

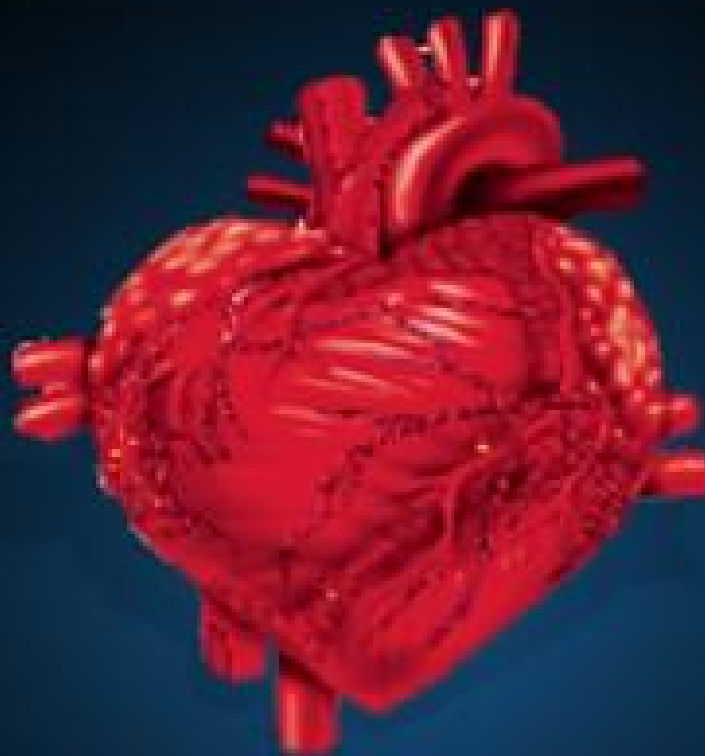
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The Association of Uncarboxylated Matrix Gla Protein with Mitral Annular Calcification in Patients without Significant Coronary Artery Disease

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Abstract

Objective: Mitral annular calcification (MAC) is associated with systemic calcification and cardiovascular disease (CVD) events. Matrix Gla protein (MGP) is a strong inhibitor of vascular and soft-tissue calcification and reduced levels of its circulating precursor, uncarboxylated MGP (ucMGP), was found associated with vascular calcification in pilot studies. **Methods and Results:** In this study, which includes 86 outpatients with no significant coronary artery and chronic kidney diseases, we measured serum ucMGP levels and evaluated MAC using echocardiography. In participants with MAC ($n = 44$), serum ucMGP levels were lower than the control group ($n = 42$) (216.1 ± 154.1 vs. 390.2 ± 256.3 , $P = 0.001$, respectively). The patients with MAC were divided into two groups: mild MAC group and moderate MAC group. Serum ucMGP levels were significantly lower in the moderate MAC group than the mild MAC group (139.0 ± 121.8 vs. 248.4 ± 156.3 , $P = 0.03$, respectively). **Conclusions:** In patients with MAC, serum ucMGP level was significantly low, and this association has been detected for the first time in patients with no significant coronary artery disease (CAD).

Keywords: Matrix gla protein, mitral annular calcification, uncarboxylated matrix Gla protein

INTRODUCTION

Mitral annular calcification (MAC) is a chronic, degenerative, and noninflammatory disease of the mitral valve.^[1,2] The prevalence of MAC increases with age, and MAC most frequently occurs in postmenopausal women.^[3-5] Diagnosis is made on observing the increase in opacity in the mitral valve annulus using transthoracic echocardiography (TTE). MAC may result in mitral stenosis, mitral regurgitation, infective endocarditis, atrial arrhythmias, and heart block. It is one of the known independent risk factors for systemic embolism and stroke. MAC severity as measured by the thickness of the valve in M mode is linearly correlated with the risk of stroke.^[6,7] Along with other calcific valvular processes, MAC is associated with a high prevalence of risk factors for the development of coronary atherosclerosis.^[8] Framingham trial, which studied the correlation between MAC and cardiovascular mortality and morbidity, established that there is a relationship between MAC and cardiovascular event, cardiovascular death, and all-cause mortality.^[9]

Matrix Gla protein (MGP) is an extracellular matrix protein whose synthesis depends on Vitamin K, and it inhibits vascular calcification by binding to calcium ions. The primary sites of synthesis of this most important protein that regulates vascular calcium metabolism are cartilage, lung, heart, kidney, vascular smooth muscle cells, and calcific atherosclerotic plaque.^[10,11] MGP knock-out mice are characterized by severe vascular calcification and die prematurely due to spontaneous aortic rupture.^[12] In a pilot study, it was found that individuals with coronary atherosclerosis, aortic stenosis, and calcific uremic arteriopathy had lower ucMGP levels compared to healthy controls.^[13] A previously published study determined the correlation between MAC and serum uncarboxylated

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MGP (ucMGP) levels in patients with cardiovascular disease (CVD).^[14] The objective of the present study is to determine the independent association of serum ucMGP with MAC in outpatients with no significant CVD.

STUDY DESIGN AND METHODS

Study participants

Between 2008 and 2009, we recruited 44 patients with MAC detected by TTE. Forty-two age and gender-match, healthy volunteers with no medical comorbidities, and receiving no cardioactive medications included in the study. Patients with rheumatic heart disease, severe/significant coronary artery disease (CAD), chronic renal failure, hypertrophic cardiomyopathy, cardiac failure, severe valvular disease, and patients under statin therapy were excluded from the study. Severe CAD patients were excluded myocardial perfusion scintigraphy both MAC and control groups. We performed invasive coronary angiography both mild and moderate coronary artery patients, which detected by myocardial perfusion scintigraphy, and significant (>70% stenosis in a major coronary vessel) CAD patients were excluded from the study. Before data collection, written informed consent was obtained from each patient, and the study had been approved by the appropriate Institutional Ethics Review Committee.

All transthoracic echocardiographic examinations were performed using GE Vingmed system 5 (Horten, Norway), accompanied by electrocardiogram monitoring. Echocardiographic examination was performed in the left lateral decubitus position, in accordance with the relevant guidelines. Parasternal long and short axes, apical four chamber, apical two-chamber, and apical three-chamber windows of all patients were visualized using two-dimensional echo and color Doppler. Left ventricular end diastolic diameter (LVEDD), left ventricular end systolic diameter (LVESD), left atrial diameter, left ventricular, septal and posterior wall thickness, mitral flow velocity pulse, and continuous wave Doppler were analyzed. The studies were recorded digitally. After saving the echocardiographic data, blood samples were obtained from patients and these samples were collected in biochemistry tubes with citrate. Samples were incubated for 15 min at room temperature. Blood samples were centrifuged at 3000 rpm for 15 min; serum was separated from the plasma and stored at -80°C for the future analysis.

Measurements

Uncarboxylated matrix Gla protein

Serum ucMGP was measured by competitive enzyme-linked immunosorbent assay using VitaK BV (Maastricht, the Netherlands) as previously described.^[13] Anti-ucMGP (VitaK BV, Maastricht, The Netherlands) was conjugated to the microtiter plate through polyclonal rabbit-antimouse IgG (Dako, Heverlee, Belgium). After stringent washing, 5 mL of the serum sample or standard was mixed with tracer (biotinylated peptide consisting of residues 35–54 in human MGP), transferred to the microtiter plate, and incubated

overnight at 4°C. After washing, the plate was incubated with streptavidin-peroxidase (Zymed, Breda, The Netherlands) and stained with TMB Microwell Proxidase Substrate Kit (KPL, Gennep, The Netherlands). The process was terminated by adding H₂SO₄, and the plate was read at 450 nm. The lower limit of detection was 98 nM, and the intra-assay coefficient of variation was 6% and the interassay coefficient was 11%.

Mitral annular calcification

Using GE Vingmed system 5 (Horten, Norway) echocardiograms were obtained at rest with all standard two-dimensional views and Doppler images. MAC is defined as an echo-dense structure located at the junction of the atrioventricular groove and the posterior mitral leaflet on the parasternal long-axis, apical 4-chamber, or parasternal short-axis view. MAC was divided into three groups according to the degree of calcification; mild, moderate, and severe.

Mild – Focal echodensity increase in mitral annulus.

Moderate – Echodensity increase is <1/2 and more than 1/3 of the mitral annulus.

Severe – Calcification more than 1/2 of the mitral annulus or calcification coating left ventricular outflow tract.

Other associated characteristics

Age, sex, race/ethnicity, smoking status, medical history of hypertension, diabetes, chronic kidney disease, myocardial infarction, angioplasty, coronary bypass, and heart failure were all determined by the answers to the patient questionnaire. Laboratory measures were made using standard clinical chemistry analyzers.

Statistical analysis

The statistical analyses were carried out using the SPSS 15.0 software (SPSS Inc., Chicago, IL, USA). Parametric variables were expressed as mean ± standard deviation; while the categorical variables were expressed in percentage. Continuous variables outside the normal distribution were analyzed using the Mann–Whitney U-test, while those within the normal distribution were analyzed through Student's *t*-test. The one-way analysis of variance test was used to compare the categorical variables analyses. *P* < 0.05 was considered statistically significant.

RESULTS

Both groups were similar regarding their demographic characteristics. Hypertension prevalence was significantly higher in the group with MAC (54.5% and 33.3, *P* = 0.048). Each of the two groups had no significant differences regarding the frequency of diabetes mellitus and dyslipidemia. Left ventricular hypertrophy was observed significantly more commonly in the group with MAC (52.3 and 8.23, *P* = 0.006). Left atrial diameter was significantly larger in the group with MAC (3.3 vs. 3.1, *P* = 0.011). There were no significant differences between the two groups regarding LVEDD and LVESD [Table 1]. Serum MGP levels were significantly lower in the MAC group

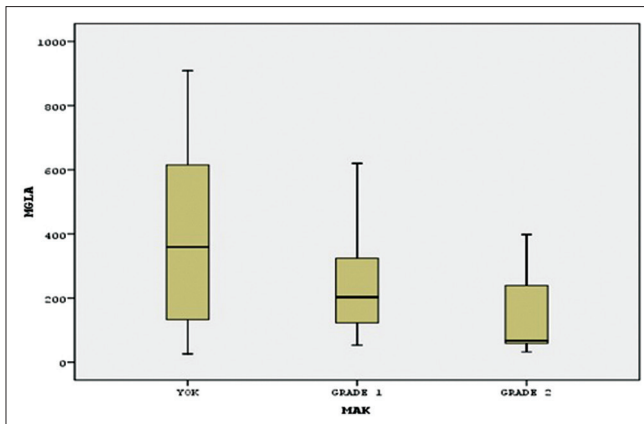


Figure 1: Serum MGP levels and the relationship between the degree of MAC

(216.1 ± 154.1 vs. 390.2 ± 256.3 , $P = 0.001$, respectively) [Table 2]. The relationship between serum MGP and MAC grade was evaluated, and it was found that there was an increase in the degree of MAC-associated reduction of serum MGP levels [Figure 1].

DISCUSSION

A previously conducted study using the same ucMGP assay demonstrated an association between lower ucMGP in people with CVD. Our study demonstrated that serum ucMGP levels were significantly lower in patients with MAC, and ucMGP levels were significantly lower even in the moderate MAC group compared to the mild MAC group. This association is detected for the first time in patients without significant CAD. A similar association was observed between ucMGP and MAC but was limited to participants with CAD. We performed myocardial perfusion scintigraphy in both MAC and control groups to exclude severe CAD. The statistical difference between mild and moderate MAC group regarding serum ucMGP levels strongly corroborated the correlation between serum ucMGP levels and dystrophic calcification.

Previous epidemiological studies evaluating the associations of ucMGP with dystrophic calcification have largely been limited to populations with end-stage renal disease and CAD, in which lower ucMGP concentrations are associated with vascular and valvular calcification and mortality.^[15-19] Here, we demonstrate an inverse association of ucMGP with dystrophic valvular calcification in a population without severe kidney disease and CAD. Together, these data suggest that ucMGP may function as an inhibitor of dystrophic calcification in other populations and is not limited to persons with end-stage renal disease and severe CAD.

CONCLUSION

In summary, ucMGLA protein concentrations are inversely associated with MAC in people without CAD and severe kidney disease. In the context of previous studies, these data corroborate the hypothesis that MGP may function as an

Table 1: Groups of patient’s demographic, clinical, and echocardiographic characteristics

	Group 1 (MAC), n (%) (mean)	Group 2 (control), n (%) (mean)	P
Age (year)	70.54	70.25	0.855
Sex			
Female	36 (81.8)	34 (81)	
Male	8 (18.2)	8 (19)	
Hypertension	24 (54.5)	14 (33.3)	0.048
Diabetes mellitus	13 (29.5)	10 (23.8)	0.803
Dyslipidemia	13 (29.5)	14 (33.3)	0.709
LVH	23 (52.3)	10 (23.8)	0.006
LA (cm)	3.3	3.1	0.011
LVEDD	4.8	4.78	0.689
LVESD	2.67	2.7	0.457

MAC: Mitral annular calcification, LVH: Left ventricular hypertrophy, LA: Left atrial, LVEDD: Left ventricular end diastolic diameter, LVESD: Left ventricular end systolic diameter

Table 2: Serum matrix gla protein levels of patients and control groups

	Group 1 (MAC)	Group 2 (control)	P
mGLA protein (pg/dl)	216.1	390.2	0.001

MAC: Mitral annular calcification

important inhibitor of dystrophic valvular calcification and that this function does not require the presence of severe CAD, kidney disease, or other traditional cardiovascular risk factors. Future studies are required to evaluate whether MGP is associated with dystrophic calcification among other vascular tissues, whether the results may be generalized to individuals without coronary heart disease, and whether MGP concentrations may predict longitudinal progression of dystrophic calcification. This study adds to a growing body of literature demonstrating that serum ucMGP levels affect the regulation of cardiac valvular calcification, and this function is not different in people without significant CAD.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

- D’Cruz I, Panetta F, Cohen H, Glick G. Submitral calcification or sclerosis in elderly patients: M mode and two dimensional echocardiography in “mitral annulus calcification”. *Am J Cardiol* 1979;44:31-8.
- Hirschfeld DS, Emilson BB. Echocardiogram in calcified mitral annulus. *Am J Cardiol* 1975;36:354-6.
- Fulkerson PK, Beaver BM, Auseon JC, Graber HL. Calcification of the mitral annulus: Etiology, clinical associations, complications and therapy. *Am J Med* 1979;66:967-77.
- Korn D, Desanctis RW, Sell S. Massive calcification of the mitral annulus. A clinicopathological study of fourteen cases. *N Engl J Med* 1962;267:900-9.
- Savage DD, Garrison RJ, Castelli WP, McNamara PM, Anderson SJ, Kannel WB, *et al.* Prevalence of submitral (anular) calcium and its

- correlates in a general population-based sample (the Framingham study). *Am J Cardiol* 1983;51:1375-8.
6. Nestico PF, Depace NL, Morganroth J, Kotler MN, Ross J. Mitral annular calcification: Clinical, pathophysiology, and echocardiographic review. *Am Heart J* 1984;107:989-96.
 7. Benjamin EJ, Plehn JF, D'Agostino RB, Belanger AJ, Comai K, Fuller DL, *et al.* Mitral annular calcification and the risk of stroke in an elderly cohort. *N Engl J Med* 1992;327:374-9.
 8. Adler Y, Herz I, Vaturi M, Fusman R, Shohat-Zabarski R, Fink N, *et al.* Mitral annular calcium detected by transthoracic echocardiography is a marker for high prevalence and severity of coronary artery disease in patients undergoing coronary angiography. *Am J Cardiol* 1998;82:1183-6.
 9. Fox CS, Vasan RS, Parise H, Levy D, O'Donnell CJ, D'Agostino RB, *et al.* Mitral annular calcification predicts cardiovascular morbidity and mortality: The Framingham heart study. *Circulation* 2003;107:1492-6.
 10. Price PA, Urist MR, Otawara Y. Matrix Gla protein, a new gamma-carboxyglutamic acid-containing protein which is associated with the organic matrix of bone. *Biochem Biophys Res Commun* 1983;117:765-71.
 11. Fraser JD, Price PA. Lung, heart, and kidney express high levels of mRNA for the vitamin K-dependent matrix Gla protein. Implications for the possible functions of matrix gla protein and for the tissue distribution of the gamma-carboxylase. *J Biol Chem* 1988;263:11033-6.
 12. Luo G, Ducey P, McKee MD, Pinero GJ, Loyer E, Behringer RR, *et al.* Spontaneous calcification of arteries and cartilage in mice lacking matrix GLA protein. *Nature* 1997;386:78-81.
 13. Cranenburg EC, Vermeer C, Koos R, Boumans ML, Hackeng TM, Bouwman FG, *et al.* The circulating inactive form of matrix Gla protein (ucMGP) as a biomarker for cardiovascular calcification. *J Vasc Res* 2008;45:427-36.
 14. Parker BD, Schurgers LJ, Vermeer C, Schiller NB, Whooley MA, Ix JH, *et al.* The association of uncarboxylated matrix Gla protein with mitral annular calcification differs by diabetes status: The heart and soul study. *Atherosclerosis* 2010;210:320-5.
 15. Schurgers LJ, Barreto DV, Barreto FC, Liabeuf S, Renard C, Magdeleyns EJ, *et al.* The circulating inactive form of matrix Gla protein is a surrogate marker for vascular calcification in chronic kidney disease: A preliminary report. *Clin J Am Soc Nephrol* 2010;5:568-75.
 16. Parker BD, Ix JH, Cranenburg EC, Vermeer C, Whooley MA, Schurgers LJ, *et al.* Association of kidney function and uncarboxylated matrix Gla protein: Data from the heart and soul study. *Nephrol Dial Transplant* 2009;24:2095-101.
 17. Cranenburg EC, Brandenburg VM, Vermeer C, Stenger M, Mühlenbruch G, Mahnken AH, *et al.* Uncarboxylated matrix Gla protein (ucMGP) is associated with coronary artery calcification in haemodialysis patients. *Thromb Haemost* 2009;101:359-66.
 18. Shioi A, Nishizawa Y. Vascular calcification in chronic kidney disease: Pathogenesis and clinical implications. *J Ren Nutr* 2009;19:78-81.
 19. Cassidy-Bushrow AE, Bielak LF, Levin AM, Sheedy PF 2nd, Turner ST, Boerwinkle E, *et al.* Matrix Gla protein gene polymorphism is associated with increased coronary artery calcification progression. *Arterioscler Thromb Vasc Biol* 2013;33:645-51.

Does Pulmonary Endarterectomy have Arrhythmia Prevention Effect?

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Abstract

Background: The aim of the present study was therefore to evaluate the evolution of electrocardiography (ECG) markers indicator of morbidity and mortality after pulmonary endarterectomy (PEA). It may be a good predictor of mortality and morbidity in chronic thromboembolic pulmonary hypertension (CTEPH) with patients who underwent PEA. PEA may be reduced risk of arrhythmia in patients with CTEPH. However, this claim must to be supported with long-term results. **Materials and Methods:** We collected demographic, ECG, and echocardiographic parameters data (baseline and after the operation) in patients undergoing PEA for CTEPH at our institution from 2009 to 2013. We assessed 62 CTEPH patients who underwent PEA. **Results:** P wave amplitude in DII, PR interval, P and QT dispersion changed significantly at 3 months after surgery. The P dispersion (17.66 ± 6.2 , $P < 0.04$) and QT dispersion (23.75 ± 11.37 , $P < 0.015$) were longer in before operation than in after operation. **Conclusions:** In our study, we found in ECG analyses of CTEPH with patients who are undergoing PEA that P dispersion, QT dispersion were changed when compared with before operation. For this reason, we think that PEA reduces the risk of atrial fibrillation and malignant arrhythmia.

Keywords: P wave dispersion, pulmonary endarterectomy, QT dispersion

INTRODUCTION

Several studies have evaluated the association between RV structure and ECG alterations in patients with either chronic thromboembolic pulmonary hypertension (CTEPH) or pulmonary arterial hypertension (PAH), which could be useful for diagnostic or prognostic purposes.^[1-6] However, it is still unknown to what extent the different ECG criteria reflect the changes in mass and volume of the right ventricle, and they are related to the RV overload determined by the elevated pressures in the pulmonary circulation. Unlike other types of pulmonary hypertension, CTEPH can be successfully treated with surgery. It is well demonstrated that pulmonary endarterectomy (PEA) allows dramatic improvements in the right heart hemodynamic profile immediately after surgery.^[7,8] On the contrary, regression of hypertrophy and restoration of regular RV systolic function requires more time and take place mainly during the first postoperative year.^[9,10] The QT interval reflects electrocardiographic (ECG) parameter of the duration of ventricular repolarization. The QT dispersion is the interleaved variability of QT interval on ECG that reflects regional differences in myocardial repolarization.

Enhanced the QT dispersion has been linked to the occurrence of malignant ventricular arrhythmias and sudden cardiac death.^[11-13] P wave terminal force in lead V1 was found to be an independent predictor of stroke in a vital trial.^[14] The aim of the present study was for this reason to evaluate the evolution of ECG parameters as potential predictors of future arrhythmias after PEA. However, this claim must to be supported with long-term results.

MATERIALS AND METHODS

The present study is a retrospective evaluation of 62 CTEPH patients who underwent PEA between 2009 and 2013 in the Marmara University Hospital by thoracic surgery and were followed up for at 6 months after surgery. Thoracic surgeon evaluated patients. Patients with Stage 4 did not perform a surgical operation. Exclusion criteria were previous

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myocardial infarction, significant left valvular heart disease, congenital heart disease, the necessity of additional cardiac surgery, persistent atrial fibrillation/flutter (three patients), and significant chronic lung disease. All patients underwent echocardiographic examination and a 12-lead ECG recording before surgery, at 6 months after surgery as part of the routine PEA follow-up protocol at our center. Conventional 12-lead ECG was recorded with the patient in supine position with commercially available ECG at a paper speed of 25 mm/s, the sensitivity of 1 mV = 10 mm, a sampling frequency of 500 Hz. Every ECG recorded and analyzed was checked by two expert cardiologists and were used to assess intra- and interobserver variability. The ECG parameters were measured: Heart rate, PR interval, QRS width, P width, and P wave amplitude in DII, P wave amplitude in aVL, P wave amplitude in V5, QT duration in DII, QT duration in aVL, QT duration in V5, P dispersion, and QT dispersion. The P wave onset and end-points were considered as the intersection of the P wave by the isoelectric line and the junction of the end-point of the P wave with the isoelectric line, respectively. The maximum P wave duration was suggested as the most extended P wave and the longest atrial conduction time, and the variation between the longest and the shortest P waves were indicated as the P wave dispersion [Figure 1]. The interval between the points of the isoelectric TP segment intercepted by the onset of the QRS complex and the descending branch of the T wave was suggested as the QT interval and was respective calculated for each derivation. The QT dispersion was determined as the variation between the longest and shortest QT intervals in any origin in the standard 12-lead ECG [Figure 2].

Ultrasound examinations were performed using commercially available echocardiographic equipment (Vivid 7 System). The following parameters were measured to study the right and left ventricle: Left ventricle ejection fraction, right ventricle tissue Doppler value (S'), myocardial perfusion index, pulmonary systolic pressure, right atrium and ventricle diameters, tricuspid annular plane systolic excursion, and degree of tricuspid regurgitation. For statistical analysis, SPSS 16.0 statistical package for Windows (SPSS Inc., Chicago, IL, USA). software was used. Categorical variables were defined as a percentage.

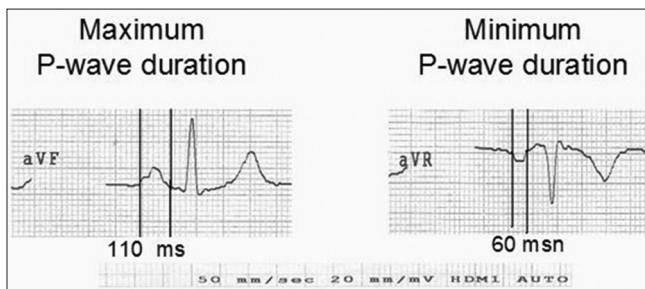


Figure 1: Two complexes extracted from 12-lead surface electrocardiography of a patient. In this case, maximum P-wave duration was observed from lead aVF and the minimum P-wave duration from lead automatic voltage regulator. Pine wilt disease was defined as the difference between the maximum and minimum P-wave durations

Quantitative variables were expressed as a mean \pm standard deviation and for the comparison of variables between two paired groups “paired sample Student T” (parametric distributed parameters) and “Wilcoxon” (for the parameters showing the nonparametric distribution) tests were used. Correlation analyses were performed by Spearman correlation test. $P < 0.05$ was accepted statistically significant.

RESULTS

The patient’s clinical characteristic are shown in Table 1. A total of 39 of the patients were of the male gender; mean age was 57 years, the vast majority had severe symptoms, 45 of the patients had a history of deep vein thrombosis, few of them had associated diseases such as chronic obstructive pulmonary disease, diabetes mellitus, and systemic hypertension. Eighty-nine percent of patients had functional Class III-IV. Hemodynamic values are shown in Table 2: the mean pulmonary arterial pressure of patients was 48.7 ± 14.9 . We assessed 62 CTEPH patients who underwent PEA. P wave amplitude (118.66 ± 2.77 vs. 109.16 ± 33.24 , $P < 0.016$) India, PR interval (157.9 ± 31.51 vs. 139.35 ± 29.28 , $P < 0.006$) P and QT dispersion changed significantly at 6 months after surgery. The P dispersion (27.93 ± 14.17 vs. 21.72 ± 11.04 , $P < 0.04$) and QT dispersion (53.37 ± 313.76 vs. 42.00 ± 18.79 , $P < 0.015$) were longer in before operation than in after operation [Table 3]. The patient’s echocardiographic values are shown in Table 4. It showed a marked reduction in RA pressure after surgery. The correlation analyses were demonstrated that there was a positive correlation between RVS’2-MPI 2 (after PEA) and P dispersion wave 1 (before PEA) [Table 5]. We have no data with PR dispersion associated with postsurgical atrial fibrillation. Overall intra- and inter-observer variability rates were similar.

DISCUSSION

The main result of the present study in patients with CTEPH is the differentiation, among the ECG markers of arrhythmia risk, of those more strictly related to the QT and P dispersion and those better reflecting the malign arrhythmia and atrial fibrillation. To the best of our knowledge, this is the first study to characterize the ECG changes in CTEPH patients

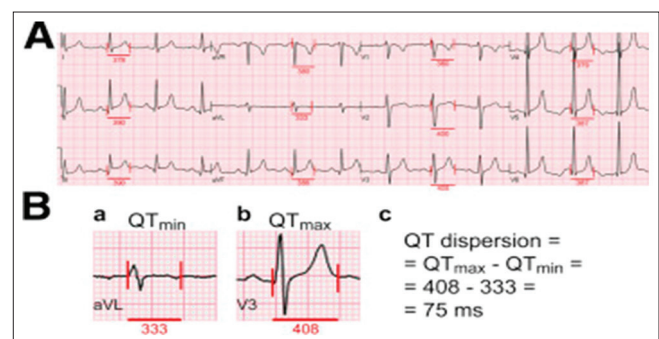


Figure 2: The QT dispersion is determined as the variation between the longest and shortest QT intervals in any origin in the standard 12-lead ECG

Table 1: Patients' clinical characteristics at baseline

	<i>n</i> (%)
Age	57±26
Male sex (<i>n</i>)	39 (62)
WHO class II/III/IV (%)	11/59/30
Previous deep venous thrombosis (<i>n</i>)	45 (72)
Systemic hypertension	18 (30)
Diabetes mellitus	4 (6)

WHO: World Health Organization

Table 2: Hemodynamic parameters of patients (before pulmonary endarterectomy)

Hemodynamic	values-average
mPAP (mmHg)	48.7±14.9
RAP (mmHg)	12.2±1.1
CO (l/min)	3.6±0.7
CI (l/min/m ²)	2.0±0.5
PVR (mmHg × min/l)	11.4±4.5
SVR (mmHg × min/l)	23.4±5.1
PVR/SVR	0.41±0.31

Data are presented as mean±SD. mPAP: Mean pulmonary artery pressure, RAP: Right atrial pressure, CO: Cardiac output, CI: Cardiac index, PVR: Pulmonary vascular resistance, SVR: Systemic vascular resistance, SD: Standard deviation

undergoing PEA, and arrhythmia-related morbidity and mortality are associated with reduced risk after surgery. Such patients are an excellent clinical model to study the effects of treatment of pulmonary hypertension on ECG markers of arrhythmia: first of all because the consequences of surgery on CTEPH patients by far exceed the impact of pharmacological therapy in other forms of pulmonary hypertension, with the only possible exception of the effects of calcium antagonists in patients with PAH responsive to vasodilators.^[15] Second because in such patients there is apparent dissociation between the hemodynamic improvement, which is immediate after surgery, and the reverse remodeling of the right ventricle, which takes time, up to inadequate preservation of the right heart during the early postoperative period, with stunning being reversible over a few months, and tethering of the right ventricular wall due to adhesion between the heart and surrounding tissues.^[15] Table 3 showed a marked reduction in RA pressure after surgery; this itself reduces the atrial stretching, which is surrogate for future remodeling and arrhythmia development.

We observed that PR interval in ECG, P wave amplitude in DII decreased significantly soon after the intervention at 6 months. Data in the literature in different forms of pulmonary hypertension indicate that a high P amplitude and a rightward-oriented QRS axis are linked to the presence of increased pulmonary pressures.^[16-18] The magnitude of the P wave has also been previously reported to be of prognostic value in patients with PAH.^[19] Finally, it has been suggested that an elevated P amplitude in lead DII, in association with changes in QRS and T wave axis, could be an important

Table 3: Patient's electrocardiography comparison between baseline (1) and 6 month (2)

	Mean±SD	SEM	95% CI of the difference	P
HR1 - HR2	17.61±1.54	3.16	-8.01	0.628
PR1 - PR2	34.69±18.54	6.23	5.82	0.006
QRS1 - QRS2	19.89±5.96	3.57	-1.32	0.105
Pwidth1 - Pwidth2	0.72±0.01	0.13	-0.24	0.902
PD21 - PD22	27.07±12.93	5.02	2.63	0.016
PaVL1 - PaVL2	28.29±6.72	5.25	-4.03	0.211
PV51 - PV52	24.44±2.83	4.46	-6.29	0.531
QTD21 - QTD22	53.43±1.06	9.92	-19.25	0.915
QTaVL1 - QTaVL2	42.29±4.55	7.85	-20.64	-0.579
QTV51 - QTV52	53.32±1.9	9.73	-18.01	0.847
Pdis1 - Pdis2	17.66±6.2	3.27	-0.51	0.04
QTdis1 - QTdis2	23.75±11.37	4.41	2.34	0.015

HR: Heart rate, PR: PR interval, QRS: QRS duration, PD2: P wave amplitude in D2 derivation, PaVL: P wave amplitude in aVL derivation, PV5: P wave amplitude in V5 derivation, QTD2: QT duration in D2 derivation, QTaVL: QT duration in aVL derivation, QTV5: QT duration in V5 derivation, Pdis: P wave dispersion, QTdis: QT dispersion, SD: Standard deviation, SEM: Standard error of mean, CI: Confidence interval

Table 4: Patient's echocardiographic values at pulmonary endarterectomy before (1) and after (2)

	<i>n</i>	Minimum	Maximum	Mean±SD
EF1	62	50,00	80,00	64.73±7.06
EF2	62	50,00	80,00	64.50±6.94
TAPSE1	62	7,00	21,00	12.11±3.47
TAPSE2	62	7,00	27,00	14.30±3.96
RVS1	62	6,00	15,00	9.30±2.52
RVS2	62	7,00	13,00	10.24±1.94
MPI1	62	0,23	1,50	0.64±0.24
MPI2	62	0,24	0,85	0.49±0.16
TRGRA1	62	1,00	3,00	2±1
TRGRA2	62	0	2,00	1±1
SPAB1	62	32,00	127,00	83.07±27.50
SPAB2	62	15,00	67,00	32.34±13.39
RA1	62	10,00	41,00	25.42±8.68
RA2	62	11,00	33,00	17.72±5.50
RVED1	62	32,00	52,00	41.66±5.43
RVED2	62	28,00	41,00	34.92±3.98

SD: Standard deviation, EF: Ejection fraction, TAPSE: Tricuspid annular plane systolic excursion, RVS²: Right ventricle systolic wave (cm/s), MPI: Myocardial Performance Index, TRGRA: Tricuspid regurgitation grade, sPAB: Systolic pulmonary artery pressure (mmHg), RA: Right atrium area (cm²), RVED: Right ventricle end diastolic diameter (cm)

determinant of treatment response in PAH patients, implying that routine ECG evaluation could be a significant contribution to the assessment of therapy response in PAH patients.^[20] The present study is in agreement with such previous findings, additionally, showing that the reduction in P wave amplitude in lead DII over the 3rd month.

The previous studies have shown that QT dispersion is an indicator for arrhythmia and CVD mortality^[20]

Table 5: Correlation analyses between right heart function parameters and electrocardiographic parameters

	QTdis1	QTdis2	Pdis1	Pdis2
TAPSE1				
Correlation	-0.282	-0.286	-0.015	-0.165
P	0.172	0.165	0.942	0.430
n	62	62	62	62
TAPSE2				
Correlation	-0.028	-0.247	0.081	0.139
P	0.895	0.233	0.701	0.508
n	62	62	62	62
RVS1				
Correlation	-0.094	-0.052	-0.091	0.179
P	0.654	0.805	0.666	0.393
n	62	62	62	62
RVS2				
Correlation	0.159	-0.380	0.571	0.226
P	0.457	0.067	0.004	0.287
n	62	62	62	62
MPI1				
Correlation	-0.123	-0.097	0.027	-0.048
P	0.568	0.650	0.900	0.825
n	62	62	62	62
MPI2				
Correlation	-0.189	-0.322	0.003	-0.062
P	0.388	0.134	0.988	0.777
n	62	62	62	62
RA1				
Correlation	0.006	0.184	-0.178	0.280
P	0.977	0.379	0.394	0.175
n	62	62	62	62
RA2				
Correlation	-0.053	0.317	-0.068	0.047
P	0.806	0.131	0.751	0.828
n	62	62	62	62
RVED1				
Correlation	0.286	-0.231	-0.070	0.315
P	0.301	0.426	0.805	0.273
n	62	62	62	62
RVED2				
Correlation	0.120	0.125	0.081	0.332
P	0.697	0.670	0.791	0.246
n	62	62	62	62

TAPSE: Tricuspid annular plane systolic excursion, RV S²: Right ventricle systolic wave (cm/s), MPI: Myocardial Perfusion Index, RA: Right atrium (cm²), RVED: Right ventricle end-diastolic diameter (cm), Pdis: P wave dispersion, QTdis: QT dispersion (1: Before operation, 2: After operation)

Tuncer *et al.*^[21] studied 25 patients with right ventricular hypertrophy without coexisting systemic hypertension, COPD, or PH who had emigrated from a high-altitude region to a low-altitude area 25 years previously and found that QT was significantly higher than in a healthy control group. Martin *et al.*^[22] found that QT was prolonged (defined as ≥ 0.45 s) in two of 25 patients with right ventricular hypertrophy without other coexisting disorders but was not statistically significant in comparison with a healthy

control group. Akgül *et al.*^[23] found that among patients with sickle cell disease, those with PH had significantly higher mean QTd than patients without PH. We discovered that QT dispersion changed a great deal at 6 months after surgery. Thereby, we believe that PEA may be diminished the risk of malign arrhythmia. QTc dispersion was found to be higher in patients without PEA than in a patient with PEA, and increased QT dispersion was not correlated with echocardiographic parameters in our study. This might be originated from our trial population is small.

Prolonged P-wave duration and increased P-wave dispersion are reported to carry an increased risk for atrial flutter or fibrillation.^[24] Many studies^[25-27] have shown that many diseases, such as PAH, bronchial asthma, diabetes mellitus, and acute rheumatic fever, in which the heart may be affected, exhibit a significantly longer P-wave duration. Large prospective clinical trials have shown that chronic atrial dilatation is an important and independent risk factor for the development of atrial fibrillation.^[28] In our study, there was a definite correlation between the MPI2-RVS2' (2: After PEA) and Pdis1 (1: Before PEA). The right ventricular systolic function may be increased as atrial stretch and preload decrease at the term of after operation.

We are aware that this study has some limitations. Foremost of these was a sample size smaller than that expected for a prospective cross-sectional study. The patients without PAH were determined by echocardiography alone, and right heart catheterization was not deemed to be ethical for these patients. This study should have an adequate number of patients in the mild, moderate, and severe groups to determine the correlation between the pulmonary artery pressure and dispersion durations.

CONCLUSIONS

Atrial and ventricular arrhythmia risks were found to be high in patients with PAH due to prolonged dispersion durations of P-wave, QT, and QTc. Further studies and multicentered studies are needed to enable an understanding of the underlying mechanisms and the diagnostic values of these electrophysiologic parameters. Physicians should pay close attention to possible atrial and ventricular arrhythmias during the clinical follow-up assessment and treatment of these patients.

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Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

- Lewczuk J, Ajlan AW, Piszko P, Jagas J, Mikulewicz M, Wrabec K, *et al.* Electrocardiographic signs of right ventricular overload in patients who underwent pulmonary embolism event(s). Are they useful in diagnosis of chronic thromboembolic pulmonary hypertension? *J Electrocardiol* 2004;37:219-25.
- Henkens IR, Gan CT, van Wolferen SA, Hew M, Boonstra A, Twisk JW,

- et al.* ECG monitoring of treatment response in pulmonary arterial hypertension patients. *Chest* 2008;134:1250-7.
3. Al-Naamani K, Hijal T, Nguyen V, Andrew S, Nguyen T, Huynh T, *et al.* Predictive values of the electrocardiogram in diagnosing pulmonary hypertension. *Int J Cardiol* 2008;127:214-8.
 4. Blyth KG, Kinsella J, Hakacova N, McLure LE, Siddiqui AM, Wagner GS, *et al.* Quantitative estimation of right ventricular hypertrophy using ECG criteria in patients with pulmonary hypertension: A comparison with cardiac MRI. *Pulm Circ* 2011;1:470-4.
 5. Kopeć G, Tyrka A, Miszalski-Jamka T, Sobień M, Waligóra M, Brózda M, *et al.* Electrocardiogram for the diagnosis of right ventricular hypertrophy and dilation in idiopathic pulmonary arterial hypertension. *Circ J* 2012;76:1744-9.
 6. Tonelli AR, Baumgartner M, Alkukhun L, Minai OA, Dweik RA. Electrocardiography at diagnosis and close to the time of death in pulmonary arterial hypertension. *Ann Noninvasive Electrocardiol* 2014;19:258-65.
 7. Mayer E, Jenkins D, Lindner J, D'Armini A, Kloek J, Meyns B, *et al.* Surgical management and outcome of patients with chronic thromboembolic pulmonary hypertension: Results from an international prospective registry. *J Thorac Cardiovasc Surg* 2011;141:702-10.
 8. Madani MM, Auger WR, Pretorius V, Sakakibara N, Kerr KM, Kim NH, *et al.* Pulmonary endarterectomy: Recent changes in a single institution's experience of more than 2,700 patients. *Ann Thorac Surg* 2012;94:97-103.
 9. D'Armini AM, Zanotti G, Ghio S, Magrini G, Pozzi M, Scelsi L, *et al.* Reverse right ventricular remodeling after pulmonary endarterectomy. *J Thorac Cardiovasc Surg* 2007;133:162-8.
 10. Reesink HJ, Marcus JT, Tulevski II, Jamieson S, Kloek JJ, Vonk Noordegraaf A, *et al.* Reverse right ventricular remodeling after pulmonary endarterectomy in patients with chronic thromboembolic pulmonary hypertension: Utility of magnetic resonance imaging to demonstrate restoration of the right ventricle. *J Thorac Cardiovasc Surg* 2007;133:58-64.
 11. Hii JT, Wyse DG, Gillis AM, Duff HJ, Solylo MA, Mitchell LB, *et al.* Precordial QT interval dispersion as a marker of torsade de pointes. Disparate effects of class Ia antiarrhythmic drugs and amiodarone. *Circulation* 1992;86:1376-82.
 12. Yunus A, Gillis AM, Duff HJ, Wyse DG, Mitchell LB. Increased precordial QTc dispersion predicts ventricular fibrillation during acute myocardial infarction. *Am J Cardiol* 1996;78:706-8.
 13. Zareba W, Moss AJ, le Cessie S. Dispersion of ventricular repolarization and arrhythmic cardiac death in coronary artery disease. *Am J Cardiol* 1994;74:550-3.
 14. Martinez-Selles M, Baranchuk A, Elosua R, Bayés de Luna A, O'Neal WT, Kamel H, *et al.* Advanced interatrial block and ischemic stroke: The atherosclerosis risk in communities study. *Neurology* 2016;87:2499.
 15. Rich S, Brundage BH. High-dose calcium channel-blocking therapy for primary pulmonary hypertension: Evidence for long-term reduction in pulmonary arterial pressure and regression of right ventricular hypertrophy. *Circulation* 1987;76:135-41.
 16. Henkens IR, Mouchaers KT, Vonk-Noordegraaf A, Boonstra A, Swenne CA, Maan AC, *et al.* Improved ECG detection of presence and severity of right ventricular pressure load validated with cardiac magnetic resonance imaging. *Am J Physiol Heart Circ Physiol* 2008;294:H2150-7.
 17. Penalzoza D, Arias-Stella J. The heart and pulmonary circulation at high altitudes: Healthy highlanders and chronic mountain sickness. *Circulation* 2007;115:1132-46.
 18. Ahearn GS, Tapson VF, Rebeiz A, Greenfield JC Jr. Electrocardiography to define clinical status in primary pulmonary hypertension and pulmonary arterial hypertension secondary to collagen vascular disease. *Chest* 2002;122:524-7.
 19. Bossone E, Paciocco G, Iarussi D, Agretto A, Iacono A, Gillespie BW, *et al.* The prognostic role of the ECG in primary pulmonary hypertension. *Chest* 2002;121:513-8.
 20. Malik M, Batchvarov VN. Measurement, interpretation and clinical potential of QT dispersion. *J Am Coll Cardiol* 2000;36:1749-66.
 21. Tuncer M, Gunes Y, Guntekin U, Aslan S, Gumrukcuoglu HA, Eryonucu B, *et al.* Association of increased QTc dispersion and right ventricular hypertrophy. *Med Sci Monit* 2008;14:CR102-105.
 22. Martin AB, Garson A Jr., Perry JC. Prolonged QT interval in hypertrophic and dilated cardiomyopathy in children. *Am Heart J* 1994;127:64-70.
 23. Akgül F, Seyfeli E, Melek I, Duman T, Seydaliyeva T, Gali E, *et al.* Increased QT dispersion in sickle cell disease: Effect of pulmonary hypertension. *Acta Haematol* 2007;118:1-6.
 24. Dilaveris PE, Gialafos EJ, Sideris SK, Theopistou AM, Andrikopoulos GK, Kyriakidis M, *et al.* Simple electrocardiographic markers for the prediction of paroxysmal idiopathic atrial fibrillation. *Am Heart J* 1998;135:733-8.
 25. Yücel O, Yildiz M, Altinkaynak S, Sayan A. P-wave dispersion and P-wave duration in children with stable asthma bronchiale. *Anadolu Kardiyol Derg* 2009;9:118-22.
 26. Köken R, Demir T, Sen TA, Kundak AA, Oztekin O, Alpay F, *et al.* The relationship between P-wave dispersion and diastolic functions in diabetic children. *Cardiol Young* 2010;20:133-7.
 27. Kocaoglu C, Sert A, Aypar E, Oran B, Odabas D, Arslan D, *et al.* P-wave dispersion in children with acute rheumatic fever. *Pediatr Cardiol* 2012;33:90-4.
 28. Psaty BM, Manolio TA, Kuller LH, Kronmal RA, Cushman M, Fried LP, *et al.* Incidence of and risk factors for atrial fibrillation in older adults. *Circulation* 1997;96:2455-61.

In-Hospital Cost Comparison of Transcatheter Closure versus Surgical Closure of Secundum Atrial Septal Defect

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Abstract

Introduction: We compared transcatheter and surgical closure of secundum atrial septal defects (ASDs) in terms of cost in this study. **Materials and Methods:** Between 2006 and 2015, 291 consecutive patients having secundum ASD, in whom percutaneous or surgical closure was performed, were included in this study. We compared the in-hospital cost of transcatheter versus surgical ASD closure in these patients. **Results:** We collected totally 291 patients, 214 transcatheter and 77 surgical closure procedures, retrospectively. Patients with a surgical closure had a longer length of stay (11.8 ± 3.8 days vs. 2.8 ± 1.6 days, $P < 0.001$). There was no in-hospital mortality in two groups. Costs denominated in Turkish lira (TL) and United States Dollar (USD) of transcatheter closure were higher than that of surgical closure (TL 10955.6 ± 183.4 vs. TL 6016.7 ± 371.9 $P < 0.001$; USD 6531.2 ± 149.62 vs. USD 3896.2 ± 234.7 $P < 0.001$). The cost of percutaneous ASD closure increase does not correlate with the dollar rate on the annual basis. This with the supplier firms has excessive profits in the first year of the study. **Conclusion:** Compared with other countries with regard to cost, transcatheter ASD closure is a more expensive treatment than surgical closure in our country.

Keywords: Cardiac surgical procedures, cost analysis, ostium secundum atrial septal defect, septal occluder device

INTRODUCTION

Atrial septal defects (ASDs) are among the most common congenital heart disease.^[1] ASD can be closed either surgically or with a transcatheter device; however, transcatheter strategy as a less invasive procedure, it has become the accepted treatment in patients with appropriate anatomy.^[2] The outcomes of percutaneous ASD closures have been compared with surgical closures. It has been shown that transcatheter ASD closure is as effective as the surgical ASD closure.^[3,4] Since transcatheter closure is commonly used in ASD, it is important to examine its cost as an important dimension of comparative effectiveness. Many small studies have previously reported that ASD closure is generally associated with lower hospital costs than that of surgical ASD closure.^[5-7] However, recently, it has been shown that surgical or transcatheter ASD closure has diversity regarding hospital costs between individual centers.^[8] We aimed to compare the costs of transcatheter and surgical ASD closure in Turkey.

MATERIALS AND METHODS

This is a retrospective study that included patients with a diagnosis of secundum ASD who were treated by transcatheter occlusion or surgical closure between December 2006 and September 2015. Our study's Ethics Committee and Institutional approval were obtained from Izmir Katip Çelebi University. For a proper cost evaluation, ASD patients with other concomitant congenital anomalies and those who underwent additional procedures such as percutaneous transcatheter coronary intervention, coronary bypass surgery, or valve operation were excluded from this study. Therefore, 214 patients with transcatheter closure and 77 patients with surgical closure were included in the study. Patient demographics, hospital length of stay (LOS),

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and total charges were evaluated using the hospital records. The complaints on application or presenting symptoms were dyspnea, palpitation, recurrent stroke, and chest pain. Concomitant valve diseases were mild-to-moderate pulmonary regurgitation/stenosis, tricuspid regurgitation, and mitral regurgitation.

The percutaneous ASD closure procedure was performed under general anesthesia using ASD closure device in accordance with the techniques described in the literature.^[9] The patients undergoing surgical treatment were operated under general anesthesia using the standard approach. The right atrium was opened following median sternotomy, and the ASD was closed with a primary suture or pericardial patch under cardiopulmonary bypass. Only one patient underwent a minithoracotomy without sternotomy. The patients were fully informed of the treatment options, which were decided on with the heart team and patients.

Bleeding complications were divided into two categories. Major bleeding was defined as the need for transfusion of >2 units of erythrocyte suspension; otherwise, it was minor bleeding. Minimal leakage was defined as leakage without associated hemodynamic complications.

The cost data were obtained directly from the accounting and resource departments of our hospital. This is a government hospital; there are no items invoiced from outside, and all cost items are invoiced to a reimbursement agency. All prices were calculated in Turkish lira (TL) and converted to the United States dollars (USD) based on the exchange rate given by the Central Bank of the Republic of Turkey on the invoice date.^[10] Considering the cost analysis of the study, the period from the day of the patients' hospitalization to the day when they were discharged was assessed. In terms of the study perspective, our work is a direct cost analysis based on the reimbursement agency (Social Security Institution).

RESULTS

Of 291 of the included patients, 214 underwent transcatheter procedures and 77 underwent surgical closure. The baseline clinical and demographic characteristics of the two groups are demonstrated in Table 1. There was no difference in terms of sex, age, or comorbidities between the two groups. The presenting symptoms were similar in the groups. The surgical closure group had longer LOS (11.8 ± 3.8 days vs. 2.8 ± 1.6 days, $P < 0.001$). There was no in-hospital mortality in either groups. The number of concomitant valve diseases was higher in the surgery group ($P < 0.05$) [Table 1].

Periprocedural complications are presented in Table 2. Minimal leakage after the procedure was seen in 7% of the patients treated with transcatheter closure. Device embolization was observed in three patients, and reintervention was performed. Dehiscence was seen in three patients after the procedure, and surgery was performed in these patients. In addition, 78% of the transcatheter patients underwent balloon sizing. The

Table 1: Baseline clinical characteristics of patients

Variable	Transkateter kapatma (n=214)	Cerrahi kapatma (n=77)	P
Age (years)	36.5±14.7	33.2±13.8	0.082
Sex (male/female)	68/146	20/57	0.400
Hypertension, n (%)	28 (13)	6 (7)	0.197
Diabetes mellitus, n (%)	9 (4)	2 (2)	0.507
Chronic renal failure, n (%)	1 (0.4)	0	0.544
Complaint on application, n (%)			
Dyspnea	100 (45)	48 (59)	0.094
Palpitation	44 (20)	18 (22)	
Recurrent stroke	2 (1)	0	
Chest pain	2 (1)	0	

Table 2: Procedural complications

Variable	Transcatheter ASD closure-(n=214), n (%)	Surgical ASD closure-(n=77), n (%)	P
Periprocedural shunt	15 (7)	0	0.016
Bleeding	4 (1.4)	50 (61)	<0.01
Pleural effusion	0	2 (2.4)	0.065
Pericardial effusion	6 (3)	11 (14)	<0.01
Pneumothorax	0	2 (2.4)	0.019
Arrhythmia	5 (2.4)	0	0.393
Repeat operation	1 (0.4)	0	0.544

ASD: Atrial septal defect

Amplatzer occluder device was used in 55%, Cardi-O-Fix occluder device was used in 42%, and BioSTAR occlude device was used in 3% of the patients. The surgical closure was performed with primary suture in 53%, and patch usage for closure was in 47% of patients. Both major and minor bleeding were more common in the surgery closure group than in the percutaneous closure group (9% vs. 3%, $P < 0.05$ and 5% vs. 0%, $P < 0.05$, respectively). The rate of pneumothorax requiring surgical intervention was higher in patients treated with surgery [Table 2].

The procedural success rate was similar between the percutaneous closure and surgical closure groups (95% vs. 99%, $P = 0.139$). In this study, the cost of transcatheter closure, denominated in TL and USD, was higher than that of surgical closure (TL $10\,955.6 \pm 183.4$ vs. TL 6016.7 ± 371.9 , $P < 0.001$; USD 6531.2 ± 149.62 vs. USD 3896.2 ± 234.7 , $P < 0.001$) [Figures 1 and 2]. The increase in the cost of percutaneous ASD closure did not correlate with the USD/TL exchange rate on an annual basis.

DISCUSSION

Following the first percutaneous ASD closure procedure, parallel to the developing technology, this technique has become an alternative to surgical therapy in the appropriate

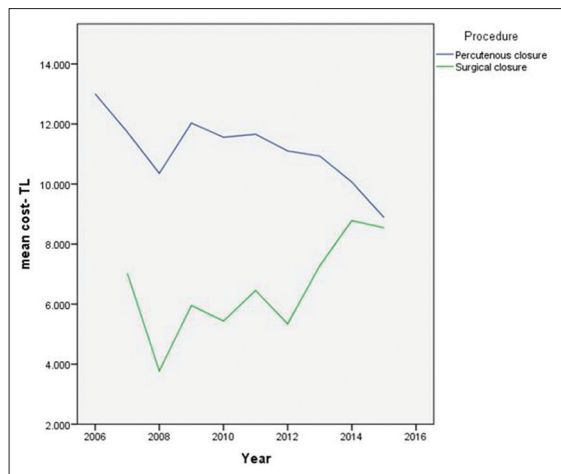


Figure 1: Turkish Lira (TL) based cost change over years in both surgical and transcatheter closure

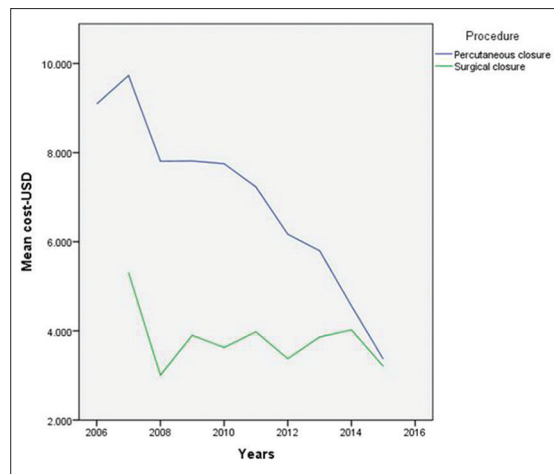


Figure 2: United States dollar (USD) based cost change over years in both surgical and transcatheter closure

direction.^[11] The outcomes of percutaneous ASD closure have been compared with those of surgical closure. It has been shown that transcatheter ASD closure is as effective as surgical ASD closure.^[3,4] However, the results of cost-effectiveness analysis for ASD closure are still considered controversial. In a Guatemalan study by Vida *et al.*,^[12] surgery costs 3.330 USD, while percutaneous closure costs 4.521 USD. Moreover, in Thomson *et al.*'s^[5] study from the United Kingdom, the surgical procedure cost was 5375 Sterling, while the percutaneous procedure cost was 5.412 Sterling. Conversely, a study carried out in the United States, by O'Byrne *et al.*,^[13] reported that the cost of operative closure was 60.992 USD, while that of transcatheter closure was 55.841 USD. From the USA again, Ooi *et al.*^[14] reported that the costs of the transcatheter procedure were lower than those of surgical closure (mean of 19.128 USD vs. 25.359 USD). In a Canadian study, Mylotte *et al.*^[7] reported that the cost of surgical closure costs 15.304 Canadian Dollars, while it costs 11 060 Canadian Dollars for the transcatheter closure group.

Based on the previous studies, transcatheter closure has lower costs compared with surgical closure. However, from Turkey, Ayık *et al.*^[15] reported that the median cost was significantly higher in the percutaneous group (10.698 TL vs. 5.572 TL). In this study, we found that the cost of transcatheter closure was higher than that of surgical closure (TL 10.955.6 ± 183.4 TL vs. 6.016.7 ± 371.9 TL, 6.531 2 ± 149 62; USD vs. 3.896.2 ± 234.7 USD, *P* < 0.001). The most noticeable finding was that, while the USD/TL exchange rate increased from 2006 to 2015, the cost denominated in TL for ASD closure devices did not increase concordantly.

Transcatheter closure has a higher price than surgical closure because an imported device is not used in the surgical option, and the operation fee is the main cost. For transcatheter closure, the main cost is the imported device for this procedure. However, in both surgical and transcatheter closures the fee paid to doctors for the operation is too low, i.e. 20%–25% of the total cost. To import an ASD occluder device depends to foreign exchange

rate, and the low value of the TL in foreign exchange is the first reason for the high prices in Turkey; the other and most noticeable reason is that, while the USD/TL exchange rate had been increasing from 1.03 to 3.03 in 2006–2015, the TL-based transcatheter ASD closure versus surgical ASD closure costs were as nearly the same. This shows that importer companies had high profits in the first few years [Figures 1 and 2].

Study limitations

Even in prospective studies, because the earnings of people can be in very large spectrum, it is difficult to standardize the cost of lost work. This is a short-term and retrospective study, so the main limitation of our study is that we could not reach the datas about patients' cost of labor loss. Therefore, we cannot know whether the cost difference between surgical and percutaneous ASD closure will be different in the long-term period.

CONCLUSION

Compared with the european countries, the high cost of imported closure devices and supplier firms' high profit rates in the percutaneous group conversely for the surgical group, lower doctor fees in Turkey and no need to imported device, in Turkey surgical closure becomes more cost-effective than transcatheter closure.

Acknowledgment

All procedures were done with the patient's approval and all authors declare that they were not involved in any conflict of interest.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Marelli AJ, Mackie AS, Ionescu-Ittu R, Rahme E, Pilote L. Congenital heart disease in the general population: Changing prevalence and age

- distribution. *Circulation* 2007;115:163-72.
2. Krasuski RA, Bashore TM. The emerging role of percutaneous intervention in adults with congenital heart disease. *Rev Cardiovasc Med* 2005;6:11-22.
 3. Hughes ML, Maskell G, Goh TH, Wilkinson JL. Prospective comparison of costs and short term health outcomes of surgical versus device closure of atrial septal defect in children. *Heart* 2002;88:67-70.
 4. Kotowycz MA, Therrien J, Ionescu-Ittu R, Owens CG, Pilote L, Martucci G, *et al.* Long-term outcomes after surgical versus transcatheter closure of atrial septal defects in adults. *JACC Cardiovasc Interv* 2013;6:497-503.
 5. Thomson JD, Aburawi EH, Watterson KG, Van Doorn C, Gibbs JL. Surgical and transcatheter (Amplatzer) closure of atrial septal defects: A prospective comparison of results and cost. *Heart* 2002;87:466-9.
 6. Baker SS, O'Laughlin MP, Jollis JG, Harrison JK, Sanders SP, Li JS, *et al.* Cost implications of closure of atrial septal defect. *Catheter Cardiovasc Interv* 2002;55:83-7.
 7. Mylotte D, Quenneville SP, Kotowycz MA, Xie X, Brophy JM, Ionescu-Ittu R, *et al.* Long-term cost-effectiveness of transcatheter versus surgical closure of secundum atrial septal defect in adults. *Int J Cardiol* 2014;172:109-14.
 8. Pasquali SK, Jacobs ML, He X, Shah SS, Peterson ED, Hall M, *et al.* Variation in congenital heart surgery costs across hospitals. *Pediatrics* 2014;133:e553-60.
 9. Wilkinson JL, Goh TH. Early clinical experience with use of the 'Amplatzer septal occluder' device for atrial septal defect. *Cardiol Young* 1998;8:295-302.
 10. Available from: http://www.tcmb.gov.tr/kurlar/kurlar_tr.html.
 11. Faella HJ, Sciegata AM, Alonso JL, Jmelnitsky L. ASD closure with the Amplatzer device. *J Interv Cardiol* 2003;16:393-7.
 12. Vida VL, Barnoya J, O'Connell M, Leon-Wyss J, Larrazabal LA, Castañeda AR, *et al.* Surgical versus percutaneous occlusion of ostium secundum atrial septal defects: Results and cost-effective considerations in a low-income country. *J Am Coll Cardiol* 2006;47:326-31.
 13. O'Byrne ML, Gillespie MJ, Shinohara RT, Dori Y, Rome JJ, Glatz AC, *et al.* Cost comparison of transcatheter and operative closures of ostium secundum atrial septal defects. *Am Heart J* 2015;169:727-3500.
 14. Ooi YK, Kelleman M, Ehrlich A, Glanville M, Porter A, Kim D, *et al.* Transcatheter versus surgical closure of atrial septal defects in children: A value comparison. *JACC Cardiovasc Interv* 2016;9:79-86.
 15. Ayik MF, Işık O, Akyüz M, Kiliç AÖ, Karakuş E, Levent E, *et al.* Cost-effectiveness analysis between surgical and percutaneous closure of atrial septal defects. *Nobel Med* 2015;11:33-6

Is it a New Late Complication of Transcatheter Aortic Valve Implantation?

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Abstract

Transcatheter aortic valve implantation (TAVI) is a novel method for patients with severe aortic stenosis at high surgical risk. Although short- and medium-term outcomes after TAVI are encouraging, long-term data on valve function and clinical outcomes are limited. Hence, our case can make a contribution to literature. An 80-year-old patient with severe aortic stenosis underwent TAVI in our clinic in October 2015. After 5 months, she admitted to our emergency department with severe dyspnea. Her symptoms were started within 2 days and getting worse day by day. Echocardiography revealed us a severe aortic regurgitation due to dislocation of the valve to the left ventricular outflow tract side. After diagnosis, aortic regurgitation was treated by valve-in-valve technique. TAVI may provide an alternative therapeutic approach to ineligible or poor surgical candidates of degenerative aortic stenosis. However, this technique also has some complications such as mortality, atrioventricular (AV) block, stroke, and coronary obstruction. Valve embolization is another rare complication of this procedure and usually can be prevented by careful preprocedure annulus measurements, stable lead positioning for rapid pacing, optimal valve positioning, full balloon inflation at the time of valve deployment, and complete balloon deflation before stopping rapid pacing. At this point, our case became important for the complication literature with its time, about 5 months. Because it is the more recently used technique, we need much more time to detect the usefulness and complications of TAVI and learn how to avoid these complications.

Keywords: Aortic stenosis, transcatheter aortic valve implantation, valve migration

INTRODUCTION

Degenerative aortic stenosis is the most commonly acquired valvular heart disease in adults, with a prevalence of 4% in patients over 80 years of age. In symptomatic patients, surgical aortic valve replacement has been the treatment of choice for 40 years.^[1] However, especially for the older ages, up to 30%–60% of cases are considered too high risk for open-heart surgery.^[2–4] Transcatheter aortic valve implantation (TAVI) has been introduced in 2002 by Cribier *et al.* to treat older surgical high-risk patients with severe symptomatic aortic stenosis.^[5]

The EuroSCORE and Society of Thoracic Surgeons (STS) score are the most widely used risk scores to predict operative mortality in cardiac surgery.^[6]

CASE REPORT

The patient with severe aortic stenosis was hospitalized; after a multidisciplinary discussion by the heart team, the patient was planned for TAVI using the Edwards SAPIEN valve through a transfemoral approach [Figure 1]. When

this procedure was administered, the patient was morbidly obese with 40.8 body mass index (BMI). After 5 months, she was admitted to our hospital with severe dyspnea and decreased effort capacity that worsened day by day. Her medical therapy was started immediately and evaluated for the reason. During her examination, echocardiography revealed us a severe aortic regurgitation due to dislocation of the valve to the left ventricular outflow tract. After hemodynamic stability facilitated, she was taken to laboratory and 26 mm CoreValve Evolut R was implanted as valve-in-valve technique [Figures 2 and 3]. No acute complication occurred; after 5-day hospitalization, she was discharged. At the second administration, her BMI was 29.2; she lost 29 kg in 7 weeks, which can be the cause of valve migration.

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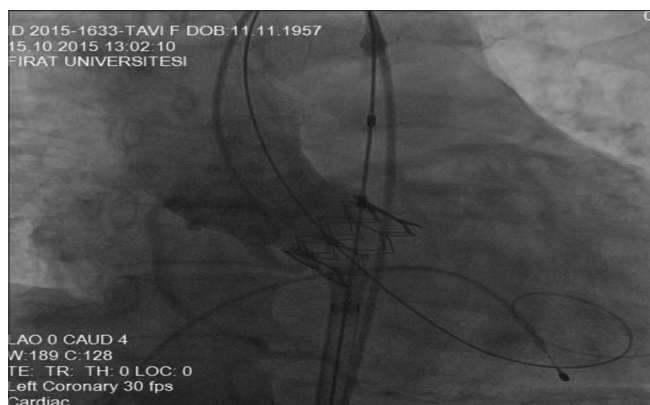


Figure 1: First transcatheter aortic valve implantation administration

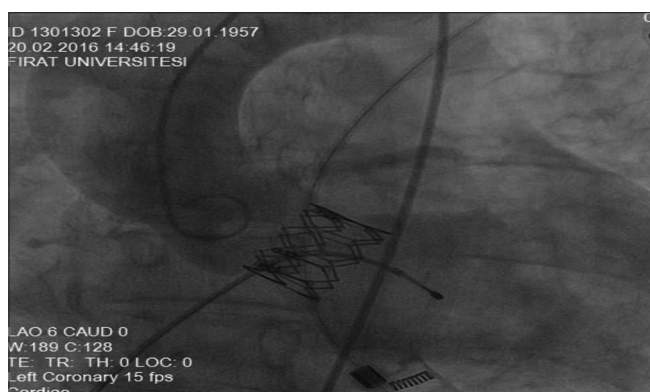


Figure 2: Migration of valve

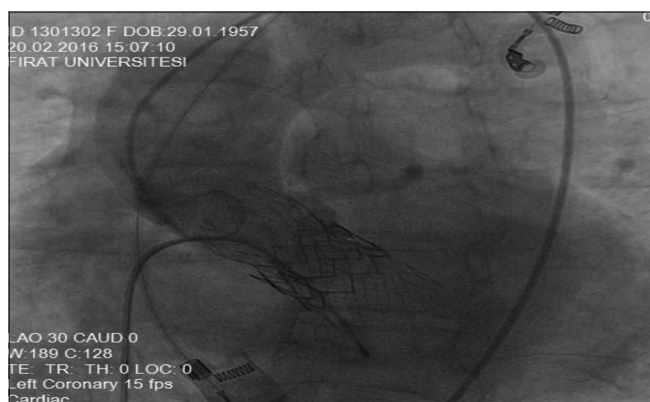


Figure 3: Valve in valve

DISCUSSION

The recently introduced Valve Academic Research Consortium 1^[7] and 2^[8] criteria may help to standardize the documentation of postoperative complications such as myocardial infarction, stroke, bleeding, acute kidney injury, vascular complications, and valve performance, as well as the risk of mortality. Malpositioning, valve migration/embolization, conversion to open surgery, renal failure, need for pacemaker implantation, stroke, and myocardial infarct are other major complications following TAVI.^[9] Blocking the coronary ostia and limiting the anterior mitral leaflet mobility and atrioventricular (AV)

conduction system are some frequently encountered perioperative complications.^[10]

Prosthesis embolization immediately after deployment is usually the result of prosthesis/annulus mismatch (implantation of a prosthesis which has been undersized for the annulus), unduly high implantation, or ejection of the device by an effective ventricular contraction during deployment. Embolization to the aorta is usually well tolerated provided coaxial wire position is maintained, preventing the valve from flipping over to obstruct antegrade flow.

Retrograde migration of the prosthetic valve following TAVI is rare. It can occur during the procedure, within the first few days after the procedure or subsequently. The first step in developing a solution is to identify the contributing factors for migration. These range from prosthesis malpositioning (i.e., too low), suboptimal valve expansion, and uneven or insufficient aortic annulus calcification, leading to inadequate prosthesis fixation, aortic paravalvular regurgitation, valve undersizing, and anatomical or functional bicuspid valves.

Transcatheter heart valve (THV) migration into the left ventricle has been described 2–43 days after deployment and is associated with cardiogenic shock or disruption of mitral valve function. Mechanisms responsible for downward THV migration can include native leaflet overhang postdeployment, exerting downward force on the THV, or limited anchoring of the THV from low deployment in a relatively large and nonseverely calcified annulus or from deployment of a THV that is too small for the native aortic valve annulus. Although rare, delayed THV migration should be suspected when there is a worsening of the patient's clinical status or unfavorable THV hemodynamic profile (increasing mean gradient or worsening regurgitation) on follow-up echocardiographic examination.

CONCLUSION

Because it is the more recently used technique, we need much more time to detect the usefulness and complications of TAVI. With the latest time of migration (about 150 days), our case became so important for the complications of TAVI.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Charlson E, Legedza AT, Hamel MB. Decision-making and outcomes in severe symptomatic aortic stenosis. *J Heart Valve Dis* 2006;15:312-21.
2. Lung B, Baron G, Butchart EG, Delahaye F, Gohlke-Bärwolf C, Levang OW, *et al.* A prospective survey of patients with valvular heart disease in Europe: The Euro Heart Survey on Valvular Heart Disease. *Eur Heart J* 2003;24:1231-43.
3. Varadarajan P, Kapoor N, Bansal RC, Pai RG. Clinical profile and natural history of 453 nonsurgically managed patients with severe aortic stenosis. *Ann Thorac Surg* 2006;82:2111-5.
4. Pai RG, Kapoor N, Bansal RC, Varadarajan P. Malignant natural history of asymptomatic severe aortic stenosis: Benefit of aortic valve replacement. *Ann Thorac Surg* 2006;82:2116-22.
5. Cribier A, Eltchaninoff H, Bash A, Borenstein N, Tron C, Bauer F, *et al.* Percutaneous transcatheter implantation of an aortic valve prosthesis for calcific aortic stenosis: First human case description. *Circulation* 2002;106:3006-8.
6. Piazza N, Wenaweser P, van Gameren M, Pilgrim T, Tzikas A, Otten A, *et al.* Relationship between the logistic EuroSCORE and the society of thoracic surgeons predicted risk of mortality score in patients implanted with the CoreValve reValving system – a bern-rotterdam study. *Am Heart J* 2010;159:323-9.
7. Leon MB, Piazza N, Nikolsky E, Blackstone EH, Cutlip DE, Kappetein AP, *et al.* Standardized endpoint definitions for transcatheter aortic valve implantation clinical trials: A consensus report from the valve academic research consortium. *Eur Heart J* 2011;32:205-17.
8. Zierer A, Wimmer-Greinecker G, Martens S, Moritz A, Doss M. Is transapical aortic valve implantation really less invasive than minimally invasive aortic valve replacement? *J Thorac Cardiovasc Surg* 2009;138:1067-72.
9. Wendler O, Thielmann M, Schroefel H, Rastan A, Treede H, Wahlers T, *et al.* Worldwide experience with the 29-mm edwards SAPIEN XT™ transcatheter heart valve in patients with large aortic annulus. *Eur J Cardiothorac Surg* 2013;43:371-7.
10. Johansson M, Nozohoor S, Kimblad PO, Harnek J, Olivecrona GK, Sjögren J, *et al.* Transapical versus transfemoral aortic valve implantation: A comparison of survival and safety. *Ann Thorac Surg* 2011;91:57-63.

Thrombus in Transit Causing Acute Massive Pulmonary Emboli Treated Successfully with Reteplase Administration

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Abstract

Acute pulmonary thromboembolism (PTE) is a leading cause of mortality and morbidity. Observation of the right atrial thrombi is a rare condition, which usually accompanies to massive PTE. Urgent treatment strategies for rapid thrombus removal are mandatory in patients presenting with acute massive PTE. In this paper, we present a patient admitting with acute massive PTE to our emergency department, in whom concomitant right atrial thrombus was successfully treated with reteplase.

Keywords: Acute pulmonary thromboembolism, reteplase, right atrial thrombi

INTRODUCTION

Pulmonary thromboembolism (PTE) is the most important emergencies in cardiovascular system with high rate of mortality without appropriate treatment.^[1] The diagnosis of PTE is difficult, and it may be overlooked because it does not emerge as of a specific clinical condition. Furthermore, in recent years, advances in diagnostic methods have also increased the frequency of diagnosis of PTE. The mortality rate in patients with PTE who cannot be diagnosed reaches 30%; this rate may be reduced to 3% when diagnosed and treated appropriately.^[2] In the majority of cases, the source of thrombus is in the deep veins of the lower extremities, especially the common femoral, superficial, femoral, and popliteal pelvic veins.

CASE REPORT

A 77-year-old woman was admitted to the emergency department with complaints of acute severe dyspnea and cyanosis. She reported that her complaints had begun 3 days ago. Before this event, she walked a long distance and done strenuous exercise. In her medical history, she had asthma. On admission, she was tachycardic (152 bpm), hypotensive (85/52 mmHg), and tachypneic (36 min⁻¹). Her oxygen saturation was 88% with oxygen mask. On physical examination, she had right ventricular S₃, 2/6 systolic murmur on tricuspid area, and bilateral severe crackles in both lungs.

Her extremities were cyanotic. On electrocardiogram, tachycardia, atrial flutter, and right axis deviation were detected. Right ventricular dilation (46 mm) and severe hypokinesis of the right ventricle lateral wall were observed on transthoracic echocardiography (TTE). A highly erratic, 44 cm × 19 mm-sized worm-like mass appearance, originating from vena cava inferior and freely floating in the right atrium, consistent with “Thrombus in Transit” (ThIT) was detected on TTE [Figure 1]. Furthermore, her pulmonary artery pressure was measured 75 mmHg. The patient was diagnosed as acute massive pulmonary emboli. Her blood sample analysis showed anemia and thrombocytopenia (hemoglobin: 10.8 g/dl and platelet: 1 04.000). Since she had massive pulmonary emboli with cardiogenic shock, we immediately decided to initiate thrombolytic and intravenous anticoagulant therapy. Reteplase (10 IU bolus dose followed by a 10 IU bolus 30 min after) and unfractionated heparin were given. Two hours after thrombolytic therapy, her blood pressure turned to normal ranges and her oxygen saturation was raised to 93%. Control TTE was performed the day after thrombolytic therapy, which revealed smaller right ventricular size (39 mm) and

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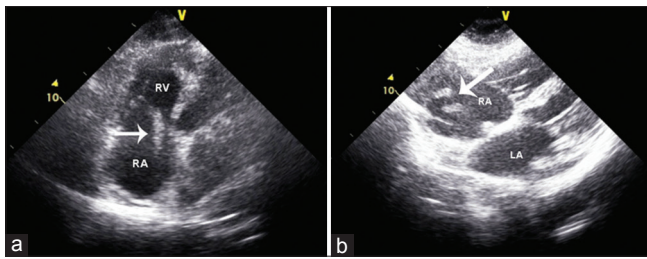


Figure 1: Apical four-chamber (a) and subcostal (b) views demonstrating highly erratic thrombus (white arrow) freely floating in the right atrium and protruding into the right ventricle. RA: Right atrium, RV: Right ventricle, LA: Left ventricle

lower pulmonary artery pressure (48 mmHg) with no visible thrombus appearance [Figure 2]. Oral anticoagulant therapy with warfarin was started on the 3rd day of her hospitalization. She was discharged on the 8th day of her admission.

DISCUSSION

Acute PTE usually occurs from deep venous thrombosis, and these thrombi migrate to the lungs through vena cava inferior and right atrium. Entrapment of thrombi in the right heart, so-called “thrombus in transit” (ThIT), is a rare finding, which is observed in only 4% of patients admitting with acute PTE. Patients presenting with ThIT in their right chambers are usually much more hemodynamically compromised than patients without ThIT.^[3] Observation of ThIT directly confirms acute PTE diagnosis, and no other imaging modality is required in the early phase for determination of management strategy. Administration of intravenous heparin alone or rapid elimination of thrombus is possible treatment choice in patients with ThIT-complicated acute PTE.^[4] On the other hand, 90-day mortality rates are significantly higher in patients treated with heparin alone; so, choosing a management strategy for rapid elimination of ThIT is highly reliable.^[3]

Catheter-based extraction, surgical removal, and thrombolytic therapy are possible choices for rapid elimination of ThIT. Since most of the patients are hemodynamically unstable, administration of thrombolytic therapy seems easier and safer. On the other hand, disconnection of the thrombi from the entrapment area before complete lysis of it may theoretically lead to massive re-emboli. Continuous and slow infusion of thrombolytic agents may be preferable for getting over of this possible complication. There are case reports showing successful lysis of ThIT with streptokinase^[5] and tissue plasminogen activator.^[6] Both agents are infused continuously in a longer period when compared to reteplase. Reteplase is approved for the treatment of acute coronary syndromes, but it has also been evaluated in individuals with acute PTE.^[7] Reteplase is the first clinically available modified tissue plasminogen activator produced by recombinant DNA technology. Reteplase preferentially activates plasminogen on the clot surface and is classified as fibrin specific. The fibrin-specific agents have longer half-lives (e.g., 11–19 min), which allow bolus administration. The recommended dose of

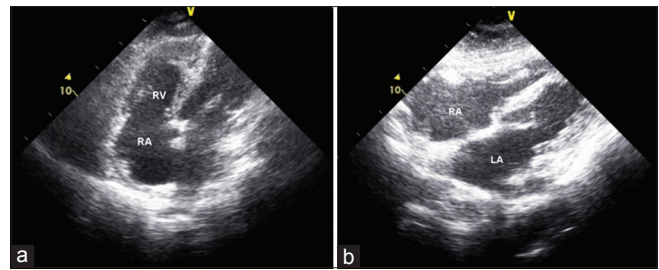


Figure 2: Apical four-chamber (a) and subcostal (b) view of the same patient after reteplase administration. No visible thrombus is seen and the right heart chambers are smaller. RA: Right atrium, RV: Right ventricle, LA: Left ventricle

reteplase is 10 U followed by a further 10 U after 30 min. Each injection must be given over a period of no longer than 2 min.^[8] Reteplase also alleviates the risk of allergic reactions associated with the first-generation thrombolytics. Our case report is demonstrating successful thrombolysis of ThIT with reteplase in a patient admitting with acute massive PTE.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

- Guidelines on the Diagnosis and Management of Acute Pulmonary Embolism. Task force on pulmonary embolism, European society of cardiology. *Eur Heart J* 2014;35:3033-80.
- Yılmaz Z, Ercan G, Recep D. Affecting factors on early mortality in elderly patients diagnosed with pulmonary embolism in emergency department. *Turk J Geriatr* 2015;18:97-103.
- Torbicki A, Galié N, Covezzoli A, Rossi E, De Rosa M, Goldhaber SZ, *et al.* Right heart thrombi in pulmonary embolism: Results from the international cooperative pulmonary embolism registry. *J Am Coll Cardiol* 2003;41:2245-51.
- Mollazadeh R, Ostovan MA, Abdi Ardekani AR. Right cardiac thrombus in transit among patients with pulmonary thromboemboli. *Clin Cardiol* 2009;32:E27-31.
- Tekin K, Çağhyan ÇE, Karaaslan O, Uysal OK, Özkan B, Çaylı M, *et al.* Witnessing a rare event: Thrombus in transit after coronary angiography. *Anadolu Kardiyol Derg* 2011;11:E22.
- Ruiz-Bailén M, López-Calder C, Castillo-Rivera A, Rucabado-Aguilar L, Ramos Cuadra JA, Lara Toral J, *et al.* Giant right atrial thrombi treated with thrombolysis. *Can J Cardiol* 2008;24:312-4.
- Meyer G, Vicaut E, Danays T, *et al.* Fibrinolysis for patients with intermediate-risk pulmonary embolism. *N Engl J Med* 2014;370:1402-11.
- Simpson D, Siddiqui MA, Scott LJ, Hilleman DE. Reteplase: A review of its use in the management of thrombotic occlusive disorders. *Am J Cardiovasc Drugs* 2006;6:265-85.

A Snare Retrieval Experience of Coil Migration in a Large Coronary Artery Fistula

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Abstract

A 45-year-old female patient was referred due to the abnormal myocardial perfusion scintigraphy showing ischemia in the inferior and lateral wall. Coronary arteries were normal, and a large fistula was detected from the proximal portion of the circumflex coronary artery (Cx) draining into the pulmonary artery. Percutaneous closure of the coronary artery fistula (CAF) was considered, and a 3 mm × 50 mm-Balt coil was planned to place the proximal portion of the fistulized artery. Unfortunately, during placement of the coil, it was opened early and migrated to the proximal segment of the Cx, the left anterior descending artery, and the distal part of the left main coronary artery. A snare was moved into the extra backup guiding catheter immediately. The migrated coil was retrieved with the snare successfully. Subsequently, 4 mm × 12 mm and 2 mm × 25 mm-Balt coils were placed in the mid portion of the fistulized artery until total occlusion was obtained. A CAF is described as a direct connection between one or more of the coronary arteries and a cardiac chamber or great vessel. The fistula may cause serious hemodynamic disturbances such as myocardial ischemia, high-flow heart failure, right ventricle volume overload, endocarditis, rupture, thrombosis, embolism, and arrhythmias. Percutaneous closure is the prior technique, in the absence of complex conditions such as multiple fistulas and large fistula branches and in cases where the fistula can be simply reached. There have been very rare data which contain complications about the percutaneous closure of CAFs.

Keywords: Coil migration, coronary artery fistula, snare

INTRODUCTION

A coronary artery fistula (CAF) is described as a direct connection between one or more of the coronary arteries and a cardiac chamber or great vessel. This is a rare abnormality and its definite incidence is unclear.^[1] Although majority of cases are asymptomatic, the fistula may cause serious hemodynamic disturbances such as myocardial ischemia, high-flow heart failure, right ventricle volume overload, endocarditis, rupture, thrombosis, embolism, and arrhythmias.^[2] The closure is required for symptomatic patients and fistulas with high-flow rate. Percutaneous closure is the prior technique, in the absence of complex conditions such as multiple fistulas and large fistula branches and in cases where the fistula can be simply reached.^[2,3] We present a rare complication of coil embolization where the coils migrated native circumflex artery. Subsequently, the coils are drawled back by a snare successfully.

CASE REPORT

A 45-year-old female patient was referred to coronary angiography due to the abnormal myocardial perfusion

scintigraphy showing ischemia in the inferior and lateral wall. Her cardiovascular examination was normal. There were no significant findings except poor R-wave progression on the electrocardiogram. Echocardiography revealed that the left ventricular ejection fraction was 65% and the left ventricular diastolic dysfunction was Grade 1. There were no serious valve diseases additively. Coronary angiography was performed to investigate ischemic origin. Coronary arteries were normal, but a large fistula was detected from the proximal portion of the circumflex coronary artery (Cx) draining into the pulmonary artery [Figure 1]. We assessed the patient's status as a coronary steal phenomenon due to the arteriovenous shunt caused by a large fistula. Percutaneous closure of the CAF was considered and a 3 mm × 50 mm-Balt coil was planned to place the proximal portion of the fistulized artery. Unfortunately, during placement of the coil, it was opened early and migrated to the

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proximal segment of the Cx, the left anterior descending artery, and the distal part of the left main coronary artery [Figure 2a]. A snare was moved into the extra backup guiding catheter immediately. The migrated coil was retrieved with the snare successfully [Figure 2b]. Subsequently, 4 mm × 12 mm and 2 mm × 25 mm-Balt coils were placed in the mid portion of the fistulized artery until total occlusion was obtained [Figure 2c].

DISCUSSION

A CAF is described as a direct connection between one or more of the coronary arteries and a cardiac chamber or great vessel. Its most commonly congenital and its definite incidence are unknown. However, an acquired fistula can be occur subsequent to chest traumas or as a complication of percutaneous coronary interventions and coronary artery bypass graft surgery.^[4] Pathological mechanisms of CAFs include variety of theories. The presence of an accessory coronary artery from pulmonary artery is one of these theories. On the other hand, embryological hypothesis has been generated such as persistence of intertrabecular spaces and fetal sinusoids, that normally obliterate to form the adult coronary capillary network.^[4] The right coronary artery is the most common origin of the CAFs with a frequency of 50%–60%. The prevalence of drainage sites of CAFs are as follows: right atrium (19%–26%), pulmonary artery (15%–20.2%), right ventricle (14%–40%), coronary sinus (7%), left atrium (5%–6%), left ventricle (2%–19%), and superior vena cava (1%).^[2] In our case, a large fistula was detected from the proximal portion of Cx artery draining into the pulmonary artery.

Most CAFs are thought to be incidentally detected on routine examination or during coronary angiography. The left-to-right shunt or the presence of coronary steal phenomenon generally determines the severity of symptoms. Exertional dyspnea is the most common symptom with a frequency of 60% for the patients with CAFs. Endocarditis in the fistula (20%), congestive heart failure (19%), angina pectoris (3%–7%),

syncope, palpitations, myocardial infarction, cardiac arrhythmias, pulmonary hypertension, hemopericardium, and sudden cardiac death are the other clinical situations which have been seen in the patients with CAFs.^[2]

Multidetector computed tomography and magnetic resonance imaging are noninvasive tools to confirm the CAF entry site and patency of shunt. Radionuclide studies can be opted to detect ischemic regions of the myocardium. If the patient has restricted myocardial ischemia territory (<10% left ventricular surface area) and is asymptomatic pharmacotherapy is the first-line treatment.^[5] According to the American College of Cardiology/American Heart Association guidelines, “percutaneous or surgical closure is a Class I recommendation for large fistulae regardless of symptoms and for small-to-moderate size fistulae with evidence of myocardial ischemia, arrhythmia, ventricular dysfunction, ventricular enlargement, or endarteritis.”^[6] In our patient, the nuclear test has confirmed her symptoms with wide myocardial ischemia territory. Hence, we decided to closure of her fistula that cause of the coronary steal phenomenon.

Percutaneous closure is the prior technique, in the absence of complex conditions such as multiple fistulas and large fistula branches and in cases where the fistula can be simply reached.^[2,3] In addition, excessive vessel tortuosity and lumen diameter are determinative parameters for surgical closure. Steel coils, umbrella devices, and covered stents are utilized for percutaneous closure of the CAFs. The selection of device and technique depend on the anatomical properties of the fistula which contain age and size of the patient, size of the occluded vessel, and catheter support for tortuosity.^[2,4] We consider the patient’s fistula characteristics and choose coil embolization through femoral approach.

In the literature, there have been very rare data which contain complications about percutaneous closure of CAFs. Armsby *et al.*, have reviewed the results of percutaneous closure in 45 patients.^[7] Unretrieved device embolization to tricuspid valve or distal pulmonary artery were seen about



Figure 1: A large fistula which was draining into the pulmonary artery from the proximal portion of circumflex coronary artery

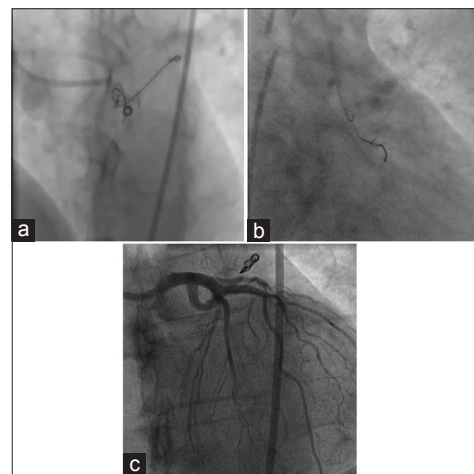


Figure 2: (a-c) The migrated coil (a). Retrieving of the migrated coil with the snare (b) Embolization of the fistulized artery with Balt coils successfully (c)

four patients in their study. Furthermore, there was only one procedure-related death (2.2%) due to embolization of a coil, the left Cx artery that led to the left Cx artery dissection.

CONCLUSION

Even if the coils do migrate, they can be retrieved with snares. This case shows the unexpected complication of percutaneous closure of CAFs and successful management of this complication using a snare.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Qureshi SA. Coronary arterial fistulas. *Orphanet J Rare Dis* 2006;1:51.
2. Challoumas D, Pericleous A, Dimitrakaki IA, Danelatos C, Dimitrakakis G. Coronary arteriovenous fistulae: A review. *Int J Angiol* 2014;23:1-10.
3. Gowda RM, Vasavada BC, Khan IA. Coronary artery fistulas: Clinical and therapeutic considerations. *Int J Cardiol* 2006;107:7-10.
4. Said SA, Nijhuis RL, Akker JW, Takechi M, Slart RH, Bos JS, *et al.* Unilateral and multilateral congenital coronary-pulmonary fistulas in adults: Clinical presentation, diagnostic modalities, and management with a brief review of the literature. *Clin Cardiol* 2014;37:536-45.
5. Sibille L, Boudousq V, Soullier C, Rossi M, Mariano-Goulart D. Tc-99m tetrofosmin SPECT in coronary cameral fistula. *Clin Nucl Med* 2009;34:473-4.
6. Warnes CA, Williams RG, Bashore TM, Child JS, Connolly HM, Dearani JA, *et al.* ACC/AHA 2008 Guidelines for the Management of Adults with Congenital Heart Disease: Executive summary: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (writing committee to develop guidelines for the management of adults with congenital heart disease). *Circulation* 2008;118:2395-451.
7. Armsby LR, Keane JF, Sherwood MC, Forbess JM, Perry SB, Lock JE, *et al.* Management of coronary artery fistulae. Patient selection and results of transcatheter closure. *J Am Coll Cardiol* 2002;39:1026-32.