original article

Clinical outcomes with transcatheter aortic valve implantation at a single cardiac center in Saudi Arabia

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BACKGROUND: Transcatheter aortic valve implantation (TAVI) has been recognized as a valid alternative to surgery for severe aortic valve stenosis (AS) in high-risk surgical patients.

OBJECTIVE: Determine first-year clinical outcomes for TAVI at Madinah Cardiac Center (MMC) in Saudi Arabia.

DESIGN: Retrospective, analytical cross-sectional.

SETTING: Tertiary cardiac care center.

PATIENTS AND METHODS: All patients who underwent TAVI for severe AS between February 2013 and December 2016 were included. Clinical, imaging, and laboratory information at baseline and at one year follow-up were analyzed.

MAIN OUTCOME MEASURES: Clinical and echocardiography outcomes at discharge, at 1-month, and at end of follow-up; one-year mortality, complications and clinical response to TAVI procedure.

SAMPLE SIZE AND CHARACTERISTICS: N=80, mean (SD) age 79.5 (10.6) years, with severe AS and high-surgical risk.

RESULTS: Fifty-five (69.2%) patients received Core valves, and 25 (30.8%) received Edward valves. Peri-procedure mortality was 3.8% and 1-year post-operative mortality was 13.8%. Ten patients (12.5%) had life-threatening or major bleeding. Nineteen (23.8%) patients had vascular complications, which were mostly minor. Fourteen patients (17.5%) developed acute kidney injury and 86% of these patients recovered. Five patients (6.25%) had pericardial effusion. Two patients (2.5%) developed endocarditis and another 2 patients (2.5%) had cerebrovascular accidents. Five patients (6.25%) received pacemakers. Mean aortic valve gradient significantly reduced from a mean (SD) 47.6 (19) mm Hg to 10.7 (6.0) mm Hg ($P<.001$). New York Heart Association functional class was significantly reduced ($P<.001$).

CONCLUSION: The TAVI experience at MCC is encouraging and comparable to international outcomes in terms of success, morbidity, and mortality rate.

LIMITATIONS: Retrospective, relatively small sample size. Rate of minor bleeding was overestimated.

CONFLICT OF INTEREST: None.

Saudi Arabia has seen a steady improvement in socio-economic status and healthcare systems as part of a brisk pace of modernization over the last 4 decades.[1] Consequently, life expectancy, now above 65 years of age, has increased and the population is aging rapidly.[1,2] The percentage of people aged 80 years and above in the total population, is projected to quadruple from 2015 to 2050.[3] Many chronic medical conditions, like diabetes mellitus, hypertension, coronary artery disease, lung disease and cancer frequently coexist in the elderly population, which pose a substantially higher perioperative risk, compared to the younger population.[4-6]

Degenerative aortic valve stenosis (AS) is the most prevalent heart valve disease in the West, affecting 2% to 7% of people above 65 years of age.[7,8] Similarly in Saudi Arabia, the incidence as well as prevalence of AS are expected to increase, due to the increase in life expectancy.[9,10] Until recently, it was common to turn down elderly patients with severe symptomatic AS and comorbidities, due to significant mortality associated with surgical aortic valve replacement (SAVR).[11-13] Studies have shown that TAVI leads to significant improvement in symptoms and survival rate in patients with severe AS, who are considered poor candidates for surgery.[13,14] Furthermore, the Placement of Aortic Transcatheter Valves (PARTNER) II trial, showed similar survival rates between TAVI and SAVR in patients with high-risk severe aortic valve stenosis.[15] In a meta-analysis, survival rates with TAVI were similar to SAVR, in patients with low or intermediate surgical risk.[15] However, TAVI was associated with more pacemaker placements and higher paravalvular regurgitation rates.[15] PARTNER III trial is currently underway to determine whether TAVI is not inferior compared with SAVR in people with severe symptomatic AS, regardless of comorbidities and age.[16]

Since the early days of TAVI in 2007, cardiologists in Saudi Arabia welcomed it as a novel therapeutic approach for patients with severe AS and at high surgical risk, and use of TAVI has spread to several cardiac centers across the country. There was intense competition among these centers for training and experience in the TAVI procedure. The high level of government financial support and the firm belief of Saudi cardiologists in this procedure, in addition to quick build-up of the supportive evidence were responsible for the success of TAVI in Saudi Arabia. Despite the wide acceptance of the TAVI procedure in Saudi Arabia there have been few publications on TAVI from Saudi Arabia, except for a few abstracts.[17,18] Therefore, we sought to describe our experience in TAVI, which was launched in our center early in 2013. The present study aimed to determine the short- and long-term clinical outcomes of TAVI at Madinah Cardiac Center in Saudi Arabia.

PATIENTS AND METHODS

This single-center retrospective study included patients who underwent the TAVI procedure between February 2013 and December 2016, at the Madinah Cardiac Center in AlMadinah Almunawwarh in Saudi Arabia. Patients were considered eligible for TAVI if they had symptomatic AS and were at high surgical risk due to comorbidities. Patients underwent TAVI after a consensus within the institutional Cardiac Care Team comprising a clinical cardiologist, interventional cardiologists, a cardiac surgeon, imaging cardiologist and cardiac anesthetist. All patients included in this analysis provided written informed consent. Baseline investigations included routine blood tests, cardiac markers, chest radiography, electrocardiogram (ECG), transthoracic echocardiography (TTE), transesophageal echocardiography (TEE), selective coronary angiography, aortography, iliofemoral angiography and computed tomography (CT) of the aorta/aortic valve and iliofemoral access. CT was used to evaluate the transfemoral approach. A minimum diameter of 6 mm was required for a CoreValve and Edwards Sapien valves. Tortuosities, as well as the degree and extent of calcifications were assessed to confirm suitability for a femoral approach. CT was the standard method for evaluation of the aortic root anatomy including aortic annulus measurements (diameter and area), the valve morphology (bicuspid or tricuspid), commissural fusion and calcification distribution, sinus maximal diameters across each sinus, sinotubular junction diameter and coronary artery height from the hinge points. Edwards Sapien (Edwards Lifesciences, Irvine, California, USA) or Medtronic CoreValve or Evolute R valves (Medtronic, Minneapolis, Minnesota, USA) were implanted using the transfemoral approach and the standard technique as previously reported. We used a high implantation position (≤5 mm from the annulus) for Core valves.[19,20] Patients stayed in the intensive care unit during the first 24-48 hours after the procedure and were then transferred to the cardiology ward, if there were no complications. Data on clinical history, laboratory investigations, ECG, TTE, TEE, and CT variables were obtained at baseline and discharge. Clinical and echocardiography outcomes at discharge, at 1 month and at the last follow up, were analyzed. Follow up was considered complete one year after the TAVI procedure. Death, stroke, permanent pacemaker (PPM) implantation, endocarditis, valve-related dysfunction paravalvular

leak, and functional status (New York Heart Association (NYHA) classification) were assessed by at least two co-investigators. Vascular complications, stage 1–3 acute kidney injury (AKI), peri-procedural increases in the cardiac enzyme creatine kinase-MB, major or life-threatening bleeding, and minor bleeding were assessed by at least two co-investigators and according to the Valve Academic Research Consortium (VARC-2); recommendations were made whenever applicable.[21] Bleeding was considered minor if there was a decrease in hemoglobin of 1 to 5 g/dL with no clinical or imaging evidence of overt bleeding and no hemodynamic instability. Major bleeding was defined as overt bleeding associated with a decrease in hemoglobin level of at least 3.0 g/dL or requiring transfusion of two or three units of blood. Life-threatening bleeding was defined as overt bleeding associated with a decrease in of hemoglobin ≥5g/dL or requiring ≥4 units of blood transfusion. AKI was defined as stage 1 when serum creatinine increased by 1.5 to 2.0 times the baseline creatinine within 72 hours of the TAVI procedure, stage 2 when serum creatinine increased by >2 to 3 times the baseline creatinine and stage 3 when the rise in creatinine was >3 times the baseline. Vascular complications (dissection, stenosis, perforation, rupture or arteriovenous fistula) were defined as minor when the vascular injury was confined to the access site and not associated with end organ damage, major bleeding, unplanned percutaneous or surgical intervention and/or death. Vascular injury was considered major if it was associated with any of the above mentioned conditions. Death was verified through hospital records and family contacts.

Categorical data were expressed as numbers and percentages, and compared using the chi-squared test or Wilcoxon signed-ranks test, as appropriate. Continuous variables were reported as mean and standard deviation for normal distributions, or as the median with minimum and maximum values for skewed distributions. Differences between means were tested using the *t* test.

RESULTS

The 80 patients included in the study had a mean age of 79.5 (10) years, severe AS of high surgical risk, and a mean Logistic European System for Cardiac Operative Risk Evaluation (EuroSCORE) of 15.0 (13.9) (**Table 1**). All survivors completed one year of follow up. Fifty-four (67.5%) were males, 46 (57.5%) had diabetes, 57 (71.2%) were hypertensive, 19 (23.5%) had renal impairment, and 44 (55%) had coronary artery disease. All patients were symptomatic: 58 (72.5%) in class III-IV and 22 (27.5%) were in class II NYHA functional class. Twenty-eight of 73 (38.4%) patients (data not available in 7) had one or more hospital admissions during the year preceding TAVI. After TAVI only 16 (21.9%) of 73 patients (4 patients subsequently died) required admission during the one-year period post-TAVI. After TAVI there was a significant improvement in NYHA scores, with 50 (72.5%) of 69 survivors in class I and 19 (27.5%) in class II during first year follow up (pre TAVI-NYHA, 2.9 (0.70); post-TAVI-NYHA, 1.3 (0.44), *P*<.001).

Baseline echocardiography parameters were consistent with severe aortic valve stenosis with a mean aortic valve area (AVA) of 0.73 (0.40) cm^2 and mean aortic valve gradient of 47.6 (19) mm Hg. After TAVI, both parameters significantly improved, mean aortic valve area increased to 1.90 (0.60) cm^2 and mean gradient decreased to 10.7 (6.0) mm Hg. Improvement of left ventricular function was evident by a significant improvement in left ventricular ejection fraction (LVEF) from 52.2 (16) to 58.3 (12) (*P*<.001) and global longitudinal strain (GLS) from -11.9 (3.8) to -13.95 (3.3) (*P*<.001). A significant reduction of pulmonary artery systolic pressure (PASP) from 48.9 (15) pre-TAVI to 41.0 (13) post-TAVI (*P*=.004) was observed. Echocardiographic measurements were obtained according to American Society of Echocardiography guidelines (**Table 2**).[22,23]

Table 1. Baseline clinical characteristics (N=80).

Clinical parameter	N (%)
Age (years), mean (SD)	79.5 (10.6)
Gender, male	54 (67.5)
Hypertension	57 (71.2)
Diabetes	46 (57.5)
Renal impairment (serum Cr >120 mmol/L)	19 (23.5)
Coronary artery disease	44 (55)
History of cardiac surgery	9 (11.2)
Obesity (BMI >30)	36 of 78 (46.2)
NYHA functional class	
II	22 (27.5)
III, IV	58 (72.5)
Atrial fibrillation	12 (15)
Signs of congestive heart failure on CXR	41 (51.2)
Logistic Euro-score, mean (SD)	15.0 (13.9)

Cr: creatinine, BMI: body mass index, CXR: chest X-ray.

Table 2. Comparison between echocardiographic parameters before and after TAVI.

Echocardiographic parameter	Pre-TAVI	Post-TAVI	*P* value
Aortic valve area (cm^2)	0.73 (0.40)	1.90 (0.60)	<.001
Aortic valve mean gradient (mm Hg)	47.6 (19.5)	10.7 (6.0)	<.001
LVEF %	52.2 (16)	58.3 (12)	<.001
LV-GLS	-11.9 (3.8)	-13.95 (3.3)	<.001
PASP	48.9 (15)	41.0 (13)	.004

LVEF: Left ventricular ejection fraction, LV-GLS: Left ventricular global longitudinal strain; PASP: Pulmonary artery systolic pressure.

Table 3. Procedural characteristics.

Procedure parameter	Measurement
Type of valve	
Edward	25 (30.8%)
Core	55 (69.2%)
TAVI combined with other angioplasty procedure	26 (32.5%)
Procedure duration (minutes)	36.9 (12.6)
Contrast volume (mL)	135 (54)
Fluoroscopy time (minutes)	23 (9)
Hospital stay (days) (median, range)	9 (4-64)

Data are mean (standard deviation) or number (percentage) unless indicated otherwise.

Fifty-five (69.2%) patients received Core valve or Evolut-R implantations and 25 (30.8%) received Edward Sapien valves. All approaches were transfemoral except one, which was through the left subclavian artery. TAVI was combined with other angioplasty procedures like coronary, aortic or peripheral arteries in 26 (32.5 %) of cases. The mean procedure time was 36.9 (12.6) minutes, fluoroscopy time 23 (9) minutes, mean contrast volume was 135 (54) mL and median duration of hospitalization was 9 (minimum 4, maximum 64) days (**Table 3**). During the TAVI procedure 3 patients (3.75%) died; an additional 8 (10%) died during the one-year follow up according to VARC II definition (**Table 4**).[21] Two patients (2.5%) had life-threatening bleeding, 8 (10%) patients had major bleeding, while most patients 64 (80%) had minor bleeding. Nineteen (23.75%) patients had vascular complications. Minor vascular complications were observed in 18 (22.5%) patients, while a major vascular complication was documented in one patient 1 (1.25%). Pericardial effusion was documented in 5 patients, three of whom died during the procedure and the effusion was related to LV laceration (two) or annular rupture (one) while in the other two patients, the effusion was related to pacemakers with no major consequences. Fourteen patients (17.5%) developed an AKI with an increment of creatinine levels >26.4 µmol/L, compared to baseline.[21] In 11 patients (13.75%) the AKI was stage 1, and in 2 (2.5%) patients were in stage 2 and 1 patient was in stage 3 and needed transient dialysis. Most of patients with AKI (n=12, 86%) recovered renal function. Five (6.3%) patients required PPM implantation, of which 3 were peri-procedural and 2 during follow up. Paravalvular leak was documented using echocardiography in 12 (15%) patients, mild in 10 (12.5%) and moderate in 2 (2.5%). None required additional procedures before the one-year follow up. Two patients (2.5%) developed endocarditis after 6 months of TAVI, which fully responded to antibiotics. Two patients had cerebrovascular accidents (CVA) within two weeks of the TAVI procedure.

DISCUSSION

Our study describes the experience of TAVI procedures in a single Saudi cardiac center. Immediate and one year follow-up clinical outcomes of high-risk patients with symptomatic AS treated with transfemoral TAVI were reported. The mean logistic EuroSCORE of our study population was 15.0 (13.9), which indicates a lower risk than the risk in early TAVI studies like the PARTNE-B trial with a mean logistic EuroSCORE of 26.4%[24] and comparable to the more recent studies like CoreValve US Pivotal High-Risk Study, which had a mean logistic EuroSCORE of 17.6%.[24-26]

All our patients, except one, underwent TAVI through the transfemoral route, which is more favorable than the transapical and other routes since it causes less trauma and can be performed under local anesthesia.[27] On the other hand, transfemoral TAVI carries a higher risk of vascular access complications, needs more volume of contrast and more exposure to radiation compared to transapical.[27-29] However, our TAVI procedures were carried out within an acceptable mean fluoroscopy time of 23 (9) minutes, but the mean amount of contrast required 135 (54) mL, was more than expected. This could be explained by the higher rate (32.6%) of performing TAVI with other angioplasty procedures, compared to other studies.[27-29] In line with almost all TAVI studies, our echocardiography data demonstrated immediate and sustained relief of pressure overload

Table 4. Complications of TAVI procedure.

Complication	Number (%)
Mortality	
Periprocedural	3 (3.8)
During follow up	8 (10.0)
Total	11 (13.8)
Stroke	2 (2.5)
Bleeding	
Major	8 (10.0)
Life threading	2 (2.5)
Acute kidney injury	
Stage 1	11 (13.75)
Stage 2	2 (2.5)
Stage 3	1 (1.25)
Total	14 (17.5)
Vascular complication	
Minor	18 (22.5)
Major	1 (1.25)
Total	19 (23.75)
Myocardial injury[a]	
Pacemaker (2 of 25 in Edwards group, 8%; 3 of 55 in Core valve group, 5.5%)	
Periprocedural	3 (3.75)
During follow up	2 (2.5)
Paravalvular leak	12 (15)
Endocarditis	2 (2.5)

[a]Peri-operative rise of CK MB >20% of baseline.

on the left ventricle, which translated into a significant increase in AVA and LVEF, in addition to significant reduction in the pressure gradient across AV, as well as improvement of PASP.[13-21]

The TAVI procedure has been examined thoroughly in many clinical studies and national registries from the US and Europe. The favorable outcomes in terms of mortality at one year and higher survival rates have been demonstrated clearly.[30-32] The PARTNER-B trial demonstrated that inoperable patients who underwent TAVI had a significantly lower one-year mortality rate compared to patients who underwent standard therapy (30.7% vs. 50.7%, respectively).[30-32] In our study cohort, the one-year mortality of 13.8% was low compared to early TAVI studies (e.g., PARTNER-B); this could be a reflection of the successful progress in TAVI procedure worldwide.[13-15] In addition, the experience of the team, adoption of the most sophisticated safe evidence-based techniques, up-to-date devices and lower-risk patients compared to those in the early TAVI studies could explain the lower mortality as well.[13-15] The improvement in NYHA functional class and reduction in the rate of readmission post-TAVI in our study, were consistent with many previous studies post-TAVI.[30-33] The widely variable incidence (10-30%) reported for major vascular complications has been linked to the risk level of patients who have undergone TAVI.[13,15] Low- and intermediate-risk groups have fewer access site complications (<10%).[34] We noted a low rate (1.25%) of major vascular complications in our cohort, as per the definitions of VARC II; this could indicate that our patients did not belong to the very high-risk group. On the other hand, the rate of minor vascular complication (22.5%) was relatively high as in many early TAVI studies.[13-16,34] The clinically evident stroke rate (2.5%) was relatively low in our cohort compared to early TAVI studies, which reported a 5% stroke rate, but comparable to recent studies with 2.5% stroke rate.[28,34] Stroke was acute (within 72 hours of TAVI), subacute (after 72 hours and within two weeks of TAVI), or late (after 2 weeks) and might be related to the mobilization of atherosclerotic debris from the aorta and aortic valve or from periprocedural atrial fibrillation.[28] The rate of bleeding in our study was comparable to that in previously reported TAVI studies: 8 patients (10%) had major bleeding, and 2 patients (2.5%) had life-threatening bleeding, while minor bleeding was common post-TAVI.[34] The reported incidence of major bleeding events ranges from 2% to 40% and severe life-threatening post-TAVI bleeding varies from 5% to 20%.[35-37] Previous studies indicated a negative impact of bleeding complications on clinical outcome of TAVI patients.[35-37] AKI was observed in 17.3% of our patients, which is consistent with the recently reported 12% to 28% incidence of AKI, post-TAVI.[38,39] AKI was associated with a four times higher post-procedural mortality.[38,39] As observed in our study, data from the PARTNER trial suggest a reduced need for renal replacement therapy after TAVI, compared to medical management (1.2% vs. 1.7%) or surgical replacement of AV (3.8% Vs 4.6%).[13-15] The rate of moderate paravalvular leak in our study was low; 2.5% patients developed moderate paravalvular leak, none developed severe leak or needed further intervention during the follow up. In a recent study by Mack et al,[40] involving PARTNER trial participants, found that moderate or severe paravalvular regurgitation was associated with decreased survival rate.[40] Paravalvular regurgitation was associated with

inadequate balloon expansion, discrepancy between aortic annular size and TAVI device, calcification of the native valve, angle of the left ventricular outflow tract to proximal ascending aorta, and deployment technique.[41] In contrast to the previously reported higher incidence of new PPM implantation with Core valves (15-20%)[28,34] compared to the incidence with Edwards SAPIEN valves (3-10%),[28-34] the total incidence of PPM implantation was lower in the Core valve group (5.5%) compared to the Edwards SAPIEN valve group (8%) in our study. Though it needs to be confirmed by further study with a larger sample size, this observation could be explained by the higher position of the implantation for the Core valve adopted by our team, compared to the reported deeper positioning of the Core valve frame in the left ventricular outflow tract, which has an increased risk of impingement and injury of the septal conduction system. Avoidance of over-sizing could be a factor in the lower rate in PPM implantation as well.[28-34] Consistent with previously reported studies, the incidence of endocarditis in our study was 2.5% during one-year follow-up. Endocarditis was seen at a mean of 6 months after the TAVI procedure, with full response to medical therapy.[30-34,37-40]

In conclusion, our experience with TAVI at a single Saudi center, the Madinah Cardiac Center, is encouraging compared to international experience in terms of clinical improvements, morbidity, and mortality. Low incidence of PPM implantations in the Core valve group of our cohort needs further study in a larger sample size in the future. The relatively small sample and retrospective design prevented more extensive characterization of the cohort characterizations. In addition, some patients from our cohort were referred from elsewhere for TAVI in our center. Those patients had insufficient documentation of preprocedure hospital admission, so some data is missing in our analysis. Minor bleeding was based on the decrease in hemoglobin levels after the procedure compared to baseline despite an absence of clinical notes explaining the blood loss in some cases, which may have overestimated the rate of minor bleeding in our cohort.

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REFERENCES

1. World Health Organization. Global status report on noncommunicable diseases (2014). [internet]. Avaiable from: http:// www.who.int/nmh/publications/ncd-status-report-2014/en/.
2. Total population of Saudi Arabia.[internet]. Available from: Https: // www.statista.com /statistics/262467/total-population of Saudi Arabia/.
3. Wan H, Daniel G, Paul Kl. Census Bureau, International Population Reports, P95/16-1, An Aging World: 2015, U.S. Government Publishing Office, Washington, DC, 2016.
4. Barnett K, Mercer SW, Norbury M, Watt G, Wyke S, Guthrie B. Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. Lancet 2012;380:437.
5. American Geriatrics Society Expert Panel on the Care of Older Adults with Multimorbidity. Guiding principles for the care of older adults with multimorbidity: an approach for clinicians. J Am Geriatr Soc. 2012;60:E1.
6. Global Burden of Disease Study 2013 Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet 2015;386:743.
7. Lung B, Baron G, Butchart EG, Delahaye F, Gohlke-Barwolf C, Levang OW, et al. A prospective survey of patients with valvular heart disease in Europe: the Euro Heart Survey on Valvular Heart Disease. Eur Heart J. 2003,24:1231-43.
8. Nkomo VT, Gardin JM, Skelton TN, Gottdiener J, Scott CG, Enriquez-Sarano M. Burden of valvular heart diseases: a population-based study. Lancet. 2006;368:1005-11.
9. Schwarz F, Baumann P, Manthey J, Hoffmann M, Schuler G, Mehmel HC, et al. The effect of aortic valve replacement on survival. Circulation. 1982;66(5):1105-10.
10. Murphy ES, Lawson RM, Starr A, Rahimtoola SH. Severe aortic stenosis in patients 60 years of age or older: left ventricular function and 10-year survival after valve replacement. Circulation. 1981;64(2 Pt 2):II184-8.
11. Vahanian A, Iung B. The new ESC/EACTS guidelines on the management of valvular heart disease. Arch Cardiovasc Dis. 2012;105:465-7.
12. Iung B, Cachier A, Baron G, Messika-Zeitoun D, Delahaye F, Tornos P, et al. Decision-making in elderly patients with severe aortic stenosis: why are so many denied surgeries? Eur Heart J. 2005;26:2714-20.
13. Leon MB, Smith CR, Mack M, Miller DC, Moses JW, Svensson LG, et al. Partner Trial Investigators. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. N Engl J Med. 2010;363:1597e1607.
14. Kondur A, Briasoulis A, Palla M, Penumetcha A, Mallikethi-Reddy S, Badheka A, et al. Meta-Analysis of Transcatheter Aortic Valve Replacement Versus Surgical Aortic Valve Replacement in Patients With Severe Aortic Valve Stenosis. Am J Cardiol. 2016;117:252e257.
15. Smith CR, Leon MB, Mack MJ, Miller DC, Moses JW, Svensson LG, Tuzcu EM. Partner Trial Investigators. Transcatheter versus surgical aortic-valve replacement in high-risk patients. N Engl J Med. 2011;364:2187e2198.
16. Leon MB, Smith CR, Mack M, Miller DC, et al. The Safety and Effectiveness of the SAPIEN 3 Transcatheter Heart Valve in Low Risk Patients With Aortic stenosis. [Internet]. Available from: https://clinicaltrials.gov/ct2/show/record /NCT02675114.
17. Al-Ahmari S, AL-Amri H, El-Watidi A, et al. One year follow up of patients who underwent transcatheter aortic valve implantation. [abstract]. J Am Coll Cardiol. 2011 April 5;57:14.
18. Masouood A, Al-Ahmari S, Alshurafa H, Alotaibi M, Alkasab S, Alabdallah M, et al. The change in mitral regurgitation severity after trans-catheter aortic valve implantation. J Saudi Heart Assoc 2015;27:10-7.
19. Grube E, Buellesfeld L, Mueller R. Progress and current status of percutaneous aortic valve replacement: results of three device generations of the Core Valve Revalving system. Circ Cardiovasc Interv. 2008;1:167-75[5].
20. Webb JG, Altwegg L, Masson JB, Al Bugami S, Al Ali A, Boone RA. A new transcatheter aortic valve and percutaneous valve delivery system. J Am Coll Cardiol. 2009;53:1855-8.
21. Leon MB, Piazza N, Nikolsky E, Black-

stone EH, Cutlip DE, Kappetein AE, et al. Standardized endpoint definitions for transcatheter aortic valve implantation clinical trials: a consensus report from the Valve Academic Research Consortium. J Am Coll Cardiol. 2011;57:253e269.

22. Baumgartner H, Hung J, Bermejo J, Chambers JB, Evangelista A, Griffin BP, et al. Echocardiographic assessment of valve stenosis: EAE/ ASE recommendations for clinical practice. J Am Soc Echocardiogr. 2009;22:1-23.

23. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, et al. Recommendations for Cardiac Chamber Quantification by Echocardiography in Adults: An Update from the American Society Of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr. 2015;28:1-392.

24. Gilard M, Eltchaninoff H, Iung B, Donzeau-Gouge P, Chevreul K, Fajadet J, et al. Registry of transcatheter aortic-valve implantation in high-risk patients. N Engl J Med. 2012;366:1705-15.

25. Moat NE, Ludman P, Belder MA, Bridgewater B, Cunningham AD, Young CP, et al. Long-term outcomes after transcatheter aortic valve implantation in high-risk patients with severe aortic stenosis: The U.K. TAVI (United Kingdom Transcatheter Aortic Valve Implantation) registry. J Am Coll Cardiol. 2011;58:2130-8.

26. D'Errigo P, Barbanti M, Ranucci M, Onorati F, Covello RD, Rosato S, et al. Transcatheter aortic valve implantation versus surgical aortic valve replacement for severe aortic stenosis: results from an intermediate risk propensity-matched population of the Italian observant study. Int J Cardiol. 2013;167 (5):1945-1952. DOI: http://dx.doi.org/10.1016/j.ijcard.2012.05.028.

27. Aguirre J, Waskowski R, Poddar K, Kapadia S, Krishnaswamy A, McCullough R, et al. Transcatheter aortic valve replacement: experience with the transapical approach, alternate access sites, and concomitant cardiac repairs. J Thorac Cardiovasc Surg. 2014;148:1417e1422.

28. Bleiziffer S, Ruge H, Mazzitelli D, Schreiber C, Hutter A, Bauernschmitt R, et al. Survival after transapical and transfemoral aortic valve implantation: talking about two different patient populations. J Thorac Cardiovasc Surg. 2009;138:1073e1080.

29. Garcia DC, Benjo A, Cardoso RN, Macedo FY, Chavez P, Azi EF, et al. Device stratified comparison among transfemoral, transapical and transubclavian access for transcatheter aortic valve replacement (TAVR): a meta-analysis. Int J Cardiol. 2014;172:e318ee321.

30. Holmes DR Jr, Brennan JM, Rumsfeld JS, Dai D, O'Brien SM, Vemulapalli S, et al. Clinical outcomes at 1year following transcatheter aortic valve replacement. JAMA. 2015;313(10):1019-28.

31. Walther T, Hamm CW, Schuler G, Berkowitsch A, Kotting J, Mangner N, et al. GARY Executive Board. Perioperative results and complications in 15,964 transcatheter aortic valve replacements: prospective data from the GARY Registry. J Am Coll Cardiol. 2015;65(20):2173-80.

32. Duncan A, Ludman P, Banya W, Cunningham D, Marlee D, Davies S, et al. Long-term outcomes after transcatheter aortic valve replacement in high-risk patients with severe aortic stenosis: the U.K. Transcatheter Aortic Valve Implantation Registry. JACC Cardiovasc Interv. 2015;8(5):645-53.

33. Kim CA, Rasania SP, Afilalo J, Popma JJ, Lipsitz LA, Kim DH. Functional status and quality of life after transcatheter aortic valve replacement: a systematic review. Ann Intern Med. 2014;160(4):243-54.

34. Abdel-Wahab M, Mehilli J, Frerker C, Neumann FJ, Kurz T, Tolg R, et al. CHOICE Investigators. Comparison of balloon-expandable vs self-expandable valves in patients undergoing transcatheter aortic valve replacement: the CHOICE randomized clinical trial. JAMA. 2014;311:1503e1514.

35. Konigstein M, Ben-Assa E, Banai S, Shacham Y, Ziv-Baran T, Abramowitz Y, et al. Periprocedural bleeding, acute kidney injury, and long-term mortality after transcatheter aortic valve implantation. Can J Cardiol. 2015;31:56-62.

36. Pilgrim T, Stortecky S, Luterbacher F, Windecker S, Wenaweser P. Transcatheter aortic valve implantation and bleeding: incidence, predictors and prognosis. J Thromb Thrombolysis. 2013;35:456-62.

36. Genereux P, Cohen DJ, Williams MR, Mack M, Kodali SK, Svensson LG, et al. Bleeding complications after surgical aortic valve replacement compared with transcatheter aortic valve replacement: insights from the PARTNER I Trial (Placement of Aortic Transcatheter Valve). J Am Coll Cardiol. 2014;63:1100-09.

37. Borz B, Durand E, Godin M, Tron C, Canville A, Litzler PY, et al. Incidence, predictors and impact of bleeding after transcatheter aortic valve implantation using the balloon-expandable Edwards prosthesis. Heart. 2013;99:860–5.

38. Aregger F, Wenaweser P, Hellige GJ, Kadner A, Carrel T, Windecker S, et al. Risk of acute kidney injury in patients with severe aortic valve stenosis undergoing transcatheter valve replacement. Nephrol Dial Transplant. 2009;24:2175–9.

39. Bagur R, Webb JG, Nietlispach F, Dumont E, De Larochellier R, Doyle D, et al. J. Acute kidney injury following transcatheter aortic valve implantation: predictive factors, prognostic value, and comparison with surgical aortic valve replacement. Eur Heart J. 2010;31:865-74.

40. Mack MJ, Leon MB, Smith CR, Miller DC, Moses JW, Tuzcu EM, et al. 5-year outcomes of transcatheter aortic valve replacement or surgical aortic valve replacement for high surgical risk patients with aortic stenosis (PARTNER 1): a randomised controlled trial. Lancet. 5;385:2477e2484.

41. Detaint D, Lepage L, Himbert D, Brochet E, Messika-Zeitoun D, Iung B, et al. Determinants of significant paravalvular regurgitation after transcatheter aortic valve: implantation impact of device and annulus discongruence. JACC Cardiovasc Interv. 2009;2:821e827