ECRONICON OPEN ACCESS

EC CARDIOLOGY

Research Article

Impact of Trans-Catheter Aortic Valve Implantation on Mitral Regurgitation Severity, and its Role in Predication Survival: A 12-Month Single Center Experience

Mohamed Imam[1], Yasser Sadek[1], Soliman Gharib[2], Mohamed Abd Elghany[2], Hossam Elhossary[2], Ghada A Kazamel[1]*, Reda Deyab[2], Tarek El Tawil[4], Hamdy Soliman[1], Ahmed Gaafar[4], Mohamed Osama[1], Hesham Amar[1], Sherif Hendawy[3] and Abela Atef[5]

[1]*Department of Cardiovascular Medicine, National Heart Institute, Cairo, Egypt*

[2]*Department of Cardiovascular Medicine, Cairo University, Cairo, Egypt*

[3]*Department of Cardio-Surgery, National Heart Institute, Cairo, Egypt*

[4]*Department of Cardio-Surgery, Cairo University, Cairo, Egypt*

[5]*Department of Anesthesia, National Heart Institute, Cairo, Egypt*

***Corresponding Author:** Ghada A Kazamel, Department of Cardiovascular Medicine, National Heart Institute, Cairo, Egypt.

Received: September 30, 2019; **Published:** October 17, 2019

Abstract

Introduction: In patients with severe aortic stenosis (AS), mitral regurgitation (MR) is a common finding. Current literature did not show the impact of trans catheter aortic valve implantation (TAVI) on MR, and accordingly, outcomes in patients with MR have not been a focus of evaluation.

In current practice, MR is usually left untreated in patients undergoing TAVI, especially in patients with severe MR who are excluded from formal evaluation.

Aim: In our study, we aim to study the impact of TAVI on MR severity, and how MR impacts clinical outcomes in the first year after TAVI (Am J Cardiol 2015).

Methods: Twenty AS patients were considered as candidates for TAVI due to inoperability on top of high surgical risk according to clinical status, and score results of Logistic EuroSCORE, and frailty score. All the patients underwent full left heart and vascular hemodynamics studies before undergoing TAVI.

After TAVI, patients were closely monitored in the cardiac intensive care unit for 48 - 72 hours with particular attention to hemodynamic status, vascular access site, renal function, infections and cardiac conduction abnormalities. We have asked our patients to attend follow-up visits at 1, 3, 6, and 12 months after discharge, when clinical and echocardiographic findings were recorded.

Results: We have recruited twenty patients for our study. Their age ranged between 51 to 96 years with a mean age of 83.3 (SD ± 6.7) years. The mean Euro SCORE Logistic was 23 ± 13, the mean STS score was 10.2 ± 9. Hemodynamics studies showed the body surface area as estimated by Cath was 0.4 ± 0.4, and mean gradient across aortic valve of 44.7 (SD ± 17) mmHg. All our patients underwent TAVI using BE Edwards valve.

In terms of outcomes, the most common complications occurred were vital hemorrhage in 1 patient (5%), minor vascular complications in 1 patient (5%), major hemorrhage in 1 patient (5%).

Conclusion: The TAVI procedure is feasible for patients with severe MR and most probably it will improve with increased risk of mortality in the first year and then the effect of mitral regurgitation on mortality is absent after the 1st year. The patients with concomitant mitral regurgitation and aortic stenosis must be fully studied in order to approve this indication (Sannino A., *et al*. 2017). The cause of the mitral regurgitation improved after TAVI procedure must be fully studied. Tissue Doppler must be added to the data studied after TAVI.

Keywords: *Trans-Catheter Aortic Valve Implantation; TAVI; Mitral Regurgitation; Severe Symptomatic AS; EuroSCORE*

Introduction

Currently, age-related calcific aortic stenosis (ARAS) is the most common cause of AS in adults. Freeman and Otto defined ARAS as irregular thickening of the aortic valve leaflets detected by echocardiography without significant obstruction (Brian R Lindman., *et al.* 2016). Aortic sclerosis is the initial stage of calcific aortic valve disease and, even in the absence of valve obstruction, is associated with a 50% increase in the risk of cardiovascular death and myocardial infarction.

Calcific ARAS shares common predispositions and risk factors with mitral annular calcification, and the two conditions often co-exist. Such shared profile includes genetic predisposition, inflammatory markers, elevated serum levels of low-density lipoprotein (LDL) cholesterol and lipoprotein (a) (LP a), diabetes mellitus (DM), smoking, and hypertension (HTN). Recent publications showed that moderate-to-severe MR in patients with ARAS is approximately 20% (BR Lindman 2016).

Functional MR can be a maladaptive consequence of AS, and it is found in patients with greater left ventricular (LV) dilatation and worse LV function; thus it reflects an underlying LV dysfunction.

Studies have shown that patients with moderate or severe MR undergoing TAVI presented with a worse baseline clinical profile, higher EuroSCORE and STS scores, more age advanced, higher prevalence of atrial fibrillation (JM Paradis 2017) and myocardial infarction. Similarly, their echocardiographic findings showed lower values of left ventricular (LV) ejection fraction (LVEF), higher LV volumes, narrower aortic valve area (AVA), and higher systolic pulmonary pressure.

MR may mask subclinical myocardial dysfunction, the similarity of LV ejection fraction between patients with moderate/severe MR and those with mild MR might indicate the absence of myocardial functional compensation. This may help to explain the higher mortality and hospitalization rates for heart failure of patients with moderate/severe MR, despite MR improvement.

According to current understanding of intra-cardiac hemodynamics: the immediate decrease in the afterload and LV pressure would be expected to result in improvement in MR. Considering such concept, we can draw parallels with SAVR, because MR is recognized as an independent risk factor influencing long-term survival in the elderly patients undergoing SAVR, and concomitant MR surgery is selectively considered in symptomatic patients undergoing AVR. For example, MV repair has been associated with improved late survival in patients with double valve disease, including the elderly and those with depressed LV function; however, simultaneous replacement of the aortic valve and MV significantly increases surgical morbidity and mortality; i.e. if MR left untreated, patients with severe AS and concomitant moderate/severe MR have a very poor prognosis.

Echocardiographic MV morphologic evaluation is critical for the assessment of mechanism and reparability. MR improvement after AVR is more likely in patients with lesser degrees of MR or in the presence of normal MV morphology, because it usually reflects the functional nature of MR. Although patients with moderate/severe MR undergoing TAVI have higher overall morbidity and mortality compared with those with lower degrees of MR, the benefit of TAVI may indeed be higher in this group [1].

Aim of the Study

In our study, we aim to provide further evidence on the impact of TAVI on the degree of MR and myocardial function.

Methods

Study population

Between May 2007 and November 2011, twenty patients underwent TAVI in our centre. They have been referred for TAVI on top of severe symptomatic AS, or aortic bio-prosthesis dysfunction; because of high surgical risk or inoperability criteria.

All patients who underwent successful trans-femoral TAVI were included in this study. However, we have excluded patients who had trans-apical TAVI, any acute attack of ACS during the follow-up period, any cause of increase of pulmonary blood pressure, and patients with aortic annulus diameter ≤ 19 mm or > 27 mm.

The patient's surgical risk was estimated using logistic EuroSCORE and STS scores, via the web-based system; in addition to clinical judgment and frailty score.

In all potential candidates to TAVI, we performed a routine check-up to evaluate the eligibility to transcatheter procedure and choose the most appropriate vascular access. Such check-up included clinical history and examination, laboratory investigations, chest X-ray and ECG.

Echocardiography

Transthoracic echocardiography was performed before and after TAVI. The color-flow Doppler measurements were performed to grade mitral regurgitation. According to echocardiographic assessment of mitral regurgitation, our patients were classified into three groups according to the severity of the mitral regurgitation: first group included patients with grade 0 and 1, while the second group those with grade 2 and finally, the third group those with grade 3 and 4.

Types of transcatheter aortic valves

Suture-less transcatheter aortic stent-valve the BE Edwards valves (Edwards Lifesciences, Irvine, CA, USA) allowing either retrograde TF (or trans-aortic) or integrate TA implantation. Sizes ranged from 23 - 29 mm.

Post-TAVI monitoring and management

After TAVI, patients remained in the cardiac intensive care unit for at least 24 hours and are closely monitored for 48 - 72 hours with particular attention to hemodynamic balance, vascular access, renal function, infections and eventual onset of cardiac conduction disturbances (especially late atrioventricular block). A transthoracic echocardiography was performed 24 - 48 hours after the procedure and pre-discharge. ECG was performed daily during hospitalization. A chest X-ray was performed during the first 24 hours to after TAVI and according clinical need after then. Blood tests were carried out every 8 hours the first day, then every 12 - 24 hours (troponin I, blood count, LDH, total and fractional bilirubin, BUN, creatinine, PT, PTT, INR, AT III). After the procedure, a dual antiplatelet regimen of aspirin 100 mg and clopidogrel 75 mg daily for 3 to 6 months, after which 100 mg of aspirin daily was prescribed indefinitely.

Follow up

Clinical and echocardiographic follow-up was data were collected at 1, 6 and 12 months and yearly thereafter. The clinical follow-up events included death from all causes, cardiac death (including all unexplained deaths), acute myocardial infarction, stroke, cardiac heart failure requiring re-hospitalization, and PPM implantation.

Statistical analysis

SPSS software (release 17.0, SPSS Inc., Chicago, U.S.) was used for all statistical analyses. Data were presented as frequencies and percentages for categorical variables and mean ± standard deviations for continuous variables. We used one way anova or the Wilcoxon signed-rank test to test continuous variables before and after TAVI procedure. All p-values were two-tailed and considered significant if its value < 0.05.

Results

Patients' profile

This study was conducted on 20 patients, their age ranged between 51 to 96 years with a mean age of 83.3 ± 6.7 years.

Risk factors' analysis shows that 4 patients (20%) had peripheral arterial disease, 10 patients (50%) had hypertension, 5 patients (25%) had diabetes, 2 patients had porcelain aorta, 1 patients (5%) had history of TIA, 12 patients (30%) underwent previous PCI, 4 patients (10%) had history of stroke, 5 patients (25%) had history of MI, 3 patients (15%) had underwent CABG, 2 patients (10%) had history of mediastinal radiation.

The mean Euro-Score Logistic for study population was 23 ± 13, the mean STS score was 10.2 ± 9.

There were 2 patients (10%) had porcelain aorta that was evident in the plain chest x-ray and was confirmed using the multi-slice CT angiography for the aorta.

ECG findings showed that 3 patients (15%) had right bundle branch block, 2 patients (10%) had left bundle branch block and 15 patients (75%) had normal sinus rhythm.

Echocardiographic results

Echocardiographic findings before and one-year after TAVI

There was no significant difference between before and after one year of TAVI regarding LVEDV, LVESV, EF% Simp., EDD, ESD, EF% Tech, LVOT (TVI), LVOT D and annulus diameter (P > 0.05). The AV pic. Decreased significantly from 71.14 ± 25.9 before TAVI to 17.8 ± 6.59 after 1 year, the AV mean gradient decreased significantly from 98.9 ± 32.14 to 9.66 ± 3.7, the AV (TVI) increased significantly from

19.7 ± 6.56 to 43.7 ± 10.43 and the aortic valve area increased significantly from 0.74 ± 1.26 to 1.78 ± 0.28 (P < 0.001 for all parameters) (See tables 1 and 2 for before TAVI status).

	Mean	SD
LVEDV	105.62	41.48
LVESV	50.68	35.84
EF simp	57.06	15.35
EDD	54.24	7.89
ESD	36.25	9.53
EF tech	59.30	14.28
AV pic	71.14	25.93
AV (TVI)	98.94	32.41
LVOT (TVI)	19.70	6.56
LVOT D	20.56	3.33
Annulus	21.45	2.01
AV area	0.74	1.26
PAP s	44.63	13.61

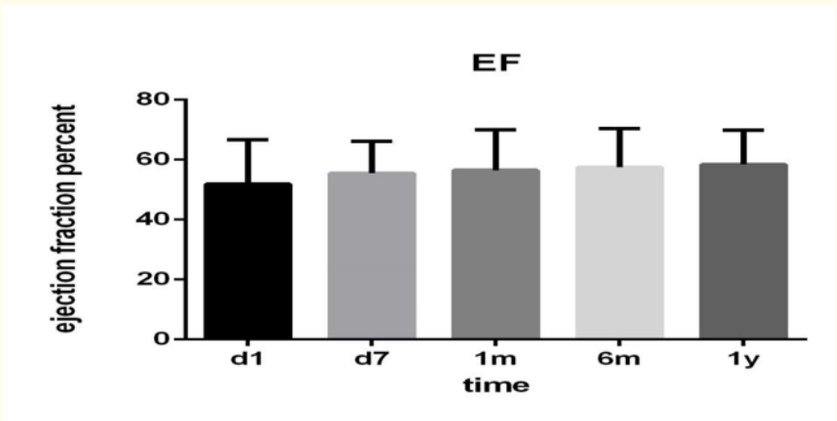
Table 1: *Echocardiographic study before TAVI among all patients.*

LVEDV: Left Ventricular End Diastolic Volume; LVESV: Left Ventricular End Systolic Volume; EF simp: Ejection Fraction by Sampson Method; EDD: End Diastolic Diameter; ESD: End Systolic Diameter; AV: Aortic Valve; TVI: Time Velocity Integral; LVOT: Left Ventricular Outflow Tract; PAPs: Pulmonary Artery Systolic Pressure.

Grade	(n)	%
None	4	20%
I	5	25%
II	5	25%
III	4	20%
IV	2	10%

Table 2: *Mitral regurgitation degree at baseline.*

MR: Mitral Regurge.



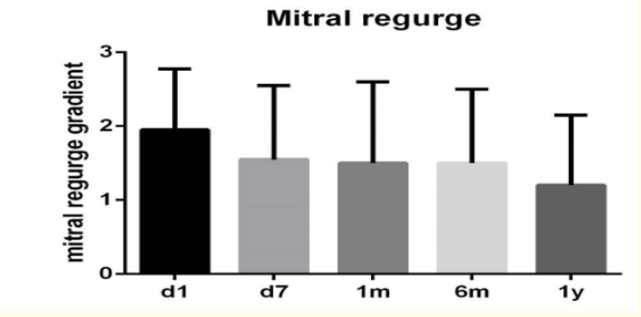
Graph 1: *Showing difference in EF between patients from day 1 to 1 year where p value was in significant (0.5) before and after TAVI.*

MR status before and one-year after TAVI

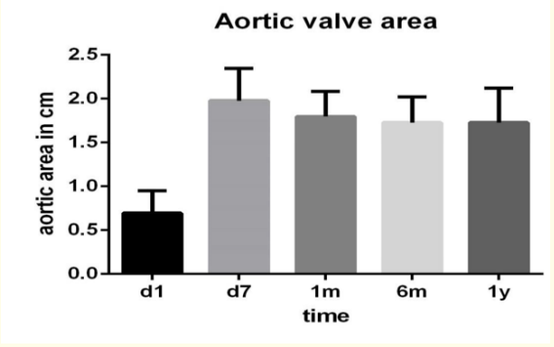
	Regurge grade	N = 20	%	N = 14	%	P value
Ao R	0	3	15%	6	43%	0.157
	1	10	50%	7	50%	
	2	6	30%	1	7%	
	3	1	5%	0	0%	
M R	0	4	15%	7	50%	0.231
	1	6	30%	5	36%	
	2	6	30%	1	7%	
	3	3	15%	1	7%	
	4	1	5%	0	0%	

Table 3: *Aortic and mitral regurgitation grade before and after 1 year of operation.*
Ao R: Aortic Reg; MR: Mitral Regurge.

Before TAVI; 1 patients (5%) had grade 0 mitral regurgitation, 3 patients (30%) had grade 1 MR, 4 patients (40%) had grade 2 MR, 1 patient (5%) had grade 3 MR and 1 patients (5%) had grade 4 MR. 12-month follow-up after TAVI showed that ; 3 patients (30%) had grade 0 mitral regurgitation, 3 patients (30%) had grade 1 MR, 2 patients (10%) had grade 2 MR, 1 patient (5%) had grade 3 MR and 1 patient (5%) had grade 4 MR and this mean that there is significant improvement in the grade of mitral regurgitation after the TAVI procedure. The results showed that there was no significant difference between the 3 groups of patients with different severity of MR regarding all the studied parameters after 1 year (P > 0.05 for all) except in comparison with on year to day 1 where there was significant p value (0.06), even in the pulmonary artery pressure that was reversible after the correction of the mitral regurgitation and this shows that most of the changes in the case of aortic stenosis was secondary to the pressure gradient that cause LV dilatation.



Graph 2: *Where was a significant difference in one year to day 1.*



Graph 3: *Shows significant p value 0f less than 0.0001 between groups.*

12-month mortality after TAVI - risk predictors for patients with MR

	Group 0/I	Group II	Group III/IV	Sig.
Mortality	1	2	3	0.042

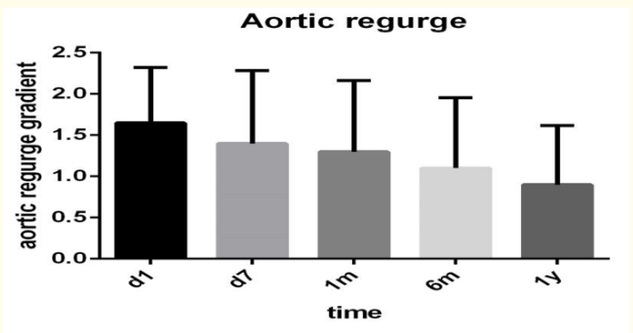
Table 4: *Mortality rate among patients with different grades of mitral regurgitation.*

12-month follow-up after TAVI showed that 6 patients died with an overall mortality rate of 35%. The mortality rate was significantly higher among patients with grade III/IV MR than that of patients with grade II, or grade 0/I MR. (P = 0.042).

The mitral regurgitation did not affect the mortality after one year because the echo data between different groups of mitral regurge became similar, so the effect of mitral regurgitation on mortality is confined to the first one year and after one year the effect on mortality is negligible because there is significant improvement in the magnitude of mitral regurgitation during the first year after the procedure.

In terms of mortality risk predication, patients with different grades of mitral regurgitation had no increase in the risk ratio of mortality 12-month follow-up after TAVI (P > 0.05). As patients with more severe mitral regurgitation had almost the same risk of mortality as patients with less severe degree of mitral regurgitation. In other words, mitral regurgitation severity was not a significant predictors for mortality 12-month follow-up after TAVI: (RR = 1.15, P = 0.66) for grade 0/I, (RR 1.74, P = 0.75) for grade II, and (RR 1.59, P = 0.33) for grade III/IV.

History of balloon aortic valvuloplasty was significant predictors for mortality 12-month follow-up after TAVI (RR for balloon aortic valvuloplasty = 2.746, 95% CI = 1.488 – 5.06, P < 0.001). EuroSCORE logistic > 15 – 30 was a significant predictor for mortality 12-month follow-up after TAVI showed that (RR = 2.6, 95% CI = 1.17 – 5.78, P = 0.019). EuroSCORE logistic > 30 were a significant predictor for mortality 12-month follow-up after TAVI (RR = 2.728, 95% CI = 1.14 – 6.5, P = 0.024). As it was evident from the above data any cause affects the total risk of the patient before TAVI its effect is persistence even after one year.



Graph 4: *Shows significant difference in aortic regurge gradient between groups where p value is 0.004.*

Discussion

In our study, we would like to demonstrate that that MR severity improves after TAVI, especially for those with Moderate to Severe MR.

However, it is important to note that we faced some limitations, such as small number of patients recruited, retrospective data collection, being a single centre experience, using only BE Edward's valves, and relatively short follow-up period for 12-month only with less data on LV functional assessment.

Our experience shows similar results to what have been reported in other studies. Cardiovascular physiology can explain that up on reversing of AS and decreasing LV afterload, there is an abrupt reduction in the LV systolic pressure, which lowers trans-mitral systolic pressure gradient, and consequently, reduces the inertia to cause MR.

Hekimian., *et al.* [2] reported significant early improvement in MR severity in 28% of the patients seven days after TAVI, and no improvement at one-month follow-up. Webb., *et al.* [3] study showed that 24 percent of their patients' MR severity has significantly improved in at discharge and those with moderate to severe MR patients (53%) has decreased in number to 24 percent after 12 month follow-up.

On the other hand, Tzikas., *et al.* [4] reported no significant improvement in MR using color-flow Doppler in early assessment after TAVI, and that their MR condition got more severe (22% versus 17% before TAVI). However, this cannot be conclusive because their study cohort had less patients with moderate to severe MR in comparison to our study, in addition to aetiology of the MR, where in our study we have more patients with functional MR, while in Tzikas., *et al.* [4] more organic MR patients.

Similar to Tzikas., *et al.* [4] and Gotzmann., *et al.* [5] study showed that there was no significant improvement in their patients at their six-month follow-up, when 21% of their patients presented with worsened MR severity, in comparison to 26% who had a non-significant improvement in their MR severity. This can be attributed to similar patients' cohort selection as in Tzikas., *et al* [4].

In our study, aetiology of MR did not impact the improvement of the MR severity, as most of reports describes MR improvement mostly in patients with functional MR [2] and on the other hand, other studies were able to detect such impact [6].

Regarding survival following TAVI in the current study was high and similar to older reports. In a meta-analysis published in 2011, one-year survival was around 76% [7].

Conclusion

The TAVI procedure is feasible for patients with severe MR and most probably it will improve with increased risk of mortality in the first year and then the effect of mitral regurge on mortality is absent after the 1st year.

Our study represents our centre experiences and provides more evidence regarding the improvement of MR severity after TAVI. Such results requires to be furtherly-studied on a larger scale in terms of patient numbers and centres experiences. To allow better prediction of outcomes after TAVI.

Recommendations

To evaluate etiology of mitral regurgitation in patients before TAVI to demonstrate effects on long term mortality.

Bibliography

1. Baumgartner H., *et al*. "Echocardiographic assessment of valve stenosis: EAE/ASE recommendations for clinical practice". *European Journal of Echocardiography* 10.1 (2009): 1-25.
2. Hekimian G., *et al*. "Mitral regurgitation in patients referred for transcatheter aortic valve implantation using the Edwards Sapien prosthesis: mechanisms and early postprocedural changes". *Journal of the American Society of Echocardiography* 25.2 (2012): 160-165.
3. Webb JG., *et al*. "Percutaneous transarterial aortic valve replacement in selected high-risk patients with aortic stenosis". *Circulation* 116.7 (2007): 755-763.
4. Tzikas A., *et al*. "Changes in mitral regurgitation after transcatheter aortic valve implantation". *Catheterization and Cardiovascular Interventions* 75.1 (2010): 43-49.
5. Gotzmann M., *et al*. "Hemodynamic results and changes in myocardial function after transcatheter aortic valve implantation". *American Heart Journal* 159.5 (2010): 926-932.
6. Agnifili M., *et al*. "Interplay between mitral regurgitation and transcatheter aortic valve replacement with the core valve revalving system: a multicenter registry". *Circulation* 128 (2013): 2145-2153.
7. Badano LP., *et al*. "EAE/ASE recommendations for the use of echocardiography in new transcatheter interventions for valvular heart disease". *European Heart Journal* 32.17 (2011): 2189-2214.

Volume 6 Issue 11 November 2019