortality rate during the first 30 days (unadjusted HR: 4.68; 95% CI: 1.75 to 12.5; p = 0.002; and adjusted HR: 4.28; 95% CI: 1.37 to 13.4; p = 0.01). No difference in mortality rates until 30 days was seen between the groups with either unchanged moderate/severe MR (unadjusted HR: 2.49; 95% CI: 0.93 to 6.68; p = 0.07; and adjusted HR: 1.74; 95% CI: 0.56 to 5.36; p = 0.33), or improved MR (unadjusted HR: 1.73; 95% CI: 0.59 to 5.09; p = 0.32; and adjusted HR: 1.69; 95% CI: 0.54 to 5.28; p = 0.37).

At 1 year, again comparing patients whose MR was ≤mild before and after TAVR, the group with unchanged moderate/severe MR (unadjusted HR: 2.24; 95% CI: 1.45 to 3.47; p = <0.0001; and adjusted HR: 2.06; 95% CI: 1.26 to 3.36; p = 0.004), and the group with MR worsening after TAVR (unadjusted HR: 2.60; 95% CI: 1.52 to 4.46; p = 0.001; and adjusted HR: 2.43; 95% CI: 1.37 to 4.32; p = 0.002) showed higher rates of all-cause mortality, whereas no difference in mortality was seen if MR improved after TAVR (unadjusted HR: 1.13; 95% CI: 0.66 to 1.94; p = 0.66; and adjusted HR: 1.17; 95% CI: 0.67 to 2.05; p = 0.59). These findings remained over the course of 5-year follow-up (Fig. 2): unchanged moderate/severe MR (unadjusted HR: 1.70; 95% CI: 1.26 to 2.30; p = 0.001; and adjusted HR: 1.66; 95% CI: 1.17 to 2.34; p = 0.004); and MR worsening (unadjusted HR: 2.13; 95% CI: 1.44 to 3.17; p = <0.0001; and adjusted HR: 1.97; 95% CI: 1.29 to 3.00; p = 0.002) conferred higher mortality rates; whereas no association with mortality increase was seen in the group with improved MR (unadjusted HR: 1.10; 95% CI: 0.78 to 1.54; p = 0.55; and adjusted HR: 1.09; 95% CI: 0.75 to 1.58; p = 0.67) compared with ≤mild pre- and post-TAVR mitral regurgitation.

## 4. Discussion

In the present national multicenter registry-based study, concomitant moderate or severe baseline MR was present in 18% of TAVR recipients with severe aortic stenosis. As expected, moderate or severe MR at baseline was associated with lower calculated aortic valve area, pulmonary hypertension, the presence of atrial fibrillation and lower LV ejection fraction. When adjusting for these factors, and others, the presence of double valve disease at baseline was associated with greater mortality during 1 year and 5 years of follow up. Improvement in MR, which occurred in 50% of subjects, translated into improved short- and long-term survival. Survival to 5 years among those with MR improvement was similar to those with ≤mild MR at baseline. Conversely, patients with worsening MR after TAVR showed increased early mortality, which persisted during 5 years of follow-up at a level comparable to the group with unchanged moderate/severe MR throughout the course. The sole predictor of MR improvement in our data was the absence of ≥moderate paravalvular aortic regurgitation. Mitral regurgitation mechanism, whether functional or organic, was not associated with MR improvement.

**Table 2**
Predictors of MR improvement and MR worsening by 7 days after TAVR, compared to MR severity at baseline.

| | MR improved Univariate | MR improved Multivariate | MR worsened Univariate | MR worsened Multivariate |
|---|---|---|---|---|
| Sex | OR 0.96 (p = 0.87) | OR 1.11 (p = 0.71) | OR 1.04 (p = 0.87) | OR 0.86 (p = 0.56) |
| Balloon vs. self-expanding device | OR 1.57 (p = 0.074) | OR 1.59 (p = 0.084) | OR 0.26 (p < 0.0001) | OR 0.28 (p < 0.0001) |
| LV EF < 50% | OR 1.28 (p = 0.31) | OR 1.39 (p = 0.22) | OR 1.52 (p = 0.097) | OR 1.66 (p = 0.057) |
| Paravalvular AI (≥moderate) | OR 0.40 (p = 0.034) | OR 0.54 (p = 0.18) | OR 4.3 (p < 0.0001) | OR 2.8 (p = 0.001) |
| Functional vs. degenerative MR | OR 0.87 (p = 0.56) | OR 0.96 (p = 0.89) | N/A | N/A |
| No atrial fibrillation | OR 1.50 (p = 0.095) | OR 1.56 (p = 0.075) | – | – |
| Atrial fibrillation | – | – | OR 2.1 (p = 0.004) | OR 2.05 (p = 0.006) |

Values are derived from univariate and multivariate regression analysis with odds ratios (OR) and p-values for each variable. MR improved denotes improvement of MR severity from moderate/severe to ≤mild. MR worsened denotes worsening of MR severity from ≤mild to moderate/severe.

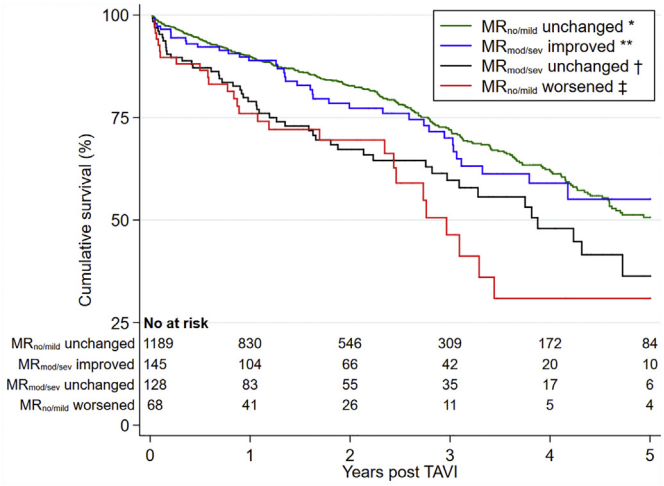


**Fig. 2.** Mortality according to mitral regurgitation change after TAVR. Kaplan-Meier curves for 5-year all-cause mortality according to MR evolution from baseline to pre-discharge echocardiogram within 7 days after TAVR. *HR 1.0 (reference); **HR 1.09 (95% CI, 0.75–1.58) p = 0.67; †HR 1.66 (95% CI, 1.17–2.34) p = 0.004; ‡HR 1.97 (95% CI, 1.29–3.00) p = 0.002.

### 4.1. Prognostic long-term impact of baseline MR

The presence of moderate or severe baseline MR was associated with a 42% increased risk for death from any cause during the first year following TAVR, and a 29% increased mortality over the course of 5 years following TAVR compared to those with no or mild baseline MR. This association did not reach statistical significance during the first 30 days after TAVR, which may be due to the relatively low early mortality rates in both groups.

Previous analyses on the impact of baseline MR among TAVR recipients have shown both an increase in early mortality [11–15] as well as no such association [16–19]. These discrepancies may stem from small sample sizes, a loss of follow up among patients with baseline moderate to severe MR, and the fact that some of these studies reported the impact of severe MR only [13,15] whereas others reported the effect of moderate to severe MR [12,14,17–19]. However, larger meta-analyses [4–6] and registries [11,20] have shown significantly increased mortality both at 30 days and 1 year after TAVR [4–6]. As an exception, a study from the French registry showed no significant association between MR and 3-year survival [21]. However, in that registry only 2% of patients displayed moderate or severe baseline MR, which may indicate negative selection of patients with MR. Our findings are concordant with the large meta-analyses, adding to the negative prognostic impact of baseline MR until 5 years after TAVR.

### 4.2. Improved MR

Meta-analyses have shown that up to half of concomitant significant MR improves after TAVR [4,22], but the effects of such an improvement have been poorly understood. Many of the previous studies on the evolution of MR following TAVR have been small in sample size [23–28], some evaluating little more than half of the study sample with follow-up echocardiograms [19,23,26]. The timing of the follow up echocardiograms has also been heterogeneous. However, in a study by Hekimian et al. [26] no change in MR severity was found between 7 days and 1 month after TAVR. Likewise, no substantial change in MR degree was found between discharge and 1 to 6 months after TAVR in a recent study by Cortés et al. [29] The same study did not demonstrate a survival benefit among those with improved MR after TAVR, which may be due to low statistical power and the fact that MR improvement was defined differently.

In the present study we evaluated MR status at baseline and within 7 days after TAVR. Data was available in 90% of the cohort comprising 1541 individuals, and MR improvement was defined as a clinically significant reduction from moderate/severe pre-TAVR MR to ≤mild post-TAVR MR. As a novel finding, we report that improvement of MR after TAVR is associated with improved survival compared to persisting moderate/severe MR or worsening MR. In effect, the risk carried by MR at baseline is mitigated if MR improves: the mortality rate of the group with MR improvement converges with the group with persisting ≤mild MR by 1 year, and remains so over the course of 5 years after TAVR. In a post-hoc sensitivity analysis we added PVL to the multivariate survival analysis, and tested for interaction between pre- to post-procedural MR severity and PVL. The association between MR degree, whether improved, worsened or unchanged, and survival at 1 year or 5 years after TAVR was not significantly altered after adjustment for PVL, and there was no interaction between MR degree and PVL (p for interaction = 0.85, see Supplementary appendix).

### 4.3. Residual and worsened MR

Residual MR has been found to increase mortality after TAVR [5]. The concept of residual MR, however, does not take into account that approximately 8% of baseline MR worsens after TAVR [4]. In our cohort 5% of those with ≤mild MR before TAVR deteriorated to moderate/severe MR after TAVR. Mortality at 30 days after TAVR was increased only for the group with worsened MR. However, when adjusting also for PVL only a trend for increased 30-day mortality remained in this group (p = 0.07, see Supplementary appendix). Importantly, residual, i.e. unchanged moderate/severe MR after TAVR was associated with an approximately 2-fold increase in mortality during 5 years of follow-up compared to those with persisting ≤mild MR. MR worsening translated into similar 5-year mortality rates, albeit with a trend towards even worse survival than the group with residual MR. The latter may be partly explained by the more sudden onset of volume overload caused by peri-procedural MR worsening in an often concentrically hypertrophied left ventricle. In contrast, the former scenario with a chronic MR coexisting with aortic stenosis may allow for a more favorable physiological response to MR after TAVR.

### 4.4. Predictors of MR change

Improvement of moderate or severe pre-TAVR MR has been shown to be greater in patients who have received balloon-expandable valve prosthesis [4,28]. In addition, absence of atrial fibrillation, absence of pulmonary hypertension, functional MR, low LVEF, LV end-systolic diameter >36 mm, mean gradient >40 mm Hg and absence of mitral annular calcification have been found to predict improvement of mitral regurgitation following TAVR [4,11,12,26,28,29,30]. Meanwhile, worsening of MR after TAVR has been associated with moderate-severe paravalvular aortic regurgitation [31].

In our material MR improvement was associated with absence of moderate-severe paravalvular aortic regurgitation, but only in the univariate analysis. The fact that functional MR mechanism was not associated with MR improvement probably reflects a large fraction of mixed MR etiologies in the TAVR population, where degenerative calcified MR often coexists with mitral annular dilatation and atrial fibrillation. Worsening of MR, which affected roughly 5% of TAVR recipients, was however associated with the presence of moderate-severe paravalvular aortic regurgitation, as well as with atrial fibrillation and the use of self-expanding valve prosthesis. Importantly, all the self-expanding prostheses were of the first generation of Medtronic CoreValve. Although this self-expanding device has now been replaced by newer and enhanced versions, the association is interesting since it remained highly significant even after adjustment for PVL. This may suggest other avenues of MR worsening, such as implantation depth with potential distortion of the anterior mitral apparatus. However, since no data was available to

explore these hypotheses, they remain open for future inquiry. Finally, our data suggest that a TAVR device with low PVL rates is preferred for patients with preexisting moderate or severe MR since the risk carried by MR and PVL are additive, reflecting the challenge of an often hypertrophic ventricle to cope with the volume overload of both MR and PVL.

## 5. Study limitations

The main limitation of this study stems from its register-based nature with a selection of cases amenable to catheter-based therapy. Also, data is reported by participating centers without an independent adjudication committee, except for mortality, which was extracted from the National Civil Registry with 100% capture. The absence of a centralized imaging core lab may have led to non-differential misclassification of echocardiographic parameters. Although data on MR degree after TAVR are based upon the first available echocardiogram within a week after the procedure, a certain degree of survival bias is inevitable. Finally, a set of unmeasured confounders may exist.

## 6. Conclusions

Concomitant moderate or severe mitral regurgitation at baseline affects roughly a fifth of TAVR recipients with severe aortic stenosis, and is associated with increased all-cause mortality up to 5 years after TAVR. The evolution of MR after TAVR appears to determine whether the mortality risk carried by baseline MR is either reversed by an improvement in MR severity; or accentuated by worsening MR; or remains in moderate/severe post-TAVR MR. Hence, the change in mitral regurgitation severity after TAVR confers important prognostic information, beyond the notion of seeing MR as a static phenomenon at baseline. Therefore, baseline MR should not render patients ineligible for TAVR, but future studies should assess whether percutaneous treatment of moderate/severe post-TAVR MR would translate into improved survival.

## Declaration of Competing Interest

Dr. Feldt has received consulting fees from Orion Pharma and Pfizer. Rodney De Palma, Henrik Bjursten, Petur Petursson, Niels Erik Nielsen, Thomas Kellerth, and Johan Nilsson report no relationships that could be construed as a conflict of interest. Dr. Jönsson has served as a proctor for Medtronic. Dr. Rück has served as a proctor for Boston Scientific and has received consulting fees from Medtronic and Edwards. Dr. Settergren has served as a proctor for Abbott, Boston Scientific and has received consulting fees from Medtronic. No specific funding support is associated with this manuscript.

The authors declare no relationships with industry related to this paper.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcard.2019.07.075.

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