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RESEARCH

ASSESSMENT OF P WAVE/QT INTERVAL DISPERSION, TP-E INTERVAL, TP-E/QT RATIO AFTER TRANSCATHETER AORTIC VALVE IMPLANTATION IN GERIATRIC PATIENTS WITH AORTIC STENOSIS

Abstract

Introduction: One of the most important reasons for a high mortality and morbidity rate in geriatric patients with calcific aortic stenosis is arrhythmias. Transcatheter aortic valve implantation is an alternative to conventional aortic valve surgery for high-risk patients because of its less-invasive nature. Although hemodynamic and functional recoveries are established after transcatheter aortic valve implantation, whether it leads to a decrease in the risk of atrial fibrillation, ventricular arrhythmia and sudden cardiac death remains unclear. Thus, this study aimed to evaluate the risks associated with aortic stenosis by assessing the rates of P wave dispersion for estimating the atrial fibrillation risk and QT interval dispersion, Tp-e interval, and Tp-e/QT ratio for ventricular arrhythmia and assessing sudden cardiac death risk before and after implantation.

Materials and Method: In a retrospective study, a total of 39 subjects [14 males (35.89%) and 25 females (64.11%); mean age=81.51±8.79 years] were enrolled. P wave/QT interval dispersion, Tp-e interval and Tp-e/QT ratio values before and 3rd months after implantation were calculated and compared.

Results: There was a statistically significant decline in P wave/QT interval dispersion, Tp-e interval, Tp-e/QT ratio values between preoperative, and 3rd, months (43.72±7.78 vs. 35.15±8.92, 61.64±17.36 vs. 49.41±12.64, 84.59±7.64 vs. 73.21±6.46, 0.21±0.01 vs. 0.18±0.01, respectively, p<0.001 for all comparisons).

Conclusion: P wave/QT interval dispersion, Tp-e interval and Tp-e/QT ratio were shown to be attenuated after transcatheter aortic valve implantation. These results indirectly offer that there may be a reduction in risk of atrial fibrillation, ventricular arrhythmias and sudden cardiac death.

Keywords: Aortic Valve Stenosis; Atrial fibrillation; Death, Sudden, Cardiac; Transcatheter Aortic Valve Replacement

ARAŞTIRMA

AORT DARLIĞI OLAN GERİATRİK HASTALARDA TRANSKATETER AORT KAPAK İMPLANTASYONU SONRASI P DALGA/QT İNTERVAL DİSPERSİYONU, TP-E İNTERVAL VE TP-E/QT ORANININ DEĞERLENDİRİLMESİ

Öz

Giriş: Kalsifik aort darlığı olan geriatrik hastalarda mortalite ve morbiditenin önemli bir sebebi de aritmilerdir. Transkateter aort kapak implantasyonu daha az invaziv olması sebebi ile yüksek riskli hastalarda konvansiyonel cerrahiye alternatifdir. Transkateter aort kapak implantasyonu sonrası fonksiyonel ve hemodinamik düzelme olduğu iyi bilinmektedir, ancak implantasyon sonrası atriyal fibrilasyon, ventriküler aritmi ve ani kardiyak ölüm riskinde azalma olup olmadığı net değildir. Bu çalışmanın amacı bu riskleri değerlendirmektir. Bu amaçla atriyal fibrilasyon riskini tahmin etmek için P dalga dispersiyonu, ventriküler aritmi ve ani kardiyak ölüm riskini tahmin etmek için ise QT interval dispersiyonu, Tp-e interval ve Tp-e/QT oranı ölçülerek transkateter aort kapak implantasyonu öncesi ve sonrası karşılaştırılmıştır.

Gereç ve Yöntem: Çalışma geriye dönük olarak yapıldı. Transkateter aort kapak implantasyonu yapılan toplam 39 hasta çalışmaya dahil edilmiştir [14 erkek (%35.89) ve 25 kadın (%64.11); ortalama yaş: 81.51±8.79 yıl]. P dalga dispersiyonu, QT interval dispersiyonu, Tp-e interval ve Tp-e/QT oranı transkateter aort kapak implantasyonu öncesi ve sonrası (3. ayda) hesaplanmış ve karşılaştırılmıştır.

Bulgular: Transkateter aort kapak implantasyonu öncesi ve 3 ay sonrasında bakılan P dalga dispersiyonu, QT interval dispersiyonu, Tp-e interval ve Tp-e/QT oranı değerlerinde istatistiksel olarak anlamlı azalma olmuştur (43.72±7.78 vs. 35.15±8.92, 61.64±17.36 vs. 49.41±12.64, 84.59±7.64 vs. 73.21±6.46, 0.21±0.01 vs. 0.18±0.01, sırasıyla, p<0.001 tüm karşılaştırmalar için).

Sonuç: Transkateter aort kapak implantasyonu sonrası P dalga dispersiyonu, QT interval dispersiyonu, Tp-e interval ve Tp-e/QT oranı değerleri azalmaktadır. Bu sonuçlar bize dolaylı olarak atriyal fibrilasyon, ventriküler aritmiler ve ani kardiyak ölüm riskinde azalma olabileceğini düşündürebilir.

Anahtar sözcükler: Aort kapak darlığı; Atriyal fibrilasyon; Ölüm, Ani, Kardiyak; Transkateter aort kapak replasmanı

INTRODUCTION

In the elderly population, calcific aortic stenosis is a major health-related problem. Mortality and morbidity rates are remarkably high after serious aortic stenosis becomes symptomatic (1). One of the most important reasons for a high mortality rate in patients with calcific aortic stenosis is malignant ventricular arrhythmias. Studies have revealed that sudden cardiac death risk is also high in patients with serious symptomatic aortic stenosis (2). Except for ventricular arrhythmias, the prevalence of atrial fibrillation (AF) that accounts for mortality and morbidity is elevated in elderly patients with symptomatic serious aortic stenosis (3-5).

In recent years, the use of transcatheter aortic valve implantation (TAVI) has gained considerable acceptance for patients considered inoperable because of a high surgical risk posed by their age and other comorbid conditions. Transcatheter aortic valve implantation is an alternative to conventional aortic valve surgery for high-risk patients because of its less-invasive nature. Moreover, patients receiving TAVI have been shown to exhibit evident recoveries in their hemodynamic status and functional capacities (6,7).

Several studies have reported that the attainment of P-wave dispersion (PWD), a difference between the widest and the narrowest in 12-lead electrocardiogram (ECG), demonstrates atrial remodeling and predicts AF (8). In addition, QT dispersion (QTd) is defined as the time between the longest and the shortest distances in 12-lead ECG. Apparently, QTd plays a role in estimating ventricular repolarization abnormalities and ventricular arrhythmias (9). Some other studies have reported the time between the points where T wave peaks and is deep in 12-lead ECG (Tp-e), thereby better predicting the ventricular repolarization abnormality (10). Furthermore, the ratio of Tp-e to QT (Tp-e/QT) exhibits repolarization abnormality (11).

Although hemodynamic and functional recoveries are established after TAVI, whether it leads to a decrease in the risk of ventricular arrhythmia and sudden cardiac death remains unclear. Thus, this study aimed to evaluate the risks associated with TAVI by assessing the rates of PWD for estimating the AF risk and QTd, Tp-e, and Tp-e/QT for ventricular arrhythmia and assessing sudden cardiac death risk before and after TAVI (in 3 months).

MATERIALS AND METHOD

This was a retrospective study in which the records of 50 patients who underwent TAVI between January 1, 2012, and November 30, 2017 were reviewed. Patients ineligible for surgical aortic valve replacement because of symptomatic serious aortic stenosis and high surgical risk were considered eligible for TAVI. Transcatheter aortic valve implantation was performed by a multidisciplinary cardiac team (cardiologist, cardiovascular surgeon, and anesthesiologist) on patients with EuroSCORE of ≥20% or the Society of Thoracic Surgeon Score of ≥10%. Baseline demographic characteristics of all patients were recorded as echocardiographic characteristics.

The exclusion criteria in this study were as follows: patients with a history of permanent pacemaker implantation in the first 3 perioperative or postoperative months, the existence of persistent AF, exit depending on any cause within the first 3 perioperative or postoperative months, using any medication that affects the QT distance, and using an antiarrhythmic drug in the perioperative period. Based on these criteria, 2 patients with persistent AF, 2 with permanent pacemaker implantation in the perioperative period, and 7 who died either during the operation or in first 3postoperative months were excluded. Thus, the remaining 39 patients were included. For all patients, their 3-month preoperative and postoperative ECGs, PWD, QTd, Tp-e, and Tp-e/QT ratios were reviewed and compared.

Next, echocardiographic data were evaluated on the basis of the American Society of Echocardiography (12) and European Association of Cardiovascular Imaging using standard two-dimensional (2D) and Doppler evaluation. Then, delta (Δ) values were obtained by deducting 3 months' values from baseline values for the left ventricular end diastolic diameter (LVEDD), left ventricular end-systolic diameter, left atrial diameter (LAD), interventricular septum (IVS), right atrial diameter, right ventricular diameter (RVD), PWD, QTd, Tp-e interval, and Tp-e/QT ratio. Furthermore, the ejection fraction (EF) was calculated using the modified Simpson method. In this study, LVEDD and LAD were measured in the parasternal long-axis imaging.

Transcatheter aortic valve implantation

All TAVI procedures were completed under general anesthesia in an operating room. In all patients, the transfemoral access was attained by puncturing the common femoral artery under fluoroscopic guidance. After the insertion of the delivery sheath, balloon aortic valvuloplasty was accomplished with rapid ventricular pacing for both balloon sizing and stenotic valve dilatation, after which an Edwards SAPIEN heart valve or Medtronic core valve was placed with rapid ventricular pacing following the valve positioning based on fluoroscopy. Then, anti-thrombotic therapy with aspirin (100 mg) and clopidogrel (75 mg) was prescribed for up to 1 month; aspirin was continued alone after the first-month control.

Electrocardiographic features

Standard ECG (25 mm/s and 10 mm/mV) was retrospectively reviewed. Electrocardiogramwas performed when a patient was in the supine position, and electrodes were placed at standard sites (13). All ECG recordings were scanned and recorded as digital media. In addition, all images were amplified 400´ using Adobe Photoshop software to minimize faults during measurements, which were executed by 2cardiologists who were blinded to the patient and control groups. For each parameter, measurements were created from 3 consecutive beats in every derivation, and the average of these measurements was recorded. Then, PWD was assessed by evaluating the difference between the duration of the widest and the narrowest P waves in the ECG. The QT interval was assessed as the interval between the start of the Q wave and the end of the T wave. Next, QT corrected (CQT) on the authority of the heart rate was evaluated using the Bazett's formula: CQT=QT√ (R–R interval). The Tp-e interval was measured in precordial leads by evaluating the interval between the point where the T wave makes a peak and the point where it ends. Finally, the Tp-e/CQT ratio was calculated from these parameters.

Statistical analysis

Variables are presented as mean±sd or median (range, interquartile range [IQR]) for continuous data and as proportion for categorical data. Continuous variables with normal distribution were analyzed with paired sample t test. Shapiro Wilk test was used to identify whether continuous variables were normally distributed. Two-sided p values <0.05 were considered significant. The degrees of association between continuous variables were evaluated by using Pearson or Spearman's correlation tests as appropriate. Independent determinants of PWD and QTD were determined by standard multiple linear regression analysis. A two-sided p<0.05 was accepted as significant. Statistical analysis was performed using commercially available computer program (SPSS version 21.0 for Windows; SPSS, Inc., Chicago, Illinois, US).

RESULTS

In this study, 39 patients [14 males (35.89%) and25 females (64.11%); mean age: 81.51±8.79 years] were enrolled. Table 1 summarizes baseline demographic characteristics of the study cohort. A statistically significant difference was observed between TAVI and the mean aortic valve and maximum aortic valve gradients compared at 3 months postoperatively ($p<0.001$, for both comparisons). Likewise, EFs pre- and postoperatively exhibited statistically significant differences. Table 2 summarizes comparisons of echocardiographic parameters before and after TAVI in the study patients. All parameters exhibited a statistically significant decrease in the 3 months' values before and after TAVI procedure of PWD, CQTd, Tp-e, and Tp-e/CQT parameters ($p<0.001$, for all comparisons). Table 3 presents pre- and postoperative values of these parameters and their comparison, with their changes shown in Fig. 1. Table 4 presents the results of correlation analysis between changes in echocardiographic measurements and those in PWD, CQTd, Tp-e, and Tp-e/CQT measurements. The correlation analysis revealed a statistically significant correlation between ΔPWD and ΔLVEDD, ΔLVESD, ΔIVS, and ΔLAD (r=0.47, p=0.003; r=0.402, p=0.011; r=0.381, p=0.017; and r=0.543, $p<0.001$, respectively); between ΔCQTd and ΔLVEDD, ΔLVESD, and ΔIVS (r=0.648, $p<0.001$; r=0.655, $p<0.001$; and r=0.379, p=0.017, respectively); between ΔTp-e and ΔLVEDD, ΔLVESD, and ΔIVS (r=0.419, p=0.008; r=0.375, p=0.019; and r=0.333, p=0.038, respectively); and between the ΔTp-e/CQT ratio and ΔLVEDD, ΔLVESD, and ΔIVS (r=0.677, $p<0.001$; r=0.754, $p<0.001$; and r=0.4, p=0.012, respectively).

Table 1. Baseline clinical characteristics of the study population.

Characteristics	Patients (n=39)
Sex, female gender, n (%)	25 (64.11)
Age (years)	81.51±8.79
Body mass index (kg/m^2)	26.58±2.6
Hypertension, n (%)	36 (92.3)
Diabetes mellitus, n (%)	10 (25.64)
Hyperlipidemia, n (%)	13 (33.33)
Smoking, n (%)	5 (12.82)
Coronary artery disease, n (%)	27 (69.23)
COPD, n (%)	8 (20.51)
Chronic renal disease, n (%)	7 (17.94)
Blood urea nitrogen (mg/dL)	28.31±11.22
Creatinine (mg/dL)	1.19±0.8
Hemoglobin (gr/dL)	11.92±1.97
White blood cell (/mm^3)	7376±2476
Platelets (100/mm^3)	214 (164-260)
STS Score	13.6±1.94
EuroScore	27.4±3.71
AVA (cm^2)	0.59±0.19

AVA: Aortic valve area, COPD: Chronic Obstructive Pulmonary Disease,
STS: Society of Thoracic Surgeons

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

Parameter	Before TAVI	3rd month after TAVI	p
Mean gradient (mmHg)	52.9±12.01	10.59±4.17	<0.001
Maximum gradient (mmHg)	81.72±15.79	17.44±6.06	<0.001
Ejection fraction (%)	49.67±9.2	51.77±8.08	0.005
LVEDD (mm)	45.25±2.51	42.71±1.65	<0.001
LVESD (mm)	30.92±2.10	28.56±1.97	<0.001
IVS (mm)	13.92±0.87	11.97±1.54	<0.001
LAD (mm)	40.15±3.07	37.48±2.29	<0.001
RAD (mm)	35.3±3.72	34.2±3.31	<0.001
RVD (mm)	29.25±1.69	29.02±1.38	0.083

IVS: Interventricular septum, LAD: Left atrial diameter, LVEDD: Left ventricular end diastolic diameter, LVESD: Left ventricular end systolic diameter, RAD: Right atrial diameter, RVD: Right ventricular diameter, TAVI: Transcatheter aortic valve implantation

Table 3. Comparison of PWD, CQTd, Tp-e and Tp-e/CQT ratio values before and after TAVI.

Parameter	Before TAVI	3rd month after TAVI	p
PWD (msn)	43.72±7.78	35.15±8.92	<0.001
CQTd (msn)	61.64±17.36	49.41±12.64	<0.001
Tp-e (msn)	84.59±7.64	73.21±6.46	<0.001
Tp-e/CQT ratio	0.21±0.01	0.18±0.01	<0.001

CQT: Corrected QT interval, CQTd: Corrected QT interval dispersion, PWD: P wave dispersion, TAVI: Transcatheter aortic valve implantation, Tp-e: T wave peak-end interval

Table 4. Correlation analysis of P wave/corrected QT interval dispersion, Tpe interval, Tp-e/CQT ratio and various clinical variables.

Variable	ΔPWD		ΔCQTd		ΔTp-e		ΔTp-e/CQT	
	r	p	r	p	r	p	r	p
ΔLVEDD	**0.47**	**0.003**	**0.648**	**<0.001**	**0.419**	**0.008**	**0.677**	**<0.001**
ΔLVESD	**0.402**	**0.011**	**0.655**	**<0.001**	**0.375**	**0.019**	**0.754**	**<0.001**
ΔIVS	**0.381**	**0.017**	**0.379**	**0.017**	**0.333**	**0.038**	**0.4**	**0.012**
ΔLAD	**0.543**	<0.001	0.165	0.315	0.059	0.72	0.215	0.188
ΔRAD	0.193	0.238	0.031	0.326	0.261	0.108	0.015	0.402
ΔRVD	0.016	0.921	0.118	0.474	0.231	0.156	0.117	0.48

CQT: Corrected QT interval, CQTd: Corrected QT interval dispersion, IVS: Interventricular septum, LAD: Left atrial diameter, LVEDD: Left ventricular end diastolic diameter, LVESD: Left ventricular end systolic diameter, PWD: P wave dispersion, RAD: Right atrial diameter, RVD: Right ventricular diameter, TAVI: Transcatheter aortic valve implantation, Tp-e: T wave peak-end interval.

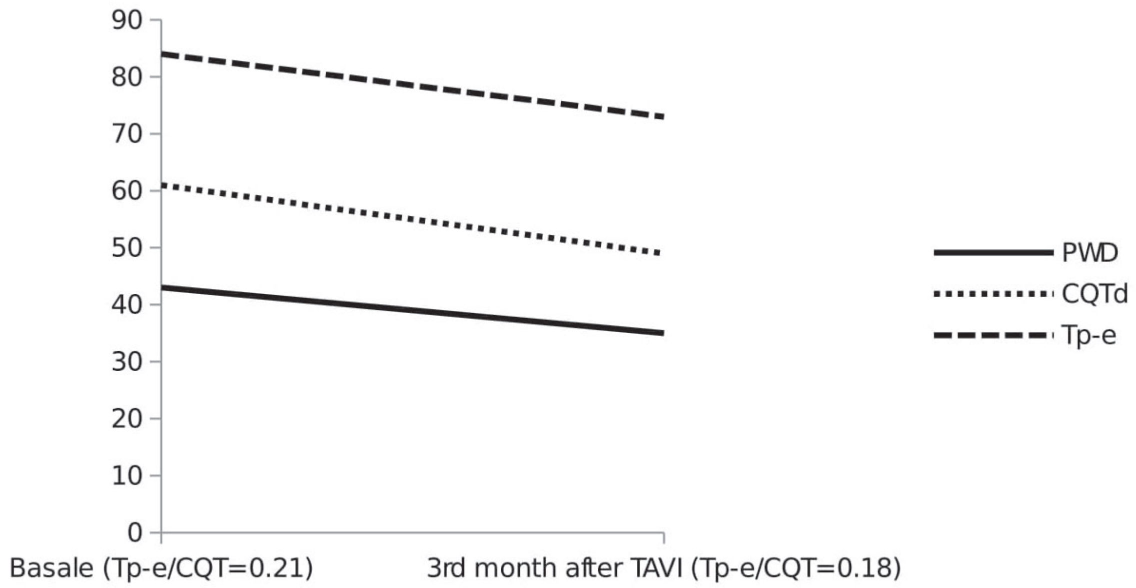

Figure 1. Change of PWD, QTDd, Tp-e and Tp-e/CQT ratio values of subjects before and after TAVI.

DISCUSSION

To the best of our knowledge, this is the first study investigating PWD, CQTd, Tp-e, and Tp-e/CQT values before and after TAVI. Based on our findings, these values exhibited a statistically significant reduction after TAVI. In addition, the change in these values correlated with that in cardiac cavities. Thus, patients with calcific aortic stenosis and conventional surgery who could not be operated because of high risk, but underwent TAVI, suggested a decline in AF, ventricular arrhythmia, and sudden cardiac death postoperatively, and this decline could be attributed to a change in the cardiac cavity after TAVI.

Patients with aortic stenosis exhibit a high prevalence of AF. In addition, approximately one-third of patients with serious aortic stenosis have paroxysmal or persistent AF. Perhaps, the presence of common risk factors, such as age and hypertension, might explain the more frequent occurrence of AF in patients with aortic stenosis (14). Besides common risk factors, another possible cause could be an increase in the left ventricular and left atrial wall pressures, resulting from aortic stenosis (15). A chronic afterload increment results in left atrial enlargement and a reduction in its functions; this enlargement during the chronic period results in fibrosis in the left atrial myocardium. Reportedly, increased left atrial fibrosis increases the risk of AF development (16). In addition, the result of the increased wall pressure in cardiac cavities after TAVI might exacerbate the risk of AF. A study has reported that advanced aortic stenosis correlated with left atrial dysfunction and that the left atrial compliance and contractility, which was assessed using speckle tracking echocardiography, significantly improved after TAVI (17). In addition, the recovered left atrium compliance and contractility might indirectly decrease in its left atrial fibrosis (17), possibly contributing to an increase in the functional and hemodynamic capacities with an increase in the left atrial contribution. Based on this study, a decrease in PWD correlates with a decrease in

LAD, which supports these explained mechanisms. These physiopathological mechanisms may result in a decreased risk of AF development after TAVI in patients with advanced-stage aortic stenosis.

Life-threatening serious ventricular arrhythmia in patients with advanced-stage aortic stenosis increases the incidence of sudden cardiac death (1). Reportedly, an increase in the chronic afterload is associated with a decrease in the left ventricular systolic function and left ventricular hypertrophy with high systolic ventricular overload (18). In addition, a decrease in the left ventricular EF resulting in high systolic overload in patients with serious aortic stenosis correlates with complex ventricular arrhythmias (19).

A study has reported an elongation in the recovered QT interval in patients with aortic stenosis with low EF (20). Kasapkara et al. have reported that QTd decreased in the first week after TAVI in 100 patients with serious aortic stenosis and that ventricular arrhythmia risk might be decreased in these patients. In addition, they inferred that the decrease could be a consequence of a reduction in left ventricular hypertrophy after TAVI (21). Notably, surgical conventional aortic valve replacement in patients with serious aortic stenosis reduces the risk of ventricular arrhythmia in the long-term follow-up. Some studies have attributed this decrease to a decrease in the diameter of muscle fibers, resulting in a reduction in the ventricular mass (2, 19). Moreover, a decline of approximately 43% in the left ventricular mass during the first 2 years after surgery occurs in patients with serious aortic stenosis undergoing surgical replacement (22). An increased left ventricular mass increases the oxygen need and is associated with myocardial ischemia (23). Reportedly, ischemia is decreased in patients with surgically recovered aortic stenosis (24). Ischemia developing in the hypertrophic left ventricular might increase the repolarization defect and ventricular arrhythmia and sudden cardiac death risk. Besides, an increase in interstitial fibrosis in hypertrophic myocardial tissue and increased fibrosis results in electrical conduction abnormalities. This study suggests that ECG parameters that indicate the ventricular repolarization abnormality are associated with echocardiographic parameters that indirectly imply that the left ventricular size and mass are due to the mechanisms described above.

This study has some limitations. First, the number of patients examined was low, which necessitates further studies with more number of patients to validate our findings. Second, the follow-up time was relatively short, and the long-term effects of these findings remain unclear. Patients might develop silent arrhythmias, which clinicians and patients cannot feel, making it difficult to detect these arrhythmias.

In conclusion, this study establishes that the3 months' control after TAVI, PWD, CQTd, TP-e, and TP-e/CQT ratios decreases, which are proportional to the decrease in the diameter of the cardiac cavity, measured using echocardiography. Accordingly, ventricular repolarization abnormalities, ventricular arrhythmias, and sudden death risks decrease in elderly patients with serious aortic stenosis after TAVI.

Conflict of interest

The authors declare that they have no conflicts of interest. The authors have indicated they have no financial relationships relevant to this article to disclose.

Ethical approval

All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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