TRANSCATHETER AORTIC VALVE IMPLANTATION IN PATIENTS WITH LEFT ATRIAL APPENDIX THROMBUS

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Aim. The transcatheter aortic valve implantation (TAVI) which developed in the recent years has become an alternative for surgery. However, in spite of new developments the process based vascular and neurological complications still remain to be a problem with elderly patients who also tend to have many co-morbid conditions. With this study we aimed to evaluate the TAVI efficacy and reliability on patients with scarcely relative contraindication and with intracardiac thrombus who are mostly left out of the study.

Methods and Results. There has been a successful TAVI process conducted in our clinic for antiplatelet and anticoagulation for 6 cases in which thrombus was seen in left atrial appendix (LAA) via transesophageal echocardiography (TEE) and which are not suitable for surgical valve replacement due to atrial fibrillation (AF) and severe AS comorbid reasons. Edwards SAPIEN XT valve was implanted to all patients transfemorally with general anaesthesia. The process was facilitated successfully and no major/minor stroke was observed in post-process early period, and 9 month controls, in average.

Conclusion. Other than AS, also AF, whose frequency increases with age, is an important risk factor for neurological complications. In patients who has AF and AS the source of the cardioembolic focus is mainly LAA. The post-TAVI antiplatelet and anticoagulation treatment is not clear for these patients. We tried to show that TAVI process is reliable in terms of the risk of stroke, in careful processing and suitable anticoagulation treatment for the patients with AF, AS and LAA in this first case study in literature, as far as we know.

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Key words: transcatheter aortic valve implantation, atrial fibrillation, left atrial appendix, thrombus, stroke.

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ТРАНСКАТЕТЕРНАЯ ИМПЛАНТАЦИЯ АОРТАЛЬНОГО КЛАПАНА У ПАЦИЕНТОВ С ТРОМБОЗОМ УШКА ЛЕВОГО ПРЕДСЕРДИЯ

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Цель. Транскатетерная имплантация аортального клапана (ТИАК), которая развивалась в последние годы, стала альтернативой для хирургии. Однако, несмотря на новые разработки, сосудистые и неврологические осложнения, лежащие в основе процесса, по-прежнему остаются проблемами у пожилых пациентов, которые, как правило, имеют много сопутствующих заболеваний. В данном исследовании мы стремились оценить эффективность и надежность ТИАК у пациентов с опасными противопоказаниями и с внутрисердечными тромбами, которые в большинстве случаев не включаются в исследования.

Методы и Результаты. Имелись успешные ТИАК, проведенные в нашей клинике для антитромбоцитарного и антикоагулянтного лечения 6 случаев, в которых тромб был замечен в ушке левого предсердия (LAA) с помощью чреспищеводной эхокардиографии, и которые являются не пригодными для выполнения хирургической операции по замене клапана вследствие фибрилляции предсердий (ФП) и тяжелого стеноза аорты (СА). Клапан Edwards SAPIEN XT был имплантирован всем пациентам трансфеморально под общей анестезией. Процесс был успешно проведен и не было отмечено большого/малого инсульта в раннем пост-операционном периоде, а также во время 9-месячного контроля, в среднем.

Заключение. СА, как и ФП, чья частота увеличивается с возрастом, являются важным фактором риска развития неврологических осложнений. У пациентов, которые уже имеют ФП и СА, кардиоэмболический акцент делается, в основном на LAA. Антитромбоцитарное и антикоагулянтное лечение после ТИАК для этих пациентов — не ясно, Мы постарались показать, что операция ТИАК является надежной с точки зрения риска инсульта, при тщательном уходе и подходящей антикоагулянтной терапии для пациентов с ФП, СА и тромбом в LAA, что в литературе впервые описано, насколько нам удалось установить.

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Ключевые слова: транскатетерная имплантация аортального клапана, мерцательная аритмия, левого предсердия приложение, тромб, инсульт.

Introduction

The frequency of aortic stenosis (AS) gradually increases along with the increase in the life span. AS is seen in abut 2–4% of the age >65 years population in Europe and North America [1]. Surgical aortic valve replacement (SAVR) is done by low operative mortality on the absence of severe comorbid conditions. Recovery of symptoms and increase in life spans are seen in patients who have AVR. Accordingly, 30% of the patients cannot have SAVR due to left ventricular dysfunction, older ages and comorbid conditions [2]. First transcatheter aortic valve implantation (TAVI) application on humans in 2002, developed in a fast manner to become a significant treatment option for surgery in inoperable patients or those who has high risk. According to the only randomized clinical study on this issue, PARTNER study, it has been shown that TAVI is superior to treatment in inoperable patients and could be a significant alternative in SAVR in patients carrying high risk [3, 4]. As well as it is a less invasive process when compared to surgery, major vascular complications and stroke is seen more often in TAVI process when compared to a surgical group. TAVI relative stroke risk increases when there are risk factors such as intensified calcification in valve, atheroma burden on aortic arch, elderly age, carotid artery stenosis, atrial fibrillation (AF) and intracardiac thrombus [5]. Therefore pres-

ence of thrombus within the intracardiac or left ventricular is indicated as exclusion criteria in choosing the patients for TAVI in the recent published studies [6, 7]. However, there is no data regarding the presence of thrombus in left atrial appendix (LAA).

Thus, in this study we aimed to show the reliability of TAVI process in terms of the risks of stroke along with appropriate anticoagulation and careful interference on patients with in AF, severe AS and thrombus LAA. In our knowledge this publication is the first study in the literature.

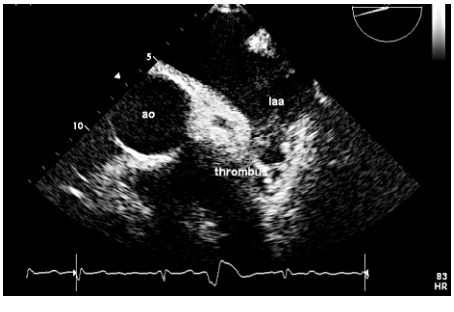
Material and methods

In our clinic TAVI process was applied to high risk carrier 70 patients with severe calcific AD and comorbid causes for surgical valve replacement between the dates July 2011 and December 2012. TEE was applied to 66 patients, not to the other 4 (one having oesophagus stenosis, the other having oesophagus varicose and the last two was undergone local anaesthesia) before the process. Thrombus presence was found via multi slice computerized tomography (MSCT) and TEE presence LAA in 6 of the patients (Fig. 1 and 2A-B). Fourth of the patients were female as 2 of them were male and the age average was 76 years. Basal characteristics of the patients and data regarding the TAVI process are given on Table 1. In echocardiography the average valve area was determined to be 0,7 cm^2, and the average mean gradient to be 50,6 mmHg. One of the patients had coronary artery disease which required revascularization and asymptomatic carotid artery disease in right internal carotid artery which caused 80% stenosis. A bare metal stent was implanted to the severe stenosis in the patient's circumflex artery before TAVI. Another patient had a mitral valve replacement 10 years ago and wasn't receiving an enough anticoagulation treatment. All of the patients were carrying high risk in terms of surgical means and they were accepted to be inoperable by the evaluations done by the cardiovascular surgeons. All patients were informed and their approval was taken before the process. An ethical approval was granted from the ethical committee of our hospital. TEE and MSCT were done to all of the patients before the process and it was evaluated for their compliance and additional pathology in valve morphology, aortic annulus, coronary ostium-annulus distance, calcification degree, and peripheral arteries. All six of the patients, thrombus was identified in LAA via TEE, MSCT. TAVI process was planned for all patients via transfemoral ways. Warfarin treatment was stopped for the patients who were previously using warfarin due to AF or mitral valve replacement, and enoxaparin 1 mg/kg treatment was started as two doses a day for the bridge treatment before the process. Along with this acetylsalicylic acid (ASA) and clopidogrel treatment was started for all of the patients. TAVI was applied when the international normalize ratio (INR) value was determined to be <1,5. For the appropriate access route was specified both doing MSCT and peripheral angiography before TAVI. TAVI was done transfemorally by using 14F Prostar XL (Prostar™ XL14Fr; Abbott Vascular, Abbott Park, IL, USA) vascular closing device for all 6 cases and under general anaesthetics along with TEE. During the process it was heparinised together to obtain the activated clotting time of the patients to be 250–300 seconds. Edwards SAPIEN XT (Edwards Lifesciences, Irvine, CA, USA) valve was implanted in an appropriate position to be 23 mm in four patients, 26 mm in one and 29 mm in the other patient.

Figure 1. Image of thrombus in left atrial appendix (showed with an arrow) via multi slice computerise tomography.

Results

The process was finished successfully for all of the patients. No post-TAVI vascular complication was observed. As no bleeding was observed in none of the patients, one patient was treated with a unit of erythrocyte suspension and the other was treated with two units, after the process. The patients were evaluated by the neurology



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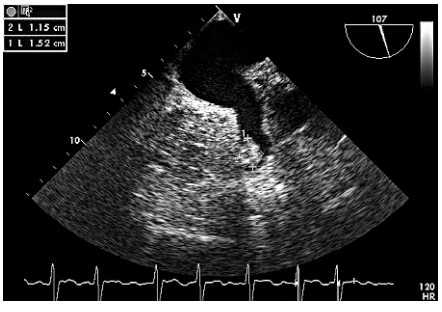

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Figures 2A and B. Images of thrombus in left atrial appendix via transoesophageal electrocardiography.

Table 1

Basal characteristics of the patients

Characteristics	1st Case	2nd Case	3rd Case	4th Case	5th Case	6th Case
Age	81	70	73	80	81	70
Gender	Female	Female	Male	Female	Female	Male
STS score	12,8	10,3	13,5	12,3	12,9	13,7
Logistic EURO score	31,87	39,7	56,23	26,38	29,49	30,06
NYHA	3	4	3	3	3	4
CVD	No	Yes	No	No	No	No
AVA cm^2	0,5	0,8	0,7	0,7	0,8	0,7
Aortic Valve mean gradient (mmHg)	72	41	52	51	47	41
LVEF%	65	45	35	65	65	25

Abbreviations: STS — Society of Thoracic Surgeons, NYHA — New York Heart Association, CVD — cerebrovascular disease, AVA — aortic valve area, LVEF — left Ventricular Ejection Fraction.

department after the process. The patient follow-ups showed no major/minor stroke development. The aortic valve average mean gradients were measured to be 9 mmHg after the process. None of them showed any moderate or severe paravalvular aortic regurgitation. Warfarin treatment was started after the process and INR was tracked to be 2.0–2.5 for 1 month under warfarin+clopidogrel dual treatment. After a month clopidogrel treatment was stopped and warfarin treatment was continued. No major or minor stroke was observed or no moderate or severe paravalvular aortic deficiency was developed according to the patient follow-ups of approximately 9 months (6 patient follow-ups, respectively 16, 15, 8, 8, 7, 2 months). All of the patients showed significant improvements in their functional capacities and no major undesired event was developed during the follow-ups.

Discussion

In our publication which is the first study in the literature, we presented the successfully applied TAVI process without developing any stroke on the patients with thrombus in LAA and AF. Rhythm of all 6 patients to which TAVI was applied was AF and thrombus presence in LAA was seen in the TEE and MSCT conducted. No major/minor stroke was observed for neither of the patients as a result of the appropriate coagulation and successful process. No major adverse event (death, stroke, myocardial infarction, haemorrhage) during the 9 month follow-ups of the patients.

AS is a degenerative disease whose frequency increases gradually in the elderly and which decreases the survival rate in a fast manner as it becomes symptomatic. A certain treatment is the valve replacement. Although, the rates of the patients which cannot be operated to get a surgical valve replacement is 30–40% due to an elderly age and frequency of comorbid conditions [2]. It was first said in European Society of Cardiology (ESC) latest valve guidelines that TAVI process, which was first started to be applied on humans in 2002 and took place in the real world due to its fast development, can be an alternative to SAVR on patients carrying high risk [7]. However, in spite of these developments some patient groups cannot be benefitted enough from this treatment. The latest ESC valve guidelines included the ones having thrombus within the left ventricular in the absolute contraindications group. Intra cardiac thrombi were listed in the contraindication group within the latest American College of Cardiology (ACC) TAVI consensus. However, it does not mention the ones having left atrium or LAA thrombi. Although, overall proneness is to refrain to conduct this on these patients [3, 6, 7]. While determining the major stroke rates of 3.8% on day 30 and 5.1% on year 1 in cohort A from the PARTNER study, which is the only randomized controlled study, the cohort B showed major stroke rates to be 5% on day 30 and 8.4% on year 1. Along with this, within the studies done with diffusion-weighted magnetic resonance imaging the rates of silent ischemia was found to be 68–84% (DW-MRI) while the clinical importance of silent ischemia was not stated to be clear. It is known that the half of the stroke were related to the procedure and the other half develops within the 12 months after the procedure, and the post-process high risk period for stroke is the first 24 hours [3,9,10]. Emboli might be observed in every stage of the TAVI process such as left heart catheterisation, catheter manipulations, thrombus formation around the catheter or the sheath, calcified aortic valve tear up during balloon valvuloplasty, valve position and implantation and the extended time period after the process [11]. Age, hypertension, diabetes, calcified ascending aorta, female gender, story of stroke, AF and the degree of the atheroma plates in the aortic arch are included in the risk factors for emboli [6,12]. New AF related to TAVI which causes an increase in post procedural stroke risk for 3.9 times was determined to be 7.5% in the transfemoral arm, 11.5% in the transapical arm of cohort A, and 0.7% in cohort B of PARTNER [3,12].

AS and AF are both conditions that are highly probable to be found together and that increases in frequency as the age gets older. AF is responsible for most of the neurological complications seen in elderly ages and the cardioembolic focus is mainly on the thrombus in LAA. The effect and

reliability of anticoagulation towards the prevention of thromboembolism in AF is known for many years. In spite of this there is no standardized anticoagulation protocol for the TAVI applied patients having AF yet. In order to achieve a successful process in TAVI the TAVI related stroke risk should be minimised. In order to obtain this it should start with a pre-TAVI patient evaluation. Along with this, since the potential TAVI patients hold for many risk factors for cerebrovascular events, the risk classification and transfemoral/transapical approach should be specified by using all the techniques in imaging [11]. We have done risk evaluations for the patients by applying TEE, MSCT and peripheral angiography in terms of both appropriate access route determination and emboli. Appropriate antiplatelet and anticoagulation to be done before and after the process are the building blocks of the treatment. In our cases clopidogrel and warfarin was given for one month for the INR to be 2.0–2.5, and only warfarin treatment was applied after a month. Additionally new emboli protecting devices are being developed (e.g., Embrella [Edwards Lifesciences, Inc., Irvine, CA, USA], Claret [Claret Medical, Inc. Santa Rosa, CA, USA], SMT Embolic Deflection Device) in order to prevent process related emboli and the human studies regarding these are promising [12].

As far as we know no TAVI case is found for patients with AF and thrombus in LAA in the literature. There is only one statement for 2 cases of having AF along with either AS and no thrombus in LAA. As there were warfarin contraindication in these cases TAVI and LAA shut down process was applied in one to be within the same session and in the other one to be in different sessions [13,14]. Since there was no warfarin contraindication in our cases, after the process was successfully finished the follow-ups continued under the treatment of warfarin.

Conclusion

TAVI is a developing treatment method which shows a promise to be an alternative to surgery in the treatment of patients with symptomatic severe AS. Along with the technology, and the upcoming developments in valve systems, procedural techniques and periprocedural treatments it can be applied more safely. Along with the operators to become more familiar with TAVI and the new upcoming studies the groups that will benefit from this treatment can be better identified. With this study we have shown that TAVI can be safely applied without observing any early or late stage stroke on patients with atrial fibrillation, advanced age and thrombus in LAA, which are significant risk factors for stroke. However, the reliability of TAVI would be stated more clearly for these patients with randomized controlled studies which more patients attend to and holding for a longer follow up time period.

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