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Transcatheter aortic valve replacement in patients with severe aortic valve stenosis and concomitant mitral valve regurgitation – 5 years follow-up

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ABSTRACT

Objectives: To investigate the change in severity of mitral regurgitation (MR) after transcatheter aortic valve replacement (TAVR) and its effect on 5-year mortality.

Background: There is inconsistency in literature on pre-existing MR influencing long-term survival in patients who undergo TAVR.

Methods: Patients who underwent TAVR at the University Hospital Schleswig-Holstein (USKH) Campus Kiel between March 2009 and February 2018 have been enrolled. Echocardiography determined the degree of MR before and within 7 days after TAVR. Patients were divided into two groups according to their MR at baseline: MR-grade ≤ 2 (non-relevant MR, nr-MR) and baseline MR-grade > 2 (relevant MR, r-MR). Primary endpoint was a composite of MR baseline influence on mortality and MR reduction and its' impact on mortality.

Results: A total of 820 patients (642 nr-MR and 178 in r-MR) were included in this study. Of these, 167 patients showed an improvement in MR-grade. Thereof 106 (63.5 %) referred to r-MR with a significant decrease in mean MR-grade ($p < 0.01$). Systolic pulmonary artery pressure (sPAP) ($p < 0.01$) and NT-proBNP ($p = 0.03$) decreased in patients who had an improvement. There was no significant difference in 5-year mortality for MR at baseline ($p = 0.35$) or reduction in mortality for r-MR patients with an MR improvement compared to patients with worsening or equal MR status ($p = 0.80$).

Conclusion: In patients undergoing TAVR, 63.5 % of patients with MR-grade ≥ 2 at baseline showed an improvement of grade of MR after TAVR with reduction of their sPAP and NT-proBNP values but there was no significant difference in mortality.

1. Introduction

Transcatheter aortic valve replacement (TAVR) is an established method for the treatment of high-risk inoperable patients with severe symptomatic aortic valve stenosis (AS) [1]. While AS is the most treated valve disease in the western world, up to 20 % of patients with AS simultaneously suffer from concomitant relevant mitral regurgitation (MR), leading to a worse patient prognosis and higher mortality [2,3]. In the presence of severe AS, diagnostic and echocardiography approaches are challenging in assessing the actual severity of MR and interactions must be considered [2].

Due to a lack of prospective RCTs, ESC/EACTS and ACC/AHA guidelines do not provide strong recommendations on approaching high-risk inoperable patients with severe AS and concomitant primary and secondary MR [4]. Most of those patients present with older age and more frequently comorbidities such as higher prevalence of atrial

Abbreviations: TAVR, transcatheter aortic valve replacement; MR, mitral regurgitation; r-MR, Relevant MR; nr-MR, Non relevant MR; sPAP, systolic pulmonary artery pressure; AS, aortic stenosis; AF, atrial fibrillation.

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fibrillation (AF) or prior myocardial infarction [5,6]. In inoperable patients undergoing TAVR, reassessment of mitral regurgitation is recommended [2,4]. Timing of such reassessment and the impact of TAVR on improvement, none-improvement or deterioration of MR remains uncertain. Staged procedures with TAVR and transcatheter interventional therapy of the MR may be feasible and reduce symptoms and mortality but there is insufficient experience to allow robust recommendations [7]. While some studies suggest a significant improvement in MR by performing TAVR and reducing the need for a transcatheter therapy of the MR, there is also data showing contrary results [7]. Those patients should carefully be monitored after TAVR, and timing of interventional therapy of the MR should be on point at risk–benefit assessment. In patients with persisting symptomatic severe MR after TAVR, interventional therapy of the MR should be considered. The primary objective of this study was to assess the change in MR severity of MR in patients with severe AS undergoing TAVR and its influence on patient survival.

2. Methods

2.1. Study population

This retrospective study investigated patients who were treated with a transfemoral TAVR at the University Hospital Schleswig-Holstein, Campus Kiel between March 2009 and February 2018 and who formally agreed to use their treatment data for research purposes. The study was approved by the local ethics committee at the University Hospital Schleswig-Holstein – (reference number: D529/16).

2.2. Procedural details

Patients included in this study were diagnosed with severe symptomatic AS in need of treatment (aortic valve area $<$ 1,0 cm, mean aortic pressure gradient $\geq$ 40 mmHg or peak aortic jet velocity $\geq$ 4.0 m/s) Eligible candidates for TAVR were selected by a multidisciplinary heart team, which classified the patients based on clinical aspects but also on surgical risk scores (logistic Euro-Score, the STS-Score or the Euro-II-Score). Prior to TAVR, left and right heart catheterisations were performed and relevant (70 % proximal) coronary artery stenoses were treated. Postprocedural follow up was performed until discharge and in our ambulatory section. The long-term follow-up data were collected by means of annual telephone calls. In patients, who died during follow-up, the exact time and cause of death were ascertained and documented.

For our analyses, we divided our study population into two groups according to baseline MR (defined according to the American Society of Echocardiography recommendations) [8]. One group includes patients without MR or patients with presumed clinically non relevant MR (MR $\leq$ Grade 2), hereinafter referred to as non-significant MR “nr-MR”. Patients with a higher grad of MR (MR $\geq$ Grade 3) were included in the other group (referred to as high MR “high-MR”).

2.3. Statistical analysis

Frequency tables were performed to describe frequency distribution. Metric variables were analysed as median with interquartile ranges, whereas nominal and ordinal data was expressed by absolute numbers and percentages. X^2-test and Fisher‘s exact test was performed for nominal and ordinal data to detect significant differences between the groups. Metric variables were evaluated by Mann-Whitney-U-Test for independent samples or with Wilcoxon-Test for dependent samples. Survival was pictured by Kaplan-Meier graphs and life tables. Significant differences in mortality were analysed by the Log-Rank-Test. All tests were 2-tailed and a p-value $<$ 0.05 was considered to be statistically significant. Statistical analysis was performed using SPSS Statistics 29.

3. Results

3.1. Baseline characteristics

In our analysis, 820 patients who underwent TAVR at the UKSH between March 2009 and February 2018 were included. Patient characteristics are summarised in Table 1.Table 2..

Nr-MR group included 642 patients with none or mild MR-grade at baseline, while the r-MR group included 178 patients with moderate or severe MR at baseline. From this group, 32 patients (18 %) had a primary MR.

In comparison of the two groups, patients of r-MR were significantly more often female, had higher risk-scores, higher sensitive Troponin levels (hs-TnT), higher median NT-proBNP levels, as well as a higher incidence of AF. Patients in the r-MR group had more patients with impaired LV-EF among the Group of LV-EF $<$ 35 % and $>$ 55 % and significantly higher sPAP levels (see Fig. 1 and Fig. 2).

3.2. Periprocedural data and complications

Regarding intervention, there was no significant difference between the two groups in terms of procedural duration, access route, valve type and size (see Table 3). Periprocedural complications (defined by VARC-III-criteria) are displayed in Table 4. Acute kidney failure was documented more frequently in r-MR group.

3.3. Postprocedural remodelling: Change in MR and cardiac function

Overall, there was a significant reduction in MR in pre- and 7-day

Table 1
Baseline characteristics.

	Total	nr-MR	r-MR	p
Characteristic	(n = 820)	(n = 642 / 78 %)	(n = 178 / 22 %)	
Median age (IQR) – yr	81 (78; 86)	81 (77; 86)	82 (78; 86)	0.31
Male sex	373 (45.5)	308 (48.0)	65 (36.5)	**0.01**
BMI in kg/m^2	27 (24; 29)	27 (24; 29)	27 (23; 30)	0.29
Pre-existing conditions				
Diabetes	263 (32.1)	208 (32.4)	55 (30.9)	0.71
Hyperlipoproteinemia-	436 (53.2)	347 (54.0)	89 (50.0)	0.34
Hypertension	744 (90.7)	588 (91.6)	156 (86.6)	0.11
AF	357 (43.6)	259 (40.4)	98 (55.1)	**<0.01**
Previous cardiac surgery	147 (17.9)	116 (18.1)	31 (17.4)	0.83
COPD	139 (17.0)	112 (17.5)	27 (15.2)	0.46
PAOD	136 (16.6)	107 (16.7)	29 (16.3)	0.90
Cerebrovascular diseases	158 (19.3)	128 (20.0)	30 (16.9)	0.37
Dialysis	13 (1.6)	10 (1.6)	3 (1.7)	0.90
NYHA functional class				
I	31 (3.8)	30 (4.7)	1 (0.6)	**0.01**
II	195 (23.9)	159 (24.8)	36 (20.5)	0.23
III	470 (57.6)	368 (57.5)	102 (58.0)	0.91
IV	120 (14.7)	83 (13.0)	37 (21.0)	**0.01**

BMI: Body-mass index, COPD: Chronic obstructive pulmonary disease, PAOD: peripheral arterial occlusive disease, NYHA: New York Heart Association Classification

Table 2
Baseline laboratory parameters, echocardiography parameters and risk scores.

	Total (n = 820)	nr-MR (n = 642 / 78 %)	r-MR (n = 178 / 22 %)	p
Laboratory parameters at baseline				
Mean Hs-TnT [ng/l](SD)	73.7 (454.6)	68.2 (478.7)	95,5 (344.8)	< **0.01**
Mean NT-proBNP [ng/l] (SD)	4131.4 (7473.0)	3577.8 (7108.7)	6249.3 (8427.9)	< **0.01**
Mean Creatinine [µmol/l] (SD)	119.3 (77.4)	118.9 (80.4)	120.8 (65.1)	0.06
Est.GFR (MDRD)				**0.02**
G4/G5 (<30 ml/min)	94 (11.5)	72 (11.2)	22 (12.4)	0.67
G3b (30–45 ml/min)	178 (21.7)	124 (19.3)	54 (30.3)	< **0.01**
G3a (45–60 ml/min)	294 (35.9)	241 (37.5)	53 (29.8)	0.06
G1/G2 (>60 ml/min)	245 (29.9)	198 (30.8)	47 (26.4)	0.25
Echocardiography parameters at baseline				
Mean AVA in cm^2 [SD]	0.7 (0.2)	0.7 (0.2)	0.7 (0.2)	0.13
Pre AR-Category				
none	545 (66.5)	436 (67.9)	109 (61.2)	0.23
trace	87 (10.6)	72 (11.2)	15 (8.4)	0.37
mild	38 (4.6)	26 (4.0)	12 (6.7)	0.10
severe	13 (1.6 %)	6 (0.1)	7 (3.9)	< **0.01**
LV ejection fraction				< **0.01**
< 35 %	70 (8.5)	47 (7.3)	23 (12.9)	**0.02**
35–45 %	113 (13.8)	81 (12.6)	32 (18.0)	0.08
46–54 %	156 (19.0)	118 (18.4)	38 (21.3)	0.44
≥ 55 %	422 (51.5)	347 (54.0)	75 (42.1)	< **0.01**
Mean sPAP (mmHg) (SD)	45.8 (14.6)	52.6 (15.6)	43.8 (13.6)	< **0.01**
Risk Scores				
Log. Euroscore (%) mean, SD	19.8 (12.5)	19.4 (12.7)	21.4 (11.7)	< **0.01**
Euroscore II (%) mean, SD	6.4 (5.2)	6.1 (5.1)	7.5 (5.4)	< **0.01**
STS Score (%) mean, SD	5.5 (3.7)	5.4 (3.6)	6.1 (3.8)	**0.02**

HsTnT: Highly sensitive troponin-T, NT-proBNP: N-terminales pro brain natriuretic peptide, AVA = Aortic valve area, GFR = glomerular filtration rate, AR: Aortic regurgitation, sPAP: systolic pulmonary artery pressure.

post procedural measurement ($p < 0.01$). This reduction was mainly driven by the r-MR group ($p < 0.01$). Mean MR grade for the r–MR group was 3.1 and declined to 2.5, indicating an overall class switch from moderate to mild ($p < 0.01$). For the group of patients with clinical nr-MR there was no class switch ($p < 0.01$).

Postprocedural MR presented unchanged in 558 patients (68.0 %), improved in 167 (20.4 %) and worsened in 95 patients (11.6 %). Regarding the nr–MR group, 495 of 642 (77.1 %) patients presented with an unchanged MR, 61 (9.5 %) had an improvement and 86 (13.4 %) suffered from worsening. For r–MR, 63 out of 178 patients (35.4 %) showed no changes in MR, while 106 (59.6 %) showed an improvement and 9 (5.1 %) showed worsening (see Fig. 1). There was a significant difference in pairwise comparison resulting in significant more patients with MR improvement among the group of r–MR and significant more patients with unchanged ($p < 0.01$) or worsened ($p < 0.01$) MR among the group of nr-MR. These effects were widely consistent regarding MR improvement after 1 year. Comparing 7-day MR status with 1-year MR status, 207 patients (25.2 %) remained unchanged, 35 patients (4.3 %) improved, and 49 patients (6.0 %) had a worse MR status. There is a loss of follow-up of 522 patients (63.7 %) due to ambulatory follow-up examinations.

In the r-MR group more patients improved with a secondary MR,

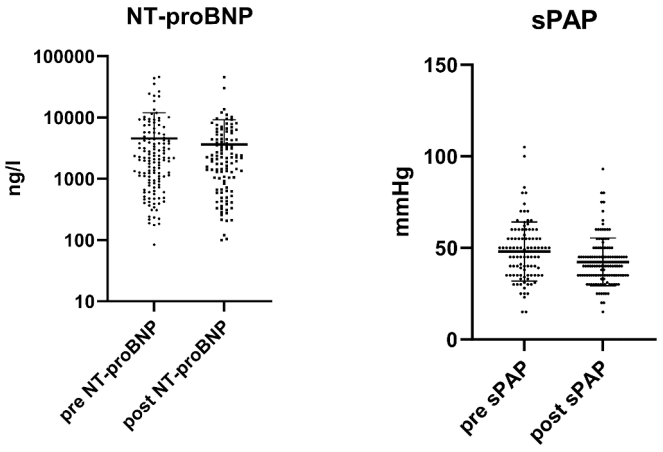

Fig. 2. Significant changes of sPAP and NT-proBNP in patients with improvement in MR. Changes of NT-proBNP and sPAP pre and post TAVR in patients with improved MR status.

Table 3
Procedural data.

	Total	nr-MR	r-MR	p
	(n = 820; %)	(n = 642 / 78; %)	(n = 178 / 22; %)	
Procedure data				
Mean duration [min] (SD)	75.7 (36.3)	75.8 (36.3)	75.5 (36.6)	0.75
Access route				0.98
Transfemoral	552 (67.4)	433 (67.4)	119 (67.2)	0.96
Transaortal	164 (20.0)	127 (19.8)	37 (20.9)	0.74
Transapikal	103 (12.6)	82 (12.8)	21 (11.9)	0.77
Valve type				0.60
CoreValve Evolut R	178 (21.7)	134 (79.1)	44 (24.7)	0.27
Sapien XT	213 (26.0)	170 (26.5)	43 (24.2)	0.53
Sapien 3	366 (44.6)	290 (45.2)	76 (42.7)	0.56
Other	63 (7.7)	48 (7.5)	15 (8.4)	0.67
Mean valve size [mm] (SD)	26.4 (2.4)	26.4 (2.4)	26.4 (2.5)	0.97

Min: minutes.

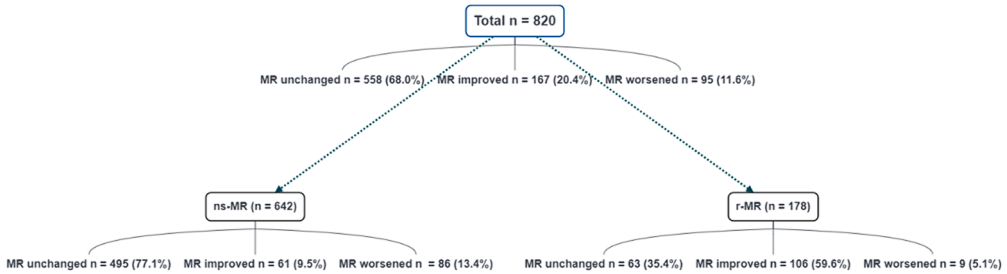

Fig. 1. Change in MR Grade within 7 days. Flow chart documenting inclusion criteria and the number of individuals included in the study groups.

Table 4
Periprocedural complications.

	Total	nr-MR	r-MR	p
VARC-III criteria	(n = 820; %)	(n = 642 / 78 %)	(n = 178 / 22 %)	
Mortality (at 30 days)				
Total	26 (3.2)	20 (3.1)	6 (3.4)	0.86
Myocardial infarction	8 (1.0)	6 (0.9)	2 (1.1)	0.82
Stroke				
Total	14 (1.7)	12 (1.9)	2 (1.1)	0.50
Disabling	7 (0.9)	6 (0.9)	1 (0.6)	0.63
Bleeding				
Total	105 (12.8)	76 (11.8)	29 (16.3)	0.12
life-treating	16 (2.0)	10 (1.6)	6 (3.4)	0.12
Acute kidney failure – no. (%)	50 (6.1)	32 (5.0)	18 (10.1)	**0.01**
Vascular complications				
Total	81 (9.9)	65 (10.1)	16 (9.0)	0.65
Major	14 (1.7)	8 (1.2)	6 (3.4)	0.05
Arrythmias				
Total	230 (28.0)	180 (28.0)	50 (28.1)	1.00
new pacemaker	59 (7.2)	48 (7.5)	11 (6.2)	0.55
Conversion to open surgery	4 (0.5)	2 (0.3)	2 (1.1)	0.17
renewed intervention (valve in valve)	9 (1.1)	8 (1.2)	1 (0.6)	0.44

however this effect was not statistically significant (60 % vs 53 %, p = 0.06). From the group of patients with rMR, four patients received interventional MR-Treatment after TAVR, all of them had secondary MR.

Corresponding to baseline data, there still was a significant higher NTproBNP ($p < 0.01$), higher sPAP ($p < 0.01$) and worse ejection fraction regarding LV-EF category < 35 % ($p < 0.01$) and ≥ 55 % ($p < 0.01$) for patients in the r-MR group seven days after intervention. Among the cohort of improved MR (n = 167) patients showed a significant reduction in NT-proBNP (p = 0.03) and sPAP ($p < 0.01$) in comparison to patients with worsened or unchanged MR (Fig. 2). Patients with worsened or unchanged MR-status presented higher NT-proBNP levels after TAVR compared to baseline but this was not significant (see Fig. 2). Table 5.

3.4. Survival after TAVR

Maximum follow-up duration was 10.5 years and median follow up duration was recorded for 3.4 years. Death was recorded for 299 patients (36.5 %). Regarding mortality there was a lower median survival (6.1 years) for patients in r-MR vs. nr-MR (7.0 years). This effect was not statistically significant (p = 0.35).

Within r–MR group there was a higher median survival in years for patients with improved MR (6.1 years) compared to patients with unchanged or worsened (5.5 years) but this effect failed to be significant (p = 0.80) (see Figs. 3 and 4). Regarding 1-year MR status these findings are robust and there is no overall significant higher survival for patients with improvement versus patients with unchanged or worsened MR (p = 0.89).

4. Discussion

We conducted this study in the field of TAVR and we observed its influence on concomitant MR. We found a reduction in MR mainly among patients with r-MR (MR-grade ≥ 2) which is consistent with retrospective *meta*-analysis by Nombela-Franco and Sethi et al. [9,10]. This effect was promptly observable within 7 days. There was a significant reduction in sPAP and NT-proBNP levels in those patients with improvement compared to patients with worsening or unchanged MR status. We observed a lower median survival for patients in r-MR vs ns-MR at baseline and there was a higher median survival for patients with

Table 5
Post TAVR laboratory parameters, echocardiography parameters.

	Total (n = 820)	nr-MR (n = 642 / 78 %)	r-MR (n = 178 / 22 %)	p
7d Laboratory parameters				
Hs-TnT (ng/l) mean, SD	164.7 (327.6)	172.7 (352.1)	135.1 (211.2)	0.54
NTproBNP (ng/l) mean, SD	4093.8 (7603.9)	3867.8 (7735.8)	4927.2 (7066.0)	**<0.01**
Creatinine (µmol/l) mean, SD	115.3 (77.3)	114.3 (79.4)	118.6 (69.3)	0.13
Est. GFR (MDRD)				**0.01**
G4/G5 (<30 ml/min)	77 (9.4)	53 (8.3)	24 (13.5)	**0.03**
G3b (30–45 ml/min)	149 (18.2)	108 (16.8)	41 (23.0)	0.06
G3a (45–60 ml/min)	244 (29.8)	201 (31.3)	43 (24.2)	0.07
G1/G2 (>60 ml/min)	270 (32.9)	219 (34.1)	51 (28.7)	0.17
7d Echo parameters				
AR-Category				0.23
0	468 (57.1)	374 (58.3)	94 (52.8)	0.19
1	279 (34.0)	216 (33.6)	63 (35.4)	0.66
2	20 (2.4)	13 (2.0)	7 (3.9)	0.15
3	1 (0.0)	1 (0.0)	0 (0.0)	0.60
LV ejection fraction (LV-EF)				**<0.01**
< 35 %	70 (8.5)	43 (6.7)	27 (15.2)	**<0.01**
35–45 %	94 (11.5)	66 (10.3)	28 (15.7)	0.05
46–54 %	145 (17.7)	110 (17.1)	35 (19.7)	0.48
≥ 55 %	428 (52.2)	356 (55.5)	72 (40.4)	**<0.01**
Mean sPAP [mmHg] (SD)	43.5 (14.1)	42.1 (13.5)	48.3 (15.2)	**<0.01**

HsTnT: Highly sensitive troponin-T, NT-proBNP: N-terminal pro brain natriuretic peptide, AVA = Aortic valve area, GFR = glomerular filtration rate, AR: Aortic regurgitation, sPAP: systolic pulmonary artery pressure.

improvement in their MR grade, but these results failed to be significant.

In line with previous investigations, a higher portion of patients with severe AS and concomitant moderate to severe MR, who undergo TAVR, show significant improvement of the degree of MR after TAVR [5,9,11,12].

4.1. Coincidence of aortic stenosis and mitral regurgitation and prognostic predictors

Every fourth to fifth patient of the study population suffered from moderate or severe MR in addition to AS which is coherent with recent publications [12,13]. The r-MR group presented significant higher rates of AF, lower LV-EF and had higher perioperative risk scores. Meta-analysis by Sethi et al. presented higher MR grade was associated with lower LV-EF and higher perioperative risk scores.

Regarding AF, analysis by ÓOnofrio and Toggweiler et al. also showed higher rates among patients with higher MR grade. Concordant with Toggweiler et al. AF may present as predictor for MR worsening. Gertz et al. determined the term of „atrial functional MR“ and could prove that ablation and restoration of sinus rhythm improves atrial functional MR [14].

Left ventricular fractional area change, mitral annular calcification, left ventricular volume and mass and left atrial volume index have been described as univariable predictors for MR after surgical aortic valve replacement [12,15–17]. Further, our analysis shows that NT-proBNP and sPAP did significantly decrease in patients with improvement. As shown by Seoudy et al. among 704 patients undergoing TAVR, NT-pro-BNP is a strong risk predictor for survival. They introduced the term of “responders” and “nonresponders” for patients with decrease or increase in NT-pro-BNP levels post TAVR [18]. Abdel-Wahab demonstrated higher mortality among 1432 TAVR patients with elevated sPAP [19]. In fact, little is known about the predictive sensitivity of NT-proBNP and sPAP for MR reduction. Regarding mortality both predictors seem to be

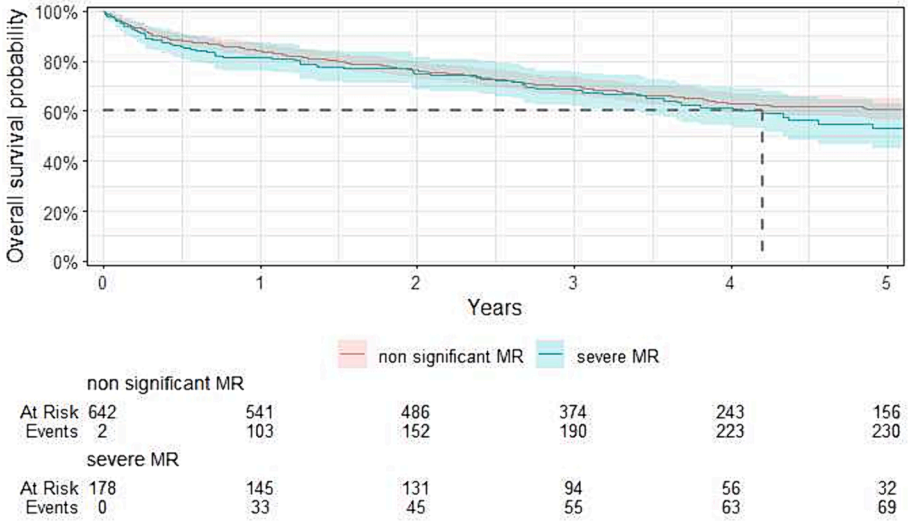

Fig. 3. Kaplan-Meier curve in relation to baseline MR. Kaplan-Meier surveillance curve in relation to baseline MR and 5 years follow-up.

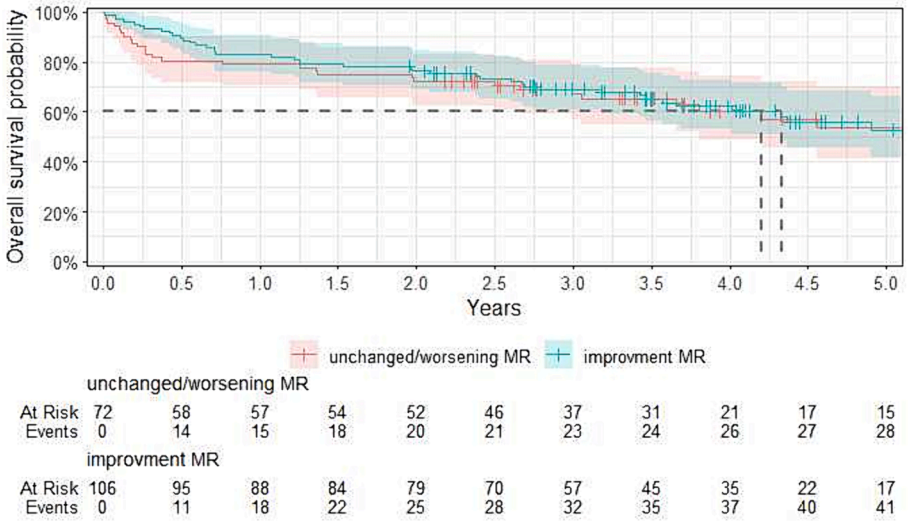

Fig. 4. Kaplan-Meier curve in relation to MR status after 7 days. Kaplan-Meier surveillance curve for unchanged/worsening MR vs improved MR status.

valid after TAVR and this may be co-effected by MR reduction and cardiac remodeling.

4.2. Change in the degree of MR after TAVR

In line with the *meta*-analysis by Sethi et al. we found a significant reduction in MR after TAVR. Those effects where traceable within 7 days, instead to other studies where effects were described at 30 days or even later. We found conclusive and relatable rates of MR-improvement [10,11]. Cortés et al. included also a TTE at discharge in their design, but they did not report the rates of high-grade MR at discharge after TAVR dependent on the previously formed groups of high-grade MR at baseline versus low-grade MR at baseline [12]. Toggweiler et al. did also observe direct effects on MR reduction within an observational median of 3 days (before discharge). Misleading, in their conclusion, they reported their results on 1-year follow up, where MR improvement had slightly declined [5]. Vena contracta as single predictor for MR indicated improvement within 24 h after the procedure and persisted for at least six months in an analysis by Durst et al. [16]. Another publication by Khawaja et al. stated a significant MR reduction in those patients with grade 3–4 MR. Contrary to a prompt MR evaluation, there assessment was performed 30 days post TAVR. Interestingly, MR reduction persisted with no significant difference in 1 year follow-up [13].

In conclusion, the biggest reduction in MR apparently seems to take place during the hospital stay where TAVR procedure was performed but we still do not know if there is further improvement and when to target persisting symptomatic MR. For example, Witberg et al. published a multicentre registry summarizing a median interval for transcatheter mitral valve repair of 164 days post TAVR [7].

4.3. Survival

Moderate to severe MR after TAVR is a predictor for mortality [9,11,13]. We assumed that reduction in MR after TAVR would have a significant influence.

Sethi et al. *meta*-analysis showed that we do not have strong evidence to determine the impact of MR at baseline on mortality in TAVR [10]. Only five out of the 21 studies included in the *meta*-analysis showed an association between MR and mortality [10]. Our results are in line with the majority of the included studies, we did not find a significant better prognosis in patients with non-relevant MR at baseline.

We could not prove an impact of MR improvement on survival. In

contrast, a *meta*-analysis by Charkavarty et al. described that a severe residual MR after TAVR was associated with a significant increase in mortality [11]. We could not find any obvious difference to the included studies, as the key demographic data were comparable. The most striking difference was the timing of echographic follow-up (7d vs 30d) and thus the assessment of mitral regurgitation after TAVR. From our data it remains unclear whether the MR improvement after TAVR is stable or evolves again by the 30d timepoint and explains the different outcomes in terms of mortality.

5. Limitations

The study concept of this work corresponds to a single centre study, from which the risk of systematic errors emanates. It is a retrospective observational study which may not take sufficient account of the influence of possible confounders. For some parameter analyses of the follow-up, a decimated number of data was available compared to the total number of patients pre-procedurally, which could limit the statistical power of the corresponding analyses. Our echocardiographic data must be viewed against the background of a subjective assessment of different examiners and could therefore vary in their comparability. For the 1-year echocardiography follow-up in particular, it must be mentioned that we were only able to collect this data from 36.3 % of patients. The reason for this was that the patients received their follow-up care in an outpatient setting from other health care providers. For the survival analysis, the data was collected directly from the patients, so there was little loss of follow-up in the first two years.

6. Conclusion

TAVR can significantly reduce MR, in particular in those patients with moderate to severe MR. This effect was significant among echocardiographic and cardiac biomarkers. We could not prove a significant effect on long-term mortality regarding MR reduction and this field remains controversial.

The knowledge that a higher-grade MR could improve so comprehensively after TAVR suggests a stepwise approach by TAVR followed by close meshed follow-up.

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CRediT authorship contribution statement

Rafael Henrique Rangel: Writing – original draft, Conceptualization. **Jakob Christoph Voran:** Conceptualization. **Hatim Seoudy:** Conceptualization. **Theresa Villinger:** Writing – original draft, Formal analysis. **G. Lutter:** Writing – review & editing. **T. Puehler:** Writing – review & editing. **Felix Kreidel:** Writing – review & editing. **Johanne Frank:** Writing – review & editing. **Mostafa Salem:** Writing – review & editing. **Derk Frank:** Writing – review & editing. **Mohammed Saad:** Writing – review & editing, Validation, Supervision, Project administration, Methodology, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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