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ORIGINAL PAPER

# Long term evaluation of electromechanical delay in patients with atrial septal defect after transcatheter closure

**Ahmet Öz[1] · Emre Aruğaslan[2] · Tufan Çınar[1] · Muhammed Keskin[1] · Mert Ilker Hayıroğlu[1] · Şahin Avşar[3] · Mehmet Baran Karataş[4] · Berat Arıkan Aydın[5] · Koray Demir[6] · Barış Güngör[4] · Osman Bolca[4]**

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## Abstract

Some studies have been showed that electromechanical delay, which may pose an increased tendency to atrial fibrillation, may prolong in patients with various clinical conditions. In addition, the electromechanical delay in patients with secundum type atrial septal defect (ASD) compared to healthy people have been reported previously. Therefore, in the present study, we prospectively evaluated the mid-term and long-term effects of the transcatheter closure of secundum type ASD on the lateral atrial conduction time (PA), septal PA, tricuspid PA, left and right intra-atrial electromechanical delay (ILeft-EMD and IRight-EMD, respectively) and inter-atrial electromechanical delay (IA-EMD) measured by means of Doppler echocardiography. Our prospective study included a total of 45 secundum type ASD patients who undergone percutaneous transcatheter closure from December 2012 to April 2015. All patients underwent transthoracic echocardiography (TTE) before the closure, at sixth and twelfth months after the closure. In comparison of the EMD sixth months after the device closure, there were statistically significant decrease in lateral PA, septal PA, tricuspid PA, ILeft-EMD, IRight-EMD and IA-EMD compared to pre-device closure values. Twelfth months after the device closure, we also observed statistically significant decrease in lateral PA, septal PA, tricuspid PA, ILeft-EMD, IRight-EMD and IA-EMD compared to 6-month post-device closure values. In the present study, we observed that the atrial EMD improves after device closure and continues to improve after twelfth month following post-device closure.

**Keywords** Atrial conduction time · Doppler echocardiography · Secundum type of atrial septal defect

## Introduction

Atrial septal defect (ASD) constitutes 10% of the congenital heart diseases in newborns and this rate is approximately 30–40% in adults [1]. Based on the location of the septal defect, ASD can be classified into four types; ostium secundum, ostium primum, sinus venosus, and coronary sinus type ASD [2]. In recent years, the closure of the secundum type ASD with percutaneous transcatheter approach has been gained popularity due to the more rapid hemodynamic restoration and fewer complications compared to surgical closure [3, 4].

The atrial conduction defect tends to be more common in older patients with structural heart disease [5]. Previous studies have been demonstrated that atrial conduction time or electromechanical delay, which may pose an increased tendency to atrial fibrillation, may prolong in patients with clinical conditions such as systemic sclerosis, psoriasis vulgaris, lone atrial fibrillation and hemodynamically

✉ Ahmet Öz
drozahmet@gmail.com

1 Department of Cardiology, Sultan Abdülhamid Han Training and Research Hospital, Health Sciences University, Tibbiye Street, Uskudar/Istanbul, Turkey

2 Department of Cardiology, Sivas Numune Hospital, Sivas, Turkey

3 Department of Cardiology, Urla State Hospital, Izmir, Turkey

4 Department of Cardiology, Dr. Siyami Ersek Cardiovascular and Thoracic Surgery Research and Training Hospital, Health Sciences University, Istanbul, Turkey

5 Department of Cardiology, Sinop State Hospital, Sinop, Turkey

6 Department of Cardiology, Muş State Hospital, Muş, Turkey

insignificant rheumatic heart disease [6, 7]. Different methods have been proposed for the evaluation of atrial conduction time including P-wave dispersion measured by electrocardiography (ECG), the measurement of the time form P wave on the ECG to the beginning of Doppler A′ wave on transthoracic echocardiography (TTE) (PA), and electrophysiological studies [8–11]. The previous study demonstrated that there was electromechanical delay in the left and right intra-atrial and inter-atrial locations in patients with secundum type ASD compared to healthy people due to volume overload [12]. In light of this data, in the present study, we prospectively evaluated the mid-term and long-term effects of the transcatheter closure of secundum type ASD on the lateral atrial conduction time (PA), septal PA, tricuspid PA, left and right intra-atrial electromechanical delay (ILeft-EMD and IRight-EMD, respectively) and inter-atrial electromechanical delay (IA-EMD) measured by means of Doppler echocardiography.

## Methods

### Study population

The present prospective study included the hemodynamically significant secundum type ASD (Qp/Qs > 1.5) patients who undergone percutaneous transcatheter closure from December 2012 to April 2015. The exclusion criteria were; coronary artery disease, cardiomyopathy, structural heart disease, contra-indication to anti-platelet and anti-coagulation treatment, permeant pacemaker implantation, significant conduction defect, severe valvular heart disease, chronic obstructive lung disease, and severe right or left ventricular dysfunction. After evaluation regarding with the exclusion criteria, a total of 45 secundum type ASD patients were prospectively included in the study. The baseline demographic characteristics data for all patients were obtained from the hospital electronic database. Informed consent was obtained from all patients. This study was carried out according to the Principles of Declaration of Helsinki and it was approved by our ethics committee.

### Transthoracic echocardiography and transesophageal echocardiography

All patients underwent TTE before the closure, at sixth and twelfth months after the closure. TTE assessment was performed using S5-1 transducer (iE33; Philips Medical Systems, Andover, MA, USA) to study patients in accordance with American Society of Echocardiography guidelines [13]. Each patient was evaluated with an M-mode, 2-dimensional Doppler, and tissue Doppler echocardiography. Left ventricular ejection fraction of each patient was calculated using biplane Simpson's method. The end-systolic and diastolic diameters of the left ventricle (LV) as well as the end-systolic diameter of the left atrium (LA) were measured with M-mode echocardiography on the parasternal long axis display. LA volume was calculated with the $(A1 \times A2 \times A3 \times 0.524)$ formula using the LA dimensions measured from the parasternal long axis (anteroposterior—A1) and apical 4 chamber (mediolateral—A2, apicobasal—A3) views. From apical-4-chamber, right ventricle (RV) basal diameter was estimated at the end-diastole. The mediolateral and apicobasal diameter of the RA were estimated at the end-systole from the apical-4-chamber. The tricuspid annular plane excursion (TAPSE) was measured from the apical 4-chamber view on TTE by placing 2D cursor at the tricuspid lateral annulus and measuring the distance of systolic annular right ventricular excursion along a longitudinal line defining the end of systole as the end of T wave in the ECG. The calculation of pulmonary systolic pressure was determined primarily calculating the systolic pressure gradient peak from the right ventricle to the right atrium assessed through the simplified Bernoulli equation (4 × squared V, where V = peak systolic velocity of tricuspid regurgitation measured using continuous Doppler and then the right atrium pressure was added according to the collapse of the inferior venous cava during the inspiration) [14]. In the apical 4 chamber view, the LV-pulsed tissue Doppler imaging was performed using a 5-mm pulsed Doppler sample volume as minimum optimal gain to obtain the best signal to noise ratio. We optimized the signal filter of the spectral pulsed Doppler until the Nyquist limit was 15–20 cm/s using a transducer of 3.5–4.0 MHz in frequency. The monitor sweep speed was set at 50–100 mm/s to optimize the spectral display of myocardial velocities. On the tissue Doppler trace, PA was accepted as the time passing from the beginning of the P wave on ECG to the A′ wave on tissue Doppler trace and estimated from lateral mitral annulus named as lateral PA, form septal mitral annulus named as septal PA, and from RV tricuspid annulus named as tricuspid PA (Fig. 1). IA-EMD was described as the time difference between the lateral mitral annulus of LV and the tricuspid annulus of RV. The ILeft-EMD and IRight-EMD were described as the PA time difference between the lateral mitral annulus of LV and septal mitral annulus of LV and the PA time difference between septal mitral annulus of LV and the tricuspid annulus of RV, respectively. In order to prevent intra and inter-observer bias, the average of three measurement was calculated and the measurement was repeated by the second blindly observer. The mean values of the measurement of the two observers were taken. Transesophageal echocardiography (TEE) examinations were performed in a standard manner, with all subjects in the lateral decubitus position, using the X7-2t multiplane TEE probe (iE33; Philips Medical Systems, Andover, MA, USA) after the overnight fasting.

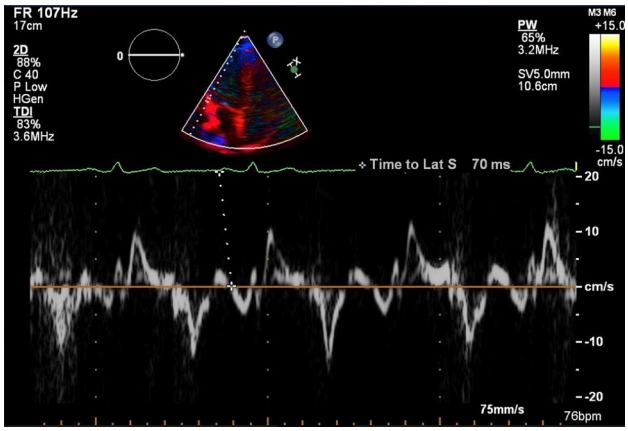


**Fig. 1** The evaluation of atrial conduction times by means of Doppler echocardiography

TEE was performed under conscious sedation with anaesthetizing the hypopharynx.

### Interventional procedure

Two types of ASD closure devices (Cocoon Septal Occluder, Vascular Innovations Co., Nonthaburi, Thailand and Cardi-o-Fix Septal Occluder, Starway Medical, PR China) were used in the study. The Cocoon Septal Occluder was deployed in 22 (48.9%) patients and Cardi-o-Fix Septal Occluder was deployed in 23 (51.1%) patients. All procedures were performed under the general anesthesia. All patients were heparinized throughout the procedure with a minimum active clotting time of 200 s prior to device insertion. TEE was used as an aid in placing the device. Balloon measurement was not performed routinely. All patients were treated with antiplatelet therapy (aspirin or in case of aspirin allergy with clopidogrel) for 6 months during the post-intervention period.

### Follow-up

The TTE was performed to all patients before the hospital discharge, at sixth and twelfth months after the procedure. Any symptomatic patient was also evaluated during the follow-up period. The total duration of the follow-up was 12 months.

### Statistical analysis

Statistical analyses were performed using SPSS version 17.0 (IBM, Chicago, Illinois). Normality of the data was analyzed using the Kolmogorov–Smirnov test. The numerical variables with a normal distribution are presented as mean ± standard deviation, whereas the categorical variables are presented as numbers and percentages (%).The changes in normally distributed variables over the time were compared using the Student t test. The changes in non-normally distributed variables over the time were analyzed using a Wilcoxon test. Categorical data were compared using the Chi-square test or the Fisher exact test. Statistical significance was defined as a p value $< 0.05$.

## Results

A total of 45 secundum type ASD patients were prospectively enrolled in the study. The mean age of the study population was 39.0 ± 12.9 years and 34 (75%) patients were female. Baseline demographic characteristics and septal defect diameter evaluated with TEE before the closure are shown in Tables 1 and 2. The mean septal defect diameter was 18.7 ± 5.9 mm. In two patients, there were a more than one septal defects, however; they were suitable for the closure with percutaneous transcatheter approach. The devices were successfully deployed in all patients. The mean

**Table 1** Baseline demographic characteristics (n = 45)

| | No./mean ± SD |
|---|---|
| Age (years) | 39.0 ± 12.9 |
| Gender (female) | 34 (75.5%) |
| Hypertension | 9 (20%) |
| Hyperlipidemia | 3 (6.6%) |
| Diabetes mellitus | 6 (13.3%) |
| Smoking | 5 (11.1%) |
| NYHA functional class 3–4 | 12 (26.6%) |
| Body mass index | 26.4 ± 4.3 |

Data are presented as mean ± standard deviation or percentage

*NYHA* New York Heart Association

**Table 2** Transesophageal echocardiographic before the closure features (n = 45)

| | Mean ± SD |
|---|---|
| $Q_P/Q_S$ ratio | 1.86 ± 0.62 |
| ASD diameter by TEE (mm) | 18.7 ± 5.9 |
| Aortic rim (mm) | 4.3 ± 2.9 |
| Posterior rim (mm) | 10.1 ± 3.9 |
| AV valve rim (mm) | 10.0 ± 2.6 |
| SVC rim (mm) | 12.0 ± 4.1 |
| IVC rim (mm) | 11.2 ± 2.8 |
| Occluder size (mm) | 22.4 ± 6.3 |

Data is presented as mean ± standard deviation

$Q_P/Q_S$ pulmonary-to-systemic flow ratio, *TEE* transesophageal echocardiography, *AV* atrio-ventricular, *IVC* inferior vena cava, *SVC* superior vena cava

diameter of deployed devices was 22.4 ± 6.3 mm. Only one local complication, the arteriovenous fistula, which was successfully repaired with surgical operation, was occurred after the procedure. During the in-hospital course, atrial fibrillation was developed in one patient and, after the thrombus was excluded with TEE examination, it was successfully restored to sinus rhythm with direct electrical cardioversion. The supraventricular tachycardia occurred in four patients during the procedure, and spontaneously terminated in all patients. After the procedure, the residual interatrial shunt occurred in three patients. The resolutions of the residual interatrial shunts were confirmed in two patients with TEE examination at twelfth months follow-up. However, one patient did not accept the TEE examination for the evaluation of the residual interatrial shunt.

The TTE findings before the closure, at sixth and twelfth months after the closure are demonstrated in Table 3. Six months after the device closure, there were statistically significant increase in the end-diastolic diameter of the LV that is 8% increase from baseline; the end-systolic diameter of the LV that is 4% form baseline. In terms of LA dimensions, 6 months after the device closure; there were statistically significant decrease in anteroposterior diameter of the LA that is 8% from baseline; in the mediolateral diameter of the LA that is 10% from baseline; in the apicobasal diameter of the LA that is 5% from baseline; and in the LA volume that is 23% from baseline. After 6 months of the device closure, there were statistically significant decrease in the basal diameter of RV that is 16% from baseline; in mediolateral diameter of the RA that is 12% from baseline; in apicobasal diameter of the RA that is 14% from baseline; in TAPSE that is 8% from baseline; and in pulmonary systolic pressure that is 33% from baseline. In comparison of the EMD sixth months after the device closure, there were statistically significant decrease in lateral PA that is 17% from baseline; in septal PA that is 18% from baseline; in tricuspid PA that is 19% from baseline; in the ILeft-EMD that is 12% from baseline; in the IRight-EMD that is 10% from baseline; in the IA-EMD that is 12% from baseline.

Twelve months after the device closure, there were no statistically significant differences in the end-diastolic and end-systolic diameter of the LV, in anteroposterior, mediolateral, and apicobasal diameters of the LA, LA volume, the basal diameter of RV, mediolateral and apicobasal diameters of the

**Table 3** Echocardiographic parameters before and after atrial septal defect occluder implantation

| Variables | Before closure (n = 45) | After ASD closure | | *P* value | |
|---|---|---|---|---|---|
| | | 6 months (n = 45) | 12 months (n = 45) | Before closure–after closure 6 months | After closure 6–12 months |
| LVEDD (mm) | 44.2 ± 3.1 | 46.2 ± 3.3 | 46.1 ± 3.7 | < 0.001 | 0.409 |
| LVESD (mm) | 26.3 ± 3.6 | 27.5 ± 3.0 | 27.2 ± 2.9 | 0.005 | 0.108 |
| IVS (mm) | 8.8 ± 1.1 | 9.0 ± 1.1 | 8.9 ± 1.2 | 0.238 | 0.654 |
| LVPW (mm) | 8.8 ± 1.1 | 8.9 ± 1.2 | 8.9 ± 1.1 | 0.760 | 0.935 |
| LA AL diameter (mm) | 37.2 ± 4.8 | 33.9 ± 4.0 | 33.7 ± 4.1 | < 0.001 | 0.019 |
| LA ML diameter (mm) | 42.3 ± 4.7 | 37.7 ± 3.7 | 37.3 ± 3.8 | < 0.001 | 0.094 |
| LA AB diameter (mm) | 52.7 ± 5.0 | 49.8 ± 4.9 | 50.1 ± 4.2 | < 0.001 | 0.313 |
| LA volume (ml/m$^2$) | 44.5 ± 13.0 | 34.1 ± 9.8 | 33.9 ± 9.8 | < 0.001 | 0.212 |
| RVEDD (mm) | 46.1 ± 4.7 | 38.6 ± 3.7 | 37.4 ± 4.1 | < 0.001 | 0.066 |
| RA ML diameter (mm) | 43.3 ± 4.5 | 37.8 ± 4.5 | 38.5 ± 4.7 | < 0.001 | 0.521 |
| RA AB diameter (mm) | 52.9 ± 5.3 | 45.1 ± 4.8 | 45.9 ± 3.8 | < 0.001 | 0.539 |
| TAPSE | 27.2 ± 1.8 | 24.8 ± 2.0 | 24.4 ± 2.0 | < 0.001 | 0.095 |
| Pulmonary arterial systolic pressure (mmHg) | 37.3 ± 10.3 | 24.8 ± 5.9 | 24.0 ± 5.4 | < 0.001 | 0.152 |
| PA lateral (ms) | 76.5 ± 8.9 | 63.3 ± 9.9 | 52.1 ± 9.7 | < 0.001 | < 0.001 |
| PA septal (ms) | 64.6 ± 8.6 | 52.9 ± 8.1 | 43.4 ± 8.3 | < 0.001 | < 0.001 |
| PA tricuspid (ms) | 55.3 ± 9.1 | 44.6 ± 8.0 | 35.9 ± 8.2 | < 0.001 | < 0.001 |
| ILeft-EMD (ms) | 11.9 ± 4.8 | 10.4 ± 4.1 | 8.8 ± 3.6 | 0.016 | < 0.001 |
| IRight-EMD (ms) | 9.3 ± 4.2 | 8.3 ± 3.5 | 7.4 ± 3.3 | 0.043 | 0.036 |
| IA-EMD (ms) | 21.3 ± 7.7 | 18.7 ± 6.5 | 16.2 ± 6.0 | < 0.001 | < 0.001 |

Data presented as mean ± SD

*LVEDD* left ventricular end-diastolic diameter, *LVESD* left ventricular systolic diameter, *IVS* interventricular septum diameter, *LVPW* left ventricular posterior wall diameter, *LA* left atrial, *AL* anterolateral, *ML* mediolateral, *AB* apicobasal, *RVEDD* right ventricular end-diastolic diameter, *RA* right atrial, *TAPSE* tricuspid annular plane systolic excursion, *PA* atrial conduction time, *ILeft-EMD* left intra-atrial electromechanical delay, *IRight-EMD* right intra-atrial electromechanical delay, *IA-EMD* inter-atrial electromechanical delay

RA, in TAPSE, and pulmonary systolic pressure in comparison with sixth months post-device closure ($p > 0.05$, for all). However, 12 months after the device closure, there were statistically significant decrease in lateral PA that is 17% form 6-month post-device closure in septal PA that is 17% form 6-month post-device closure; in tricuspid PA that is 19% form 6-month post-device closure in the ILeft-EMD that is 15% from 6-month post-device closure; in the IRight-EMD that is 10% from 6-month post-device closure; in the IA-EMD that is 13% from 6-month post-device closure (Fig. 2).

## Discussion

The present study revealed that (1) the LV diastolic and systolic diameters were progressively increased until the sixth months, after that, they remained unchanged at 12 months post-device closure. (2) The RA, LA and RV diameters were progressively decreased due to decreased volume overload until the sixth months, after that, they remained unchanged at 12 months post-device closure. (3) The lateral PA, septal PA, tricuspid PA, ILeft-EMD and IRight-EMD, and IA-EMD continued to decrease at twelfth month post-device closure.

Previous studies comparing the surgical closure with transcatheter closure in patients with secundum type ASD demonstrated that there was no statistically significant difference in terms of treatment success, however; the patients underwent transcatheter closure had a fewer complications and shorter hospital duration compared to those with surgical closure [15, 16].

The mortality rate of transcatheter closure may range from 0.5 to 1% [17–19] and some complications have been reported. In the literature, device malapposition/embolization has been the most common reported complication and it may range from 1.5% to as high as 3.5% [15, 20]. In the present study, there was no any death or device malapposition/embolization during the procedure and the follow-up period. The incidence of residual interatrial shunt after the device closure has been reported to be 3.9% in the previous studies. However, the resolution of residual interatrial shunts has been also demonstrated during the follow-up period [18]. In our study, the incidence of residual interatrial shunt after the device closure was 6.6% and the resolution of interatrial shunt in two patients were demonstrated with TEE examination at 12 months follow-up.

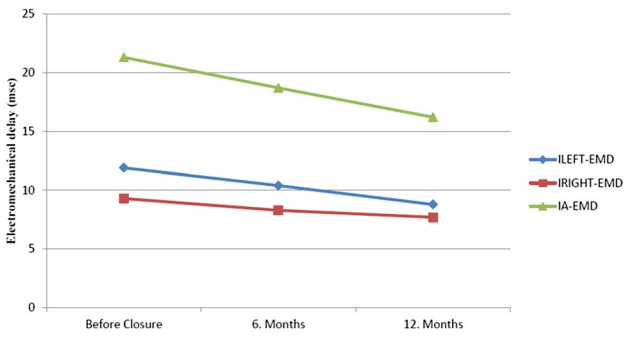


**Fig. 2** The change of electromechanical delay in patients with atrial septal defect after transcatheter closure during the follow up

The percutaneous transcatheter ASD closure may result in the right atrial and right ventricle load reduction resulting in low arrhythmic risk [21–23]. Santoro et al. demonstrated that the right atrial volume, the right atrial/left atrial volume ratio and the P-wave dispersion were significantly decreased after 6 months post-device closure in 15 secundum type ASD patients [24]. Moreover, Balcı et al. revealed that the closure of ASD by means of transcatheter approach might lead to a decrease in RV size and an increase in LV size in 19 patients at third months [25]. Similar to these previous studies, we also observed significant increase in the end-diastolic and the end-systolic diameter of the LV and significant decrease in LA volume, the basal diameter of RV, mediolateral and apicobasal diameters of the RA from baseline at sixth month's post-device closure. However, as most of the abovementioned studies had a limited follow-up, we also revealed that the aforementioned parameters did not significantly change at twelfth month post-device closure in comparison with sixth month post-device closure.

The atrial conduction time has been shown to be strongly associated with underlying diseases affecting the atrium directly or indirectly. The delayed atrial conduction time is one of the requirements for the initiation of re-entry and the development of atrial fibrillation. A number of non-invasive techniques exist that might be used for assessment of atrial conduction time including P-wave dispersion measured by ECG and by means of Doppler-echocardiography [26]. Besides that, the atrial EMD measured by tissue Doppler imaging has also been found to be well correlated with P-wave dispersion measured by ECG. In patients with secundum type ASD, increase in volume overload may cause increase in atrial diameter resulting prolonged atrial conduction time and non-homogeneous propagation of sinus impulses. Erturk et al. showed that atrial EMD measured by tissue Doppler echocardiography was significantly longer in patients with secundum type of ASD than in the control groups [12]. Therefore, the ASD closing device may have an impact on the electromechanic atrial remodeling following shunt disappearance. Recently, a study performed by Kaya et al. demonstrated that P-wave dispersion was significantly decreased in patients with transcatheter closure from baseline at 6 months. Moreover, Aslan et al. showed that the lateral PA, septal PA, tricuspid PA, ILeft-EMD and IRight-EMD, and IA-EMD did not change on the first days after the procedure, however; all aforementioned parameters were significantly decreased at 6 months post-device closure

[27]. The results of our study were similar with the results of previous study. However, our study demonstrated that aforementioned parameters also continue to decrease at twelfth month post-device closure. Similarly, the incidence of atrial arrhythmias seemed to significantly decrease over time, being recorded in about 4% of patients after post-device closure during the follow-up [28]. Therefore, the electromechanical findings continue to improve over the time, thereby probably affecting the long-term outcome of secundum type of ASD patients. In addition, these findings may be related with decrease the risk of atrial arrhythmia development in patients after post-device closure.

### Limitations of the study

The present study had a small sample size and was carried in a single center, therefore, these finding might not be generalized to all population. In addition, the Holter ECG monitoring which might detect any silent atrial arrhythmia was not done to study patients, however; all patients were evaluated with ECG during the 6 and 12 months follow-up. Since the study was non-randomized nature, the patient enrolment might potentially cause selection bias.

## Conclusion

In the present study, we observed that the EMD continue to improve after 6 months post-device closure. Therefore, atrial conduction time assessed by means of Doppler imaging should be part of the echocardiographic examination in patients after device closure during the 12 months of follow-up.

### Compliance with ethical standards

**Conflict of interest** The authors declare that they do not have any conflicts of interest.

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