Transcatheter aortic valve implantation in the presence of hematologic malignancies

Hematolojik malignite varlığında transkateter aort kapak yerleştirilmesi

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ABSTRACT

Objective: Cardiac surgery may be performed in patients with hematologic disorders, but carries an increased risk of morbidity. This series describes an experience of transcatheter aortic valve implantation (TAVI) in patients with hematologic malignancies, and highlights the technical considerations to be kept in mind.

Methods: Between June 2011 and April 2014, 133 consecutive high-risk patients with symptomatic severe aortic stenosis were treated with TAVI at our centre. Based on consensus among the local heart team, five patients with hematologic malignancies (myelodysplastic syndrome [2],chronic lymphocytic leukemia [2], Hodgkin lymphoma [1]) were considered high risk for surgery (Logistic EUROSCORE 17.2±14.0% and STS score 5.8±4.3%). Serial echocardiographic and clinical follow-ups were done pre- and post-procedure, at discharge, and at 1, 3, 6 and 12 months.

Results: Our procedural success rate was 80%. Two heart valves were implanted in one patient due to aortic embolization of the previous valve. Perforation of the right ventricle and cardiac tamponade occurred in the same patient. Mean blood transfusion requirement was 1.0±1.4 U (range: 0 to 3 U). Mean aortic valve gradient was reduced from baseline to 9.2±3.27 mmHg, and the effective orifice area was significantly increased to 1.96±0.29 cm^2. Paravalvular aortic regurgitation (AR) was absent-mild in all the patients.

Conclusion: This present series demonstrates that TAVI with a balloon-expandable valve can be performed safely and effectively and is technically feasible in high-risk patients with hematologic malignancies.

ÖZET

Amaç: Hematolojik malignitesi olan hastalarda kalp cerrahisi yapılabilir olmasına karşın artmış mortalite ve morbidite riski taşımaktadır. Bu çalışmada hematolojik maligniteli (HM) hastalarda yapmış olduğumuz transkateter aort kapak implantasyonu (TAKİ) uygulamalarımızı paylaşarak dikkat edilmesi gereken bazı noktaları vurgulamak istedik.

Yöntemler: Merkezimizde Haziran 2011 ile Nisan 2014 arasında TAKİ yapılan yüksek riskli, semptomatik aort darlığı olan ardışık 133 hastanın beşinde ek olarak hematolojik malignite (miyelodisplastik sendrom [2], kronik lenfositik lösemi [2], Hodgkin lenfoma [1]) mevcuttu. Bu hastalar hastanemiz kardiyoloji-kalp damar cerrahi konseyinde değerlendirilerek geleneksel cerrahi için yüksek riskli (Lojistik EUROSCORE: %17.2±14.0 STS skor: %5.8±4.3) oldukları belirlendi. Bu hastalara işlem öncesi ve sonrası, taburculuk esnasında, 1., 3., 6. ve 12. aylarda seri ekokardiyografik ve klinik takip yapıldı.

Bulgular: Akut işlem başarısı %80 idi. Bir hastaya bir önceki kapağın aorta embolize olması nedeniyle ikinci bir kapak takıldı. Aynı hastada daha sonra sağ ventrikül perforasyonu ve tamponat gelişti ve acil cerrahi girişim ile düzeltildi. Ortalama 1.0±1.4 U (aralık: 0 to 3 U) kan transfüzyonu ihtiyacı oldu. İşlem sonrası ortalama aort kapak basınç farkı başlangıç değerlerinden 9.2±3.27 mmHg'ya düşerken efektif kapak alanı ise 1.96±0.29 cm^2'ye yükseldi. Orta-ciddi paravalvular aort yetersizliği hiçbir hastada izlenmedi.

Sonuç: Bu çalışma hematolojik malignitesi olan yüksek riskli ciddi aort stenozu olan hastalarda TAKİ işleminin düşük komplikasyon oranları ile güvenilir ve efektif bir şekilde yapılabilir olduğunu ortaya koymaktadır.

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With the onset of symptoms, the natural history of aortic stenosis (AS) is poor. A significant number of patients with severe AS, however, are not candidates for surgical aortic valve replacement (SAVR) due to pre-existing co-morbidities, frailty or disabilities.[1] Transcatheter aortic valve implantation (TAVI) was developed as a new treatment modality to fill the gap in the treatment of patients who are not amenable to SAVR. A novel technique, TAVI was initiated by Yücel et al. in 2009 in Turkey.[2] Cardiac surgery in patients suffering from malignant hematologic disorders may be performed, but carries an increased risk of morbidity. Open heart surgery requiring cardiopulmonary bypass is especially hazardous because of the necessity for full heparinization and the destructive effects on all blood components. In these patients, an increase in bleeding complications due to anaemia and thrombocytopenia and an increase in susceptibility to infection due to leukopenia is observed.[3]

We report here on a TAVI experience in patients with hematologic malignancies and highlight the technical lessons learned.

METHODS

One hundred and thirty-three TAVIs were performed from June 2011 to April 2014 in our institution. Patient mean age was 78.5±7.2 years with a mean STS of 7.85±5.5 and mean logistic Euroscore of 23.5±16. Patient eligibility and treatment strategy were discussed by the heart team. Written informed consent was obtained from all patients and the local ethics committee approved the procedures. Five patients with hematologic malignancy underwent TAVI for severe symptomatic aortic stenosis using the Edwards SAPIEN XT (ES) balloon-expandable bioprosthesis. All patients selected for TAVI underwent screening, physical examination, transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE), baseline laboratory assays and coronary and peripheral angiography to assess anatomic suitability for TAVI and determine an optimal access strategy. All patients were prospectively followed and their clinical and echocardiographic data were recorded.

TAVI procedure

Aspirin 100 mg, and clopidogrel 300 mg were given prior to the procedure. Bioprosthesis size was determined by computed tomography (CT) angiography. Following general anesthesia (3 patients) and deep sedation (2 patients) and attainment of arterial access, anticoagulation with intravenous heparin was given to achieve an activated clotting time of at least 250–300 seconds. All procedures were performed under fluoroscopic and transesophageal guidance.

Abbreviations:

AS	*Aortic stenosis*
CLL	*Chronic lymphocytic leukemia*
SAVR	*Surgical aortic valve replacement*
TAVI	*Transcatheter aortic valve implantation*
TEE	*Transesophageal echocardiography*
VARC	*Valve Academic Research Consortium*

The femoral artery was surgically cut down (1 patient) or pre-closed (4 patients) with the Prostar® XL (ProStar™ XL10Fr, Abbott Vascular, Abbott Park, IL, USA) device. Then, aortic valvuloplasty was performed through an 18–19 Fr sheath using a balloon undersized to the aortic annulus and rapid ventricular pacing (200/min) to a target systolic pressure of less than 60 mm Hg. Following valve positioning based on fluoroscopy, an Edwards SAPIEN XT balloon expandable bioprosthesis aortic valve (Edwards Lifesciences Ltd, Newbury, Berks, UK) was deployed with rapid ventricular pacing. Percutaneous access and closure were applied in 4 patients and a surgical strategy in one. Before removal of the sheath, selective angiography was performed to assess iliofemoral artery complications. Routine periprocedural antibiotic prophylaxis was given to all patients.

Clinical follow-up

All patients were observed in the coronary care unit for at least 24 h after TAVI. Serial echocardiograms were collected at screening, post-procedure (within 24–48 hours), discharge, and at 1, 3, 6 and 12 months. Clinical follow-up of all patients was obtained over the same time periods. All adverse events were assessed according to the Valve Academic Research Consortium (VARC) classification.[4]

Statistical analysis

Statistical analyses were performed using SPSS software (version 20.0; SPSS Inc, Chicago, IL). Categorical variables are presented as frequency and percentage and were compared using the Pearson chi-square test. Continuous variables are presented as mean±SD for a normal distribution or median (interquartile range [IQR]) for a skewed distribution and compared using the Student's t test or Mann-Whitney U test. Normality of distributions was assessed using the

Shapiro-Wilks test. Statistical significance was defined as $p<0.05$.

RESULTS

The patients included were from the period December 2011 to June 2013. Informed consent forms were signed by 5 patients.

Demographics and baseline characteristics

The patients were elderly (78.4±5.5 years), commonly men (60%) and were severely symptomatic (mean NYHA class was 3–4). Patient baseline clinical characteristics are summarized in Table 1. Patients 1 and 2 were diagnosed with myelodysplastic syndrome (MDS), Patients 3 and 4 with chronic lymphocytic leukemia (CLL) and Patient 5 with Hodgkin lymphoma (HL) stage IV. Since Patients 1 and 2 had leukopenia, anemia and thrombocytopenia prior to the procedure, the hematology department was consulted. It was indicated that an interventional procedure might be performed when the necessary precautions were taken and since all of the patients had more than one year survival. Patients 3 and 4 were CLL stage 0 and had no symptoms. Patient 5 was considered as high risk for surgery by cardiovascular surgeons, and due to this and the need for the patient to undergo chemotherapy as soon as possible, it was decided to perform percutaneous aortic valve replacement. For this purpose, an erythrocyte suspension, a platelet suspension and fresh frozen plasma were prepared prior to the procedure. The logistic EuroSCORE was 17.2±14.0% (range: 6.6 to 41%) and STS score was 5.8±4.3% (range: 2.5±13.5%). Mean body mass index (BMI) was 24.1±2.6 kg/m^2. Two patients had peripheral artery disease. One patient had a history of mitral valve replacement surgery 10 years previously. No patient had coronary angioplasty or coronary artery disease and only one patient had had a cerebrovascular event (stroke/transient ischemic attack). A history of atrial fibrillation was present in 40% of patients. One patient had a permanent pacemaker before TAVI. The incidence of chronic obstructive pulmonary disease, hypertension, diabetes and smoking was 100%, 80%, 20% and 40% respectively.

Table 1. Baseline pre-procedural characteristics of patients

Patient#	All patients (minimum-maximum, mean)
Age, years	75–87 (mean 78.4±5.5)
Sex (Male/Female)	3/2
Body mass index (kg/ m²)	19.8–29.9 (mean 24.1±2.6)
STS score (%)	2.5–16.5 (mean 5.8±4.3)
Logistic EuroSCORE (%)	6.6–32.4 (mean 17.2±14.0)
NYHA functional class 3–4 degree (n)	5/5
Previous cardiac surgery	1/5
Prior myocardial infarction (n)	0/5
Prior percutaneous coronary intervention (n)	0/5
Prior permanent pacemaker (n)	1/5
Prior stroke/transient ischemic attack	1/5
Prior atrial fibrillation (n)	2/5
Peripheral artery disease (n)	2/5
Hematologic malignancy	2 MDS, 2 CLL, 1 HL
Chronic obstructive pulmonary disease (n)	0/5
Diabetes mellitus (n)	1/5
Hypertension (n)	4/5
Smoking (n)	2/5

STS: Society of Thoracic Surgeons; NYHA FC: New York Heart Academy functional class; MDS: Myelodysplastic syndrome; CLL: Chronic lymphocytic leukemia; HL: Hodgkin lymphoma.

Table 2. Pre/post procedural echocardiographic parameters of patients

Parameters	Patient				
	1	2	3	4	5
Pre-procedural					
Left ventricular ejection fraction (%)	65	60	65	38	65
Aortic mean gr (mmHg)	40	54	70	52	44
Aortic valve area (cm²)	0.7	0.9	0.7	0.7	0.6
Systolic pulmonary arterial pressure (mmHg)	40	35	50	50	35
Mitral stenosis	+	–	–	(MVR)	–
Mitral mean gr (mmHg)	3	–	–	5	–
Tricuspid regurgitation (degree)	1	1	2	1–2	1
Right ventricle tapse (cm)	1.6	1.7	2	1.2	1.6
Right ventricular ejection fraction (%)	48	54	50	35	50
Aortic regurgitation (degree)	1	0	0	1	2
Post-procedural					
Left ventricular ejection fraction (%)	65	65	65	55	65
Aortic Mean gr (mmHg)	8	10	9	5	14
Aortic valve area (cm²)	2.1	1.7	2.4	1.9	1.7
Systolic pulmonary arterial pressure (mmHg)	49	45	40	35	30
Mitral stenosis	+	–	–	(MVR)	–
Mitral mean gr (mmHg)	3	–	–	5	–
Tricuspid regurgitation (degree)	1	1	1	1–2	1
Right ventricle tapse (cm)	1.7	1.8	2.2	1.4	40
Right ventricular ejection fraction (%)	54	56	54	1,7	50
Aortic regurgitation (degree)	0	1	1	1	1

MVR: Mitral valve replacement.

Procedural and post-procedural considerations and outcome

Procedural and post-procedural considerations and outcome are given in Table 3. The distribution of implanted valve sizes was; 23 mm (20%), 26 mm (60%), 29 mm (20%). Mean procedure time was 78.8±24.3 minutes. Mean length of stay was 6.8±6.3 days. Procedural success (defined as device success with the absence of periprocedural major cardiovascular events including death, tamponade, coronary artery occlusion in the first 24 h after device implantation) was 80% (4 of 5) as defined by VARC-1. Two heart valves were implanted in Patient 1. Implant failure was related to aortic embolization. Perforation of the right ventricle with cardiac tamponade following temporary pacemaker implantation occurred in the same patient. Following immediate surgical intervention the patient survived. No major vascular complication and one minor vascular complication (pseudoaneuysm requiring compression) occurred. No annulus rupture was observed. Moreover, there were no cases of coronary occlusion. Mean blood transfusion requirement was 1.0±1.4 U (range: 0 to 3 U) (Table 4).

Pre and post-procedural echocardiographic outcomes

The pre- and post-procedural echocardiographic parameters of the patients are summarized in Table 2. Mean left ventricular ejection fraction (LVEF), mean transaortic valvular pressure gradient and mean aortic valve area (AVA) were 58±13% (range: 35 to 65%), 52±11.5 mmHg (range: 40 to 70 mmHg) and 0.72±0.10 cm² (range: 0.60 to 0.90 cm²) respectively. Mean pre-procedural systolic pulmonary artery pressure (sPAP) was 42±7.5 mmHg (range: 35 to 50

Table 3. Procedural and post-procedural considerations and outcome

Patient#	1	2	3	4	5
Aortic annulus (mm)	23	23	21	24	21
Sapien XT size (mm)	26	26	26	29	23
Procedural time (min)	120	80	72	60	62
Closure technique	Prostar	Prostar	Surgery	Prostar	Prostar
Reinflation	No	No	No	No	No
Post-TAVI length of stay (days)	18	6	4	4	3
Valve embolization	Yes	No	No	No	No
Pericardial tamponade	Yes	No	No	No	No
Vascular complications	No	Yes	No	No	No
Transfusion units of blood	3	0	2	0	0
Post-procedural atrial fibrillation	No	No	Yes	No	No

Table 4. Hematologic parameters of patients (Pre/Post-transcatheter aortic valve implantation)

	Patient#				
	1	2	3	4	5
Pre-transcatheter aortic valve implantation parameters					
Hemoglobin (g/dl)	7.7	10.5	12.2	10.8	9.6
Hematocrit (%)	22.4	32.5	35.4	32.3	29.6
Platelet (K/uL)	178	57	124	176	159
White blood cell (K/uL)	3.1	3.420	33.55	92.89	6.44
Neutrophil (K/uL)	1.64	1.02	3.91	4.32	4.85
Lymphocyte (K/uL)	0.79	0.79	28.78	86.72	0.98
Post-transcatheter aortic valve implantation parameters					
Hemoglobin (g/dl)	8.6	9.1	12.9	9.8	9.7
Hematocrit (%)	24.7	28.1	35.6	30.0	28.6
Platelet (K/uL)	112	58	81	91	82
White blood cell (K/uL)	11.04	4.97	39.98	66.65	4.5
Neutrophil (K/uL)	10.19	2.43	9.31	3.57	3.59
Lymphocyte (K/uL)	0.34	0.34	29.71	61.57	0.44

mmHg), with one patient having right ventricle dysfunction investigated by tricuspid annular plane systolic excursion measurement (TAPSE <1.4 cm).

Post-interventional echocardiography was done immediately following the procedure in the operating theatre with TEE, and repeated prior to discharge along with transthoracic echocardiography. Mean aortic valve gradient was reduced from baseline to 9.2±3.27 mmHg and the effective orifice area was increased to 1.96±0.29 cm^2. Paravalvular AR was absent or mild in all of the patients.

DISCUSSION

Average life expectancy has increased in developed and developing communities, bringing with it a significant increase in the incidence of disease at old age. Degenerative aortic stenosis is the most commonly acquired valvular heart disease in adults. In symptomatic patients, SAVR has been the treatment of choice for 40 years.[5] However, among the elderly, up to 30–60%[6,7] of cases are considered too high risk for open heart surgery. Patient selection for TAVI has re-

lied upon an interdisciplinary heart team who collectively determine patient risk for aortic valve surgery.[8,9] These decisions are often based on subjective assessments that incorporate factors beyond those captured in traditional surgical risk assessment tools[10] such as the STS score or the logistic EuroSCORE.[11] Hematologic malignancies are one disease group for which surgery cannot be performed, or performed at a high risk.

Malignancies of the hematopoietic system are encountered in all age groups, but typically in the elderly. This is particularly true for lymphocytic malignancies such as chronic lymphocytic leukemias and lymphomas. Literature on cardiac surgery in patients with hematologic malignancies is extremely rare, and most of what is available reports coronary arterial bypass grafting.[12,13] Open heart surgery in patients with hematologic malignancies is associated with several complications.

Chronic leukemia is a disease characterized by the malignant proliferation of immunologically incompetent lymphocytes. CLL is the most common type of leukemia,[14] and its patients are prone to infection.[15] Performing surgical procedures in the setting of CLL subjects the patient to even further risk of infection.[16]

Over time, it was realized that TAVI saved patients' lives not only by treating severe symptomatic aortic stenosis, but also by making the treatment of some life-threatening diseases possible. One of our patients had Hodgkin lymphoma, which is fatal if left untreated, and could not have chemotherapy due to the hemodynamic instability caused by severe degenerative AS. After TAVI, this patient was able to have chemotherapy.

Hematologic malignant diseases, especially of the lymphocytic type, mainly affect elderly patients. Over the past few years, treatment options have continued to improve and many patients with these disorders have several years of survival. Literature on cardiac surgery in patients with hematologic malignancies is extremely rare, and most of what is available reports coronary arterial bypass grafting.[12,13]

The literature contains very few case presentations on the performance of aortic valve surgery on patients with hematologic malignancies, while there are no publications on the use of the TAVI in these cases.

Patients with hematologic malignancies may undergo cardiac operations with acceptable results. However, the high perioperative morbidity rates should be kept in mind during patient selection. Because of the high risk profile, it appears reasonable to consider alternative treatment options when indications permit.

The present series demonstrates that TAVI with a balloon- expandable Edwards SAPIEN XT valve can be performed safely and effectively and is technically feasible in high-risk patients with hematologic malignancies. Issues to be considered in such patients are working in close cooperation with hematology and determining the patient's net erythrocyte, leukocyte and platelet count, using a peripheral smear, taking necessary precautions according to the patient's cell count prior to the procedure, and performing pre-procedural erythrocyte or platelet replacement on these patients if necessary.

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