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Effect of transcatheter aortic valve implantation on QT dispersion in patients with aortic stenosis

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Abstract

Background QT dispersion (QTd) is a predictor of ventricular arrhythmia. Ventricular arrhythmia is an important factor influencing morbidity and mortality in patients with aortic stenosis. Surgical aortic valve replacement reduced the QTd in this patients group. However, the effect of transcatheter aortic valve implantation (TAVI) on QTd in patients with aortic stenosis is unknown. The aim of this study was to investigate the effect of TAVI on QTd in patients with aortic stenosis. **Methods** Patients with severe aortic stenosis, who were not candidates for surgical aortic valve replacement due to contraindications or high surgical risk, were included in the study. All patients underwent electrocardiographic and echocardiographic evaluation before, and at the 6th month after TAVI, computed QTd and left ventricular mass index (LVMI). **Results** A total 30 patients were admitted to the study (mean age 83.2 ± 1.0 years, female 21 and male 9, mean valve area 0.7 ± 3 mm^2). Edwards SAPIEN heart valves, 23 mm (21 patients) and 26 mm (9 patients), by the transfemoral approach were used in the TAVI procedures. All TAVI procedures were successful. Both QTd and LVMI at the 6th month after TAVI were significantly reduced compared with baseline values of QTd and LVMI before TAVI (73.8 ± 4 ms *vs*. 68 ± 2 ms, $P = 0.001$ and 198 ± 51 g/m² *vs*. 184 ± 40 g/m², $P = 0.04$, respectively). There was a significant correlation between QTd and LVMI ($r = 0.646$, $P < 0.001$). **Conclusions** QTd, which malign ventricular arrhythmia marker, and LVMI were significantly reduced after TAVI procedure. TAVI may decrease the possibility of ventricular arrhythmia in patients with aortic stenosis.

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1 Introduction

QT dispersion (QTd) is the maximum inter-lead variation between the longest and shortest QT intervals recorded in the standard 12-lead electrocardiogram (ECG). It reflects in-homogeneity of myocardial repolarization.[1] Also, QTd could be applied as a potential prognostic tool in the detection of future ventricular tachyarrhythmic events and death.[2,3]

Aortic stenosis (AS) is the most common acquired valvular disease in elderly populations and its prevalence is rising in adults with advanced age.[4] Furthermore, symptomatic patients with severe AS have a high mortality rate.[5] Left ventricular hypertrophy due to chronic pressure load is a risk factor for ventricular arrhythmias and sudden cardiac death.[6] Increased QTd has been reported in patients with AS and it has also been considered as a potential marker for ventricular arrhythmic homogenicity and mortality. Surgical aortic valve replacement (AVR) is the gold standard treatment in patients with severe AS and has been reported to reduce QTd.[7] Transcatheter aortic valve implantation (TAVI) is an alternative procedure for patients who are not candidates for AVR.[8] However, the effect of TAVI on QTd has never been previously investigated. Therefore, the aim of this study is to investigate the effect of TAVI on QTd in patients with severe AS.

2 Methods

2.1 Study population

This prospective and observational study was conducted from January 2012 to December 2013. We enrolled 51 patients scheduled for TAVI with severe AS and who have NYHA 3–4 symptoms. Patient characteristics, including age,

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sex, weight, height and concomitant medications, were collected for all patients. Twenty-one patients were excluded from the study because they exhibited at least one exclusion criteria. Exclusion criteria for patients were as follows: coronary artery disease; atrial fibrillation or flutter; frequent (> 10/min) ventricular extra-systoles, sinus or AV node dysfunction; permanent cardiac pacemaker; abnormal serum electrolyte levels; congenital long-QT syndrome; taking any drugs influencing QT dispersion and use of antiarrhythmic drugs. Finally, our study population consisted of 30 subjects with symptomatic severe aortic stenosis.

2.2 Study protocol

All patients were evaluated by a dedicated, multidisciplinary heart team. Clinical decision-making was based on a multimodality screening assessment, including evaluation of surgical risk by logistic EuroSCORE > 20% or Society of Thoracic Surgeons score > 10%. All patients with symptomatic aortic stenosis, who were not candidates for AVR because of high surgical risk, were referred to TAVI. Clinical, electrocardiographic and echocardiographic parameters were recorded for all patients. QTd and echocardiographic variables, obtained during the pre-procedural period, were compared to the 6th month follow up data on the same patients.

2.3 Electrocardiography

Standard 12-lead ECG (25 mm/s) was recorded after a 10 min rest in the supine position before and at 6 months after TAVI. The QTd calculation was manually performed by two independent cardiologists who were blind to the patient data. The compatability of QTd were asked to stastistical analyse. If there was a difference on the results of QTd, final decision was made by consensus. The QT interval was measured from the onset of the QRS complex to the end of the T wave. In the presence of a U wave, the end of the T wave was accepted as the nadir between T and U waves. The mean of three consecutive interval measurements was used in the analysis. QTd was calculated as the difference between the longest and shortest QT interval measured in each individual ECG lead.

2.4 Echocardiography

Patients were evaluated with standard transthoracic M-mode and two dimensional echocardiographic studies before and after the TAVI procedure. Left ventricular diastolic and systolic dimensions, ventricular septal and posterior wall thicknesses were measured at the level of the tips of the mitral valve leaflet. Left ventricular mass index was calculated according to the formula: left ventricular mass index = 1.04 [(LVID + PWT + IVST) × 3 − (LVID) × 3] − 13.6 g/BSA.[9] Severe aortic stenosis was described as a mean aortic valve gradient of ≥ 40 mmHg, or an aorta valve area (AVA) of ≤ 1 cm^2.[10]

2.5 TAVI procedure

All TAVI procedures were performed under local anesthesia and deep sedation in the hybrid operating room. The transfemoral access was accomplished by puncture of the common femoral artery under fluoroscopic guidance in all patients. After insertion of the delivery sheath, balloon aortic valvuloplasty was performed with rapid ventricular pacing for both balloon sizing and stenotic valve dilatation. Subsequently, an Edwards SAPIEN heart valve was deployed with rapid ventricular pacing after the valve positioning based on fluoroscopy. Anti-thrombotic therapy with aspirin (100 mg) and clopidogrel (75 mg) was recommended up to one month and aspirin was continued alone after the first month control.

2.6 Statistical analysis

Continuous variables were expressed as mean ± SD and categorical variables were expressed as percent. The normal distribution of values was assessed by using Kolmogorov-Smirnov test and histogram. Paired-*t* test and Wilcoxon-rank test were used for continuous variables, when appropriate. Pearson or Spearman correlation coefficients were used to assess the relationship among the parameters, when appropriate. A *P*-value of less than 0.05 represented a statistically significant result. Statistical analysis was carried out using SPSS statistical software (SPSS 16.0, IL, USA).

3 Results

A total of 51 consecutive patients were enrolled in the study. After excluding 21 patients (10 patients had severe coronary artery disease, 6 patients had paroxysmal atrial fibrillation, 4 patients used antiarrhythmic drugs and one patient died because of stroke on fifty-fourth days in follow up), 30 patients were included in the final statistical analysis. TAVI was successfully performed in 21 (70%) women and 9 (30%) men without severe complications during the hospital stay and follow-up period. Demographic characteristics of the study population are presented in Table 1. Echocardiographic, electrocardiographic and clinical parameters before and after TAVI are found in Table 2. There were no differences the duration of P, PR, QRS, QT and QTc, QRS axis and heart rate before and after TAVI. However, TAVI caused a significant reduction in QTd in six month (Figure 1). Likewise, there were a significant decrease in both left

Table 1. Demographic features of study population.

	Mean ± SD	*n* (%)
Age	83.2 ± 4.1	
STS Score	22.3 ± 11.7	
LOGİSTIC EURO Score	24.6 ± 8.9	
BMI, kg/m^2	28.1 ± 6.5	
Gender, women		21 (70%)
DM		12 (40%)
Hypertension		25 (83%)
Valve size (23 mm)		21
Valve size (26 mm)		9

BMI: body mass ındex; DM: diabetes mellitus; STS: Society of the Thoracic Surgeons.

Table 2. Electrocardiographic, echocardiographic and clinical features.

	Before TAVI (*n* = 30)	After TAVI (*n* = 30)	*P*
Heart rate	77.0 ± 8	78 ± 5	0.3
P duration	94.8 ± 10.3	94.3 ± 7.6	0.5
PR interval	141.3 ± 27.2	143.4 ± 28.8	0.6
QRS duration	86.6 ± 14	87 ± 12	0.7
QRS axis	10.5 ± 36	10 ± 34	0.6
QT	409 ± 34	405 ± 24	0.4
QTc	440 ± 24	438 ± 21	0.4
QTd, ms	73.8 ± 14	68 ± 12	0.001
QTcd, ms	75 ± 14	69 ± 12	0.001
AVA	0.7 ± 0.3	–	–
Mean gradient, mmHg	51.9 ± 10.6	11.3 ± 3.4	< 0.001
EF, %	59.4 ± 9.4	60.8 ± 7.02	0.1
IVS	1.48 ± 0.1	1.45 ± 0.1	0.05
PW	1.45 ± 0.1	1.34 ± 0.1	0.5
LVMI, g/m²	198 ± 51	184 ± 40	0.04
NYHA 3-4 Symptom	30	3	< 0.001

AVA: aorta valve area; EF: ejection fraction; IVS: interventricular septum thickness; LVMI: left ventricle mass index; NYHA: NewYork Heart Association; QTcd: corrected QT dispersion; QTd: QT dispersion; TAVI: transcatheter aortic valve implantation.

ventricular mass index (198 ± 51 g/m² *vs*.184 ± 40 g/m², P = 0.04). In correlation analysis, a significant relationship was found between LVMI and QTd (r = 0.646, P < 0.001).

4 Discussion

In the present study, we investigated the effect of TAVI on QTd in patients with symptomatic severe AS. We found that QTd has reduced after TAVI procedure by the 6th month in patients with severe aortic stenosis.

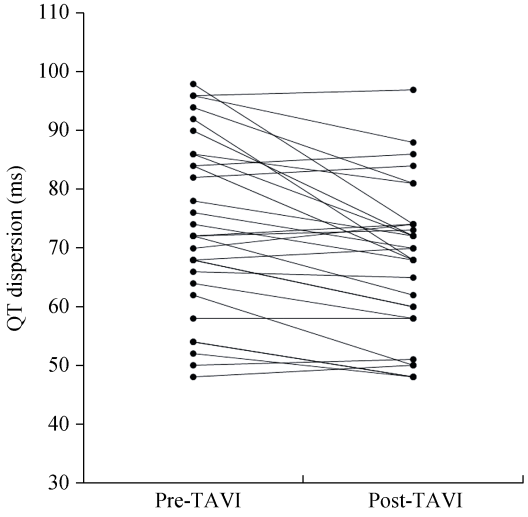

Figure 1. QT dispersion values for each patient before and after TAVI. TAVI: transcatheter aortic valve implantation.

QT dispersion is a non-invasive method which reflects a regional heterogeneity of ventricular repolarization pattern.[1] It has been reported that prolonged QTd correlates with the incidence of ventricular tachyarrhythmias and the risk of sudden death. Many disorders, such as ventricular hypertrophy, myocardial ischemia, autonomic neuropathy, electrolyte imbalance as well as anti-arrhythmic drugs, can lead to impaired repolarization homogeneity and prolonged QTd.[11]

World wide, aortic valve disease is the most common acquired valvular disease. It is well known that AS in adults has a progressive course with a long asymptomatic period.[4] The average survival period from the onset of symptoms to the time of death was approximately two years with heart failure, three years with syncope, and five years with angina.[12] Surgical AVR is currently the gold-standard treatment for patients with severe symptomatic AS. However, some patients with symptomatic severe AS are not candidates for surgery because of contraindications, or co-morbidities. They are considered as inoperable or at too high risk for surgery. TAVI is now a well-established alternative technique for these inoperable, or high risk patients.[13,14]

Malignant ventricular arrhythmias play an important role in syncope and sudden cardiac death in patients with symptomatic AS.[15] Several studies show that ventricular arrhythmia are frequent in patients with AS compared with control subjects. In the late 1960s, Schwartz, *et al*.[16] investigated electrocardiograms of patients with AS before, during, and after the development of syncopal seizures. They detected malign ventricular arrhythmias during syncopal

attack. Klein, *et al*.[17] also evaluated the frequency and grade of ventricular arrhythmias in patients with AS by 24-h ambulatory electrocardiographic monitoring. They have shown that complex ventricular arrhythmias were significantly more common than in normal control subjects.[17] These results were confirmed by later studies performed by Martinez-Useros and Sorgato.[18,19] Removal of valvular obstruction by AVR usually improves the associated symptoms. But, reported details about ventricular arrhythmia and myocardial electrical features after AVR are limited. There are two studies evaluating the effects of AVR on QT dispersion in literature. Darbar, *et al*.[7] have shown that increased QT dispersion was reduced after AVR in patients with significant aortic stenosis. These finding were later confirmed by Orlowska-Baranowska, *et al*.[20] However, the effect of TAVI on myocardial repolarization and arrhythmia is unknown.

In this study, we found a significant reduction of QTd after TAVI in patients with severe AS. Most possible explanations for our finding may be a reduction of increased myocardial mass, which is associated with some advers myocardial affects such as ischemia and fibrosis. The decrease in myocardial thickness and wall stress might restore oxygen supply and myocardial repolarization. Camici, *et al*.[21] reported that patients with left ventricular hypertrophy (LVH) had myocardial ischemia despite normal coronary angiograms. Thallium scans of patients with significant AS and normal coronary arteries often demonstrates perfusion deficits due to microvascular dysfunction.[22] In addition, Miyagawa, *et al*.[23] also have demostrated that microvascular dysfunction and ischemia can improve after aortic valve replacement in patients with severe AS. Microvascular dysfunction leads to a significant remodeling in the cellular compartments of the myocardium. At a cellular level, studies have shown that ATP sensitive potassium channels are more likely to be open during ischemia in hypertrophied myocytes compared to normal myocytes. This situation can prolong repolarization of myocardium which allowing for after-depolarizations and triggered activity that initiates ventricular arrhythmias.[24]

On the other hand, increased myocardial interstitial fibrosis is a consistent finding in LVH and has significant effects on electrical conduction.[25] Increased interstitial fibrosis can lead to abnormalities of side-to-side electrical coupling between myocardial fibres, impaired repolarization and inhomogeneity of intraventricular conduction, all of which facilitate micro-reentry and arrhythmogenesis.[26]

In our study, we found a significant reduction in both QTd and LVMI after TAVI. In addition, LVMI was also associated with QTd. Therefore, we considered that LVMI reduction may be responsible of improving QTd.

There are a few important limitations our study. First, our study population consisted of relatively small number of patients. To restrict the effect of this limitation, patients selection were made very carefully. Another major limination is that this study did not have a specific follow-up for ventricular arrhytmia after TAVI. Therefore, our results should be confirmed by further studies to determine the efficacy of TAVI on the arythmic mortality and morbidity in those patients group.

We conclude that QT dispersion which malign ventricular arrhythmia marker was reduced by the TAVI procedure in patients with severe aortic stenosis. TAVI, beyond symptom relief, may be effective in reducing ventricular arrhythmia.

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