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Title: **MICROEMBOLIC SIGNALS MEASURED BY TRANSCRANIAL DOPPLER DURING TRANSCATHETER CLOSURE OF ATRIAL SEPTAL DEFECT USING AMPLATZER SEPTAL OCCLUDER**

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ABSTRACT

Purpose: To determine the frequency and factors associated with increase in microembolic signals during transcatheter closure of atrial septal defect using Amplatzer septal occluder.

Methods: During procedure in 16 patients, we measured microembolic signals using transcranial Doppler. Procedure time was divided into 5 periods; right heart catheterization; left heart catheterization; left heart angiocardiography; sizing and long sheath placement; device placement and release. We compared numbers of microembolic signals among the 5 periods and identified factors associated with them.

Results: Mean size of septal occluder was 16 mm in diameter. Total number of microembolic signals was a median of 31.5, ranged from 3 to 113. Microembolic signals in 3 periods, left heart catheterization; sizing and long sheath placement; and device placement and release, were not significantly different from one another, but were significantly higher than those in the remaining 2 periods, right heart catheterization and left heart angiocardiography, (median was 9 in left heart catheterization; 6 in sizing and long sheath placement; 6.5 in device placement and release versus 0 in right heart catheterization and 1 in left heart angiocardiography, p less than 0.05, respectively). Importantly, the time for device manipulation positively correlated with total number of microembolic signals (r equals 0.77, p less than 0.001) though fluoroscopic time, age or size of septal occluder did not.

Conclusions: Transcatheter closure of atrial septal defect using Amplatzer septal occluder produces microemboli especially during device placement. To minimize the risk of systemic embolism, we have to decrease the time for device manipulation.

Key Words: catheter intervention; interatrial communication; systemic embolism

INTRODUCTION

Transcatheter occlusion of secundum atrial septal defects using the Amplatzer septal occluder (AGA Medical, Golden Valley, Minnesota, USA) has become an accepted first line treatment of this disease with low complication rate.[1]

However, the procedure requires placement of a guide wire and a long sheath, opening the left sided disc in the left atrium, and carries risk of microembolism. There were 2 studies concerning the formation of microemboli during this procedure evaluated by transcranial doppler. [2, 3] Ferrali et al. demonstrated microembolic signals in 33 of 35 patients who underwent percutaneous closure of interatrial communications, including 29 patients with a history of cryptogenic ischemic stroke, with the highest rate during the time when the septum was crossed with the guide wire and when the left atrial disc was deployed. [2] Also Morandi et al. reported the highest rates of microembolic signals observed during left disc opening and less during transeptal crossing, with an average count of 31 (range 3–135) and 3 (range 1–18) respectively, in 29 patients who had had a stroke or a transient ischaemic attack. [3] Though both studies showed the highest rates of microembolic signals during left disc opening, there was no information concerning the factors associated with this increased microembolic signals.

Therefore the aim of this study was to determine the frequency and factors associated with increase in microembolic signals measured by transcranial Doppler during transcatheter occlusion of secundum atrial septal defect using Amplatzer septal occluder.

MATERIALS AND METHODS

Among 21 consecutive patients who underwent successful transcatheter occlusion of atrial septal defect between February 28, 2008 and October 8, 2008, 5 patients were excluded because of signal noise or failure to detect reliable pulse waves. The remaining 16 patients were the subject of this study and patients' demographics are presented in Table 1. The indication for transcatheter occlusion of atrial septal defect was a hemodynamically significant left-to-right shunt; no patient had had cryptogenic ischemic stroke before the procedure. None of the patients had an atrial septal aneurysm. The study protocol was approved by institutional review board and all patients gave written informed consent to participate in the study.

During the entire procedure, patients were placed supine under general anesthesia and were continuously monitored with a 2.0 Mega Hertz pulsed Doppler probe that was securely placed on the left temporal area and connected to a Pioneer TC-8080 (CareFusion, San Diego, CA, USA). Sampling volume was set at the depth from 38 to 56 millimeter to detect pulse waves of the middle cerebral artery. Differentiation of microembolic signals from artifact was mainly made by automated embolic signal detection software (FS1) and was occasionally made by visual analysis of the wave-form.

Catheterization Procedure

Aspirin 3 to 5 milligram / kilogram was started 2 days before transcatheter occlusion of atrial septal defect and continued for 6 months. After introduction of sheaths, intravenously 100 Unit / kirogram of heparin was injected. Of 16 patients, 8 underwent diagnostic right and left heart catheterization as well as right

upper pulmonary venography and left ventriculography and 7 underwent just right upper pulmonary venography before the sizing of the atrial septal defect, and the remaining patient underwent transcatheter occlusion of atrial septal defect without any diagnostic catheterization or angiography. In both right and left heart diagnostic catheterization, we used a 6 French balloon catheter with side-hole (Angiographic Berman, Reading PA, USA) and left heart catheterization was performed via the atrial septal defect.

Following the diagnostic catheterization, a stiff guide wire was placed into left pulmonary vein and a sizing balloon was advanced over the wire through the defect and was inflated to measure balloon dilated defect size. The sizing balloon was withdrawn and an optimum sized long sheath was placed into left atrium over the guide wire and the selected device was placed through this long sheath. We checked activated clotting time of more than 200 seconds before device placement.

Procedure time was divided into 5 periods; right heart catheterization; left heart catheterization; left heart angiocardiography; sizing and long sheath placement; device placement and release. Also, total fluoroscopic time and device placement time, from mounting to releasing device, were recorded. We compared number of microembolic signals among 5 periods. In addition to identify factors that correlated with increase in microembolic signals, we determined correlations between total number of microembolic signals and device placement time, fluoroscopic time, age, or device size.

STATISTICAL ANALYSES

Data were presented as median and range. Friedman's test was performed for multiple independent samples

and Mann-Whitney's U test was performed for nonparametric samples. We used Pearson's correlation coefficient to determine correlation between microembolic signals and individual variables. All data analyses were performed by a commercially available statistical analysis software package (Statview 5.0, SAS Institute Inc, Cary, NC, USA and PASW 17.0, SPSS Inc, Chicago, IL, USA). A p value less than 0.05 was considered significant.

RESULTS

In 3 patients (Patient 1 to 3) including 2 patients who had to replace the device because the initial device was too small (Patient 2 and 3), we retrieved and deployed the device several times to conform and securely place the device. No patient developed any neurological signs within 72 hours after the procedure.

The total number of microembolic signals was a median of 31.5, ranged from 3 to 113 during the entire procedure. Microembolic signals in 3 periods, left heart catheterization; sizing and long sheath placement; device placement and release, were not significantly different from one another but were significantly higher than those in the remaining 2 periods, right heart catheterization; left heart angiocardiography (Table 2). This significant difference was preserved even if we looked at 8 patients who underwent all the diagnostic catheterization as well as angiocardiography (left heart catheterization, median of 6.5; sizing and long sheath placement, median of 7.5; device placement and release, median of 9.0; right heart catheterization, median of 0; left heart angiography, median of 1, $p < 0.001$, respectively). Beside left heart catheterization, cumulative number of microembolic signals in the specific time from sizing and long

sheath placement to device placement and release, was a median of 11.5 and comprised mean of 58 percent of total number of microembolic signals. As expected, 3 patients (patient 1 to 3) who required several attempts of device placement or replacement showed significantly more total microembolic signals [median microembolic signals was 63 (56 to 113) versus 22 (3 to 57) and longer device placement time [median of 13.4 (11.4 to 20) versus 4.8 (3.1 to 11.2) minutes, p less than 0.01] than the remaining 13 patients. Importantly, device placement time significantly positively correlated with total number of microembolic signals (r equals 0.77, p less than 0.001, Figure 1) though fluoroscopic time, age, or size of atrial septal defect did not correlate with total number of microembolic signals. In addition, this positive correlation (r equals 0.84, p less than 0.0002) exists even if we excluded 2 patients who required device replacement.

DISCUSSION

This study indicates that the longer the time spent for device manipulation and placement can lead to the more microembolic signals during transcatheter occlusion of atrial septal defect using Amplatzer septal occluder.

In transcatheter occlusion of atrial septal defect using Amplatzer septal occluder, microemboli occur mainly in the sequence of balloon sizing to device placement, though it occurs mainly during angiocardiography in diagnostic left catheterization in adult coronary artery disease [4] or percutaneous transluminal coronary angioplasty. [5] This difference probably explained by the different frequency of

contrast injection, because patients required only 1 or 2 angiography in this study but multiple coronary angiography with different projection are required to delineate the stenosis of coronary arteries in adult coronary artery disease or coronary intervention. Though the number of microembolic signals during this procedure may range widely depending on the study subject, indication of procedure, machine setting, or procedure protocol, our result was compatible with the observation that microembolic signals were observed mainly during the time specifically related to device manipulation and placement. [2, 3]

As the significant factor associated with increase in these microembolic signals, we found time spent on device manipulation. In this study, device placement time significantly positively correlated with total microembolic signals, and patients who required multiple manipulations of the devices including replacement showed more microembolic signals. Though device replacement should not happen so frequently, device replacement cannot be avoidable as long as an oversized device is not recommended.[6] Furthermore, there was positive correlation between device placement time and total microembolic signals even if we excluded these 2 patients who required device replacement. Therefore, we have to keep choosing device size carefully, improve our techniques,[7-10] and plan device placement procedures to decrease the total number of attempts and shorten the procedure time. Further studies are required to clarify the incidence, mechanisms, and the relationship between microembolic signals and systemic microemboli in transcatheter occlusion of atrial septal defect.

STUDY LIMITATIONS

Because we had no multi-frequency transcranial Doppler equipment available, it was virtually impossible to more accurately distinguish gaseous microembolic signals from solid microembolic signals. However, most of microembolic signals detected in this study showed bidirectional signals and, therefore, were thought to be mainly gaseous microemboli rather than solid ones.

We found no clinically detectable consequences of cerebral microemboli during or after procedure. Clinically silent cerebral ischemic events cannot be excluded because we could not offer sophisticated neuroradiological assessment such as diffusion-weighted magnetic resonance imaging. [11]

CONCLUSIONS

Microembolic signals observed during transcatheter occlusion of atrial septal defect using Amplatzer septal occluder can be can be decreased by shortening device placement time.

Figure Legend

Total number of microembolic signals significantly positively correlated with time for device manipulation (r equals 0.77, p less than 0.001).

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