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Short-term effect of transcatheter aortic valve implantation on QT dispersion

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Background/aim: Electrophysiological changes are observed following mechanical stretches due to pressure overload in patients with severe aortic stenosis (AS). The electrical instability occurs after depolarization and dispersion of repolarization. The aim of this study was to evaluate changes in ventricular repolarization following transcatheter aortic valve implantation (TAVI).

Materials and methods: The study population included 100 consecutive patients with severe AS that underwent TAVI. Electrocardiography (ECG) was performed at baseline, immediately after TAVI, and 1 week after TAVI.

Results: The mean age of the patients was 78.2 ± 7.2 years. Thirty-four (34%) of the patients were male and 66 (66%) were female. Compared to the baseline, mean QT dispersion (QTd) immediately after TAVI and 1 week after TAVI decreased significantly (82.8 ± 26.5, 75.6 ± 25.2, and 65.8 ± 28.3, respectively, $P < 0.001$). Likewise, compared to the baseline, mean corrected QTd (QTcd) immediately after TAVI and 1 week after TAVI decreased significantly (84.7 ± 25.2, 76.7 ± 30.8, and 69.1 ± 31.4, respectively, $P < 0.001$).

Conclusion: QTd is indicative of heterogeneity of ventricular refractoriness and is prolonged in patients with AS. Following TAVI, a decrease in QTd might reduce the risk of ventricular arrhythmia in patients with severe AS.

Key words: Transcatheter aortic valve implantation, QT dispersion, aortic stenosis

1. Introduction

Degenerative aortic stenosis (AS) is the most common form of acquired valvular heart disease. Patients with AS that are treated medically survive 5 years with angina, 3 years with syncope, and 2 years with heart failure (1). In patients with severe symptomatic AS, arrhythmia is the most important cause of sudden cardiac death (SCD). Left ventricular pressure overload leads to hypertrophy of the left ventricular myocardium. Increased myocardial hypertrophy with low aortic pressure impairs coronary blood flow. As a consequence, both hypertrophied and ischemic heart muscle can cause electrical heterogeneity. Heterogeneous conduction velocities or repolarization in different parts of the ventricle via the reentry mechanism can cause serious ventricular arrhythmias (2,3).

Electrical instability of heart muscle can be detected via QT dispersion (QTd) using surface electrocardiography (ECG). QTd is considered a marker of regional heterogeneity of myocardial repolarization. QTd values between 40 and 50 ms are considered normal (4), whereas higher QTd values are indicative of greater ventricular instability (5). Elevated QTd is associated with an increase in cardiovascular mortality in patients with AS, hypertrophied cardiomyopathy, myocardial infarction, dilated cardiomyopathy, and peripheral arterial disease, and in diabetic patients with autonomic neuropathy (6,7). The prevalence of complex ventricular arrhythmias is high in patients with AS. Sudden cardiac death is responsible for mortality in 30% of patients with severe AS (8). The risk of SCD is not fully understood in patients with AS, but left ventricular hypertrophy, myocardial ischemia, and myocardial fibrosis might be contributing factors (9). The aim of the present study was to investigate ventricular repolarization changes following transcatheter aortic valve implantation (TAVI) in patients with severe AS.

2. Material and methods

The study included 100 consecutive patients with severe AS that underwent TAVI. All patients also underwent transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE) to evaluate valve morphology, cardiac function, aortic annulus, coronary

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ostium-annulus distance, and calcification. Multislice computed tomography was performed before TAVI to determine peripheral vascular anatomy, as well as that of the aorta, aortic valve, and annulus.

ECG was performed at baseline, immediately after TAVI, and 1 week after TAVI via 12-lead ECG (Nihon Kohden Corporation, Cardiofax M Model ECG-1350, Tokyo, Japan), with each patient lying comfortably in the supine position. ECG was recorded at a rate of 25 mm s^{-1} and 10 mm mV^{-1} gain. The QT interval was measured from the onset of QRS to the end of the T wave. If a U wave was present, the QT interval was measured from the onset of QRS to the deep point of the curve between the T and U waves. In addition, when T waves were inverted or biphasic, the end of the T wave point was accepted as when the trace returned to the isoelectric line. Measurement of QT duration was performed manually by the same investigator. To improve accuracy, measurements were performed with calipers and a magnifying lens for defining ECG deflection. QTd was defined as the difference between the minimum and maximum QT interval. QT intervals were corrected (QTc) using Bazett's formula ($QTc = QT/(RR)^{1/2}$).

TAVI was performed using Edwards Sapien XT balloon-expandable prostheses (Edwards Lifesciences, Irvine, CA, USA). The study was approved by the Ethics Committee of Atatürk Education and Training Hospital and, prior to undergoing TAVI, all patients provided written informed consent. After clinical stabilization of the patients, they were discharged with recommendations and outpatient follow-up was done at 1 week, 1 month, and 6 months. Follow-up visits included routine physical examination, ECG, TTE, and functional capacity evaluation.

2.1. Statistics

The statistical analysis was performed using SPSS 17.0 (SPSS Inc., Chicago, IL, USA). The continuous variables are presented as mean ± standard deviation, and nonparametric variables are presented as median and interquartile ranges. Categorical variables are presented as proportion and percentage. Continuous variables before and after TAVI were compared between groups using the paired Student's t-test for normally distributed variables including QTd and QTcd values. The level of statistical significance was accepted as $P < 0.05$.

3. Results

The study population included 100 consecutive patients with severe AS that underwent TAVI. The mean age of the patients was 78.2 ± 7.2 years; 34 (34%) of the patients were male and 66 (66%) were female. Patient functional capacity according to New York Heart Association classification was class II (n = 7 [7%]), class III (n = 64 [64%]), and class IV (n = 29 [29%]). Median risk scores according to both the Society of Thoracic Surgeons and logistic EuroScore were 7.5 (4–15) and 25.3 (11–39), respectively. Among the patients, 82% had hypertension, 70% had coronary artery disease, and 27% had diabetes mellitus. Baseline characteristics of study population are shown in Table 1. TAVI was performed with a 100% procedural success rate; however, a second valve implantation procedure was needed due to technical reasons in 2 patients. After TAVI

Table 1. Baseline demographic characteristics of the study patients.

Age (years)	78.2 ± 7.2
Males/females (n)	34/66
BMI (kg m^{-2})	27.9 ± 7.6
NYHA classification	
II (%)	7
III (%)	64
IV (%)	29
STS score	7.5 (4–15)
EuroScore	25.3 (11–39)
Comorbid conditions	
Hypertension (%)	82
Diabetes mellitus (%)	27
Hyperlipidemia (%)	45
Smoker (%)	19
Peripheral arterial disease (%)	34
Coronary artery disease (%)	70
Echocardiographic parameters	
AVA (cm^2)	0.62 ± 0.17
Peak gradient (mmHg)	86.3 ± 21.7
Mean gradient (mmHg)	52.5 ± 13.9
LVEF (%)	54.0 ± 14.7
Duration to discharge after procedure (days)	7.4 (4–10)

BMI: Body mass index; NYHA: New York Heart Association; STS: Society of Thoracic Surgeons; AVA: aortic valve area; LVEF: left ventricular ejection fraction.

there were 5 cases of intrahospital mortality due to right ventricular rupture associated with rapid pacing (n = 2), left ventricular rupture due to a guidewire in the left ventricle (n = 1), postoperative bleeding via supraaortic approach (n = 1), and left main coronary artery obstruction due to calcification of aortic cusps (n = 1).

The ECG parameters of QTd and corrected QTd (QTcd) before and after TAVI are presented in Table 2. Mean QTd at baseline, immediately after TAVI, and 1 week after TAVI was 82.8 ± 26.5, 75.6 ± 25.2, and 65.8 ± 28.3, respectively. Mean QTcd at baseline, immediately after TAVI, and 1 week after TAVI was 84.7 ± 25.2, 76.7 ± 30.8, and 69.1 ± 31.4, respectively. Baseline QTd and QTcd were correlated with the mean aortic valve area ($P < 0.001$, r: −0.03). When compared to baseline QTd and QTcd, there was a significant reduction 1 week after TAVI. QTd and QTcd values at baseline and immediately after TAVI were 82.8 ± 26.5 vs. 75.6 ± 25.2 ($P = 0.044$) and 84.7 ± 25.2 vs. 76.7 ± 30.8 ($P = 0.030$), respectively. QTd and QTcd values at baseline and 1 week after TAVI were 82.8 ± 26.5 vs. 65.8 ± 28.3 ($P < 0.001$) and 84.7 ± 25.2 vs. 69.1 ± 31.4 ($P < 0.001$), respectively. QTd and QTcd values are shown in Table 2.

4. Discussion

The present findings show that QTd was elevated in patients with severe AS and left ventricular hypertrophy. The TAVI procedure resulted in improvement of QTd and QTcd values. Age-related calcific AS is a chronic and progressive disease, and it is the most common type of valvular heart disease (2%–7% of those aged >65 years) (10). The asymptomatic latent period varies widely. In patients with symptomatic severe AS, sudden cardiac death is a frequent cause of death, but it is rare in asymptomatic patients. Once symptoms begin the 5-year survival rate is only 15%–50% (10). Valve replacement is the only treatment modality that affects survival (10).

How and why AS causes SCD remains a controversial topic. Some researchers think that ventricular tachycardia due to cardiac muscle hypertrophy can cause SCD (11–13). In severe AS an increase in mechanical stretch due to pressure overload can cause myocyte hypertrophy. In addition, the cardiac renin-angiotensin-aldosterone system activates gene expression of collagen I-II and fibronectin. This likely contributes to an increase in total collagen volume in the myocardium (14). In contrast, AS impairs coronary blood flow. Hence, hypertrophied and ischemic heart muscles might cause electrophysiological changes. Electrical instability is observed as a development after depolarization and dispersion of repolarization. Prior studies showed that heterogeneity in repolarization probably predisposes to such life-threatening arrhythmias as ventricular tachycardia and ventricular fibrillation (15,16). Electrical instability of the heart muscle can be detected via QTd using surface ECG (17).

QTd is a noninvasive marker of ventricular repolarization heterogeneity. Values between 40 and 50 ms are considered normal (4), whereas a QTd of >65 ms is associated with an increased risk of ventricular tachycardia (14). The pathophysiology of prolonged QTd is not fully known (18). Arrhythmogenicity depends on modulation of ion currents, abnormal ventricular structure, and myocardial ischemia (19). Ventricular dilatation and fibrosis can affect different areas of the ventricular wall and cause an increase in dispersion of refractoriness. This hypothesis is supported by evidence of increased QTd in patients with hypertrophic cardiomyopathy, acquired long QT, uremic neuropathy, myocardial infarction, and hypertension with left ventricular hypertrophy (18). Darbar et al. reported a reduction of QTd value following aortic valve surgery and found that resolution of left ventricular hypertrophy following valve replacement might be responsible for the significant reduction in QTd (8). Another reason is the decrease in renin-angiotensin-aldosterone levels after ventricular remodeling improves (14).

QTd is a significant predictor of cardiovascular mortality. Patients with severe AS and high surgical risk undergo TAVI, and therefore this group of patients has a high cardiovascular mortality rate. In the present study, QTd and QTcd decreased significantly following TAVI; both QTd and QTcd values progressively decreased, when compared to baseline values. It could be speculated that

Table 2. QTd and QTcd before and after TAVI, based on ECG.

Electrocardiographic parameters	Baseline	Immediately after TAVI	One week after TAVI	P*	P**	P***
QTd (ms)	82.8 ± 26.5	75.6 ± 25.2	65.8 ± 28.3	0.044	<0.001	0.003
QTcd (ms)	84.7 ± 25.2	76.7 ± 30.8	69.1 ± 31.4	0.030	<0.001	0.014

*Comparison between baseline and immediately after TAVI. **Comparison between baseline and 1 week after TAVI.
***Comparison between immediately after TAVI and 1 week after TAVI.

the significant decrease in QTd and QTcd values from baseline to immediately after TAVI is indicative of the acute hemodynamic effect of TAVI. Costantino et al. showed that aortic valve implantation via TAVI facilitates a more rapid recovery of left ventricular geometry and a greater reduction in left ventricular filling pressure than conventional surgical aortic valve implantation (20). TAVI not only improves left ventricular hemodynamics but also greatly improves ventricular electrical homogeneity (20). TAVI is a new and proven alternative method for high surgical risk patients with severe AS. According to the Partner I-II trial, TAVI is an alternative to standard surgical aortic valve replacement in inoperable and high-risk surgical candidates (21,22).

In conclusion, QTd is indicative of the heterogeneity of ventricular refractoriness and is prolonged in AS patients. Following TAVI the decrease in QTd might decrease the risk of ventricular arrhythmia in patients with severe AS.

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