The Presence of Patent Foramen Ovale in the Superior Type of Sinus Venosus Atrial Septal Defect

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Abstract

Background: The superior type of sinus venous atrial septal defect (SVASD) is a rare form of the atrial septal defect (ASD) in which the upper part of the atrial septum does not exist. The presence of other cardiac anomalies such as anomalous pulmonary venous connections has been reported in this type of congenital heart disease. This study aimed to assess the presence of the patent foramen ovale (PFO) in patients with the superior type of SVASD.

Methods: This retrospective case-control study on 387 patients, consisting of 187 patients with a definite SVASD and 200 patients with problems other than the ASD, was conducted in Rajaie Cardiovascular Medical and Research Center between February 2005 and July 2014. Seven patients with inadequate data were excluded from the analysis. The presence/absence of the PFO was also evaluated in the case and control groups.

Results: The analyses were performed on 182 male and 198 female patients at a mean age of 39.07±14.41 and 51.01±15.80 years in the case and control groups, respectively. The PFO was significantly more frequent in the patients with the superior type of SVASD than in those without the condition (P<0.001). The persistence of the left superior vena cava was seen in 34 out of 180 patients with SVASD and in 1 out of 200 patients without the condition (18.9% vs 0.5%; P<0.001).

Conclusion: This study was the first to highlight the coexistence of the PFO and the superior type of SVASD. Physiological, genetic, or fetal factors may play an important role in the association between the PFO and the SVASD.

Keywords: Foramen ovale, patent; Atrial septal defect sinus venosus; Echocardiography, transesophageal

Introduction

The patent foramen ovale (PFO) is commonly considered a normal anatomic variant. During the early development, the septum primum divides the common atrium into left and right atria and remains an opening that is called the “ostium primum”. As the size of the ostium primum decreases, the ostium secundum is formed in the
septum primum. The septum secundum grows at the right side of the septum primum and covers the majority of the ostium secundum and finally, the residual foramen is the foramen ovale. The PFO is a potential source of embolism and cryptogenic stroke in young adults. During the fetal life, when the lungs cannot receive the blood flow, the blood entering the right atrium flows directly into the left atrium via the PFO. After birth, the foramen ovale fails to close and results in a left-to-right shunt in approximately 25% of the population. Contrast echocardiography with agitated saline is a useful method for a precise evaluation of the PFO. The Valsalva maneuver during contrast injection may have a clinical value for the evaluation of the PFO in patients suspected of paradoxical emboli.

The atrial septal defect (ASD) is a deficiency in the interatrial septum. The condition is categorized as the ostium secundum ASD, the ostium primum ASD, and the sinus venous atrial septal defect (SV ASD). The ostium secundum ASD is a true defect of the atrial septum which involves the fossa ovalis. The ostium primum ASD is classified as an atroventricular septal defect. In superior vena cava (SVC) type of SV ASD, a defect usually occurs at the junction of the SVC and the right atrium. There are 2 rare types of ASDs: the inferior vena cava (IVC) type of SV ASD and the unroofed coronary sinus.

In the superior type of SV ASD, which accounts for 4% to 11% of all ASDs, the upper part of the atrial septum, the SVC, and the right-sided pulmonary veins do not exist. In this type of disorder, an overriding SVC is seen on the atrial septum. The partial anomalous pulmonary venous connection (PAPVC) in some pulmonary veins, especially the abnormal drainage of the right pulmonary veins, is associated with the SVC type of SV ASD. The diagnosis of this type of ASD is more difficult than other types of ASDs and sometimes requires other diagnostic methods such as transesophageal echocardiography (TEE), cardiac magnetic resonance imaging, and multidetector computed tomography.

The purpose of this study was to investigate the coexistence of the PFO and the superior type of SV ASD. As is known, patients with the SV ASD require surgery for the correction of the cardiac anomalies. As a result, all abnormalities associated with the SV ASD such as the PAPVC and the PFO should be diagnosed before surgery.

Methods

This retrospective case-control study was conducted in Rajaie Cardiovascular Medical and Research Center. The echocardiography reports of the patients that had undergone TEE between February 2005 and July 2014 were reviewed to identify patients with the SV ASD. The case group comprised patients with the SV ASD, and the control group consisted of patients who had undergone TEE due to problems other than congenital heart diseases. The results were evaluated by 2 readers, and the presence/absence of the PFO in the TEE reports of the patients with the SV ASD was checked. The presence/absence of the PFO was also evaluated in the control group. The required information was obtained from a database maintained in the Echocardiography Ward of Rajaie Cardiovascular Medical and Research Center.

Patients were eligible if TEE confirmed a defect at the connection of the SVC to the right atrium. The presence/absence of the PAPVC, the PFO, and other congenital heart defects was recorded in all the patients. The patients with unclear reports of TEE (e.g., suspicions for the PAPVC) were excluded from the study.

Baseline transthoracic echocardiography (TTE) and TEE were performed in both the case and control groups. The two investigators assessed the echocardiography reports of the case group to diagnose the SV ASD and to determine the presence/absence of the PFO. Echocardiography was once performed by fellows training in clinical echocardiography. The echocardiograms were then reviewed again by the attending physicians of the echocardiography ward with at least 8 years of experience in clinical echocardiography.

Echocardiographic measurements, including the end-diastolic and the end-systolic diameters of the left ventricle, were performed in the parasternal long-axis view. The maximal basal right ventricular diameter was estimated in the apical 4-chamber view during the diastolic phase. The right ventricular systolic function was assessed using the tricuspid annular plane systolic excursion (TAPSE) and the velocity of the tricuspid annular systolic motion (S’). TAPSE and S’ were determined by M-mode and tissue Doppler imaging in the 4-chamber view, respectively. Stenosis and regurgitation in the heart valves were evaluated during echocardiography. In the case group, the presence of the SV ASD was proven in the bicaval view via a 2D TEE method (Figure 1A) and a color-flow Doppler study (Figure 1B).

The presence of the PFO in TTE and TEE was first investigated via 2D echocardiography and the color-flow Doppler study (Figure 2). In the control group, any doubts regarding the presence or absence of the PFO were resolved through multiple saline injections and provocative maneuvers, followed by the tracking of the bubbles crossing the foramen ovale using contrast echocardiography. A PFO was considered to be present if more than 3 contrast bubbles crossed the foramen ovale in TEE. In the case group, due to the coexistence of a defect in the atrial septum, evaluating the passage of a bubble from the right atrium to the left atrium was not sufficient and special focus was placed on the bubble cross-path for a PFO diagnosis. Therefore, the PFO was documented by 2D echocardiography, color-flow Doppler, and contrast injection. The right pulmonary
veins were evaluated in the mid-esophageal level at 0° (Figure 3) or from 90° to 110° in the bicalval view with a clockwise rotation. Both right pulmonary veins were also visualized from the mid-esophageal view at 40° to 60° (Figure 4). The left pulmonary veins were examined with a counterclockwise rotation of about 90° to 110°. Furthermore, the left upper pulmonary vein was assessed during the evaluation of the upper part of the left atrial appendage. In some cases with a dilated coronary sinus, the presence of the persistent left SVC was confirmed with visible bubbles in the coronary sinus after intravenous saline injection into the left antecubital vein.

The results were presented as the mean±the standard deviation (SD) for the continuous variables and absolute frequencies and percentages for the categorical variables. The χ² tests were applied to compare the 2 groups in terms of the categorical variables. The continuous variables were compared using independent t-tests. The correlations between the continuous variables were assessed using the Pearson correlation coefficient. The nonparametric Kolmogorov–Smirnov test was performed to assess the normal distribution of the continuous variables, and the results showed that the normality assumption was not violated (P >0.05). All the statistical analyses were conducted using SPSS 18.0 for Windows (SPSS Inc, Chicago, IL, USA). P values of 0.05 or less were considered statistically significant.
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Results

The case group was comprised of 187 patients with a definite superior type of SVASD diagnosed by TEE. Seven patients with inadequate data were excluded from the analysis. The control group consisted of 200 patients without congenital heart diseases that underwent TEE and TTE for other problems. The baseline demographic characteristics of the 2 groups are depicted and compared in Table 1. Of the 180 patients in the case group, 74 (41.1%) were male and 106 (58.9%) were female.

The frequency of female patients was significantly higher in the case group than in the control group (P = 0.012) (Table 2). The main objective of this study was to evaluate the presence of the PFO in patients with the SVASD. The presence of the PFO was significantly more frequent in the patients with the SVASD than in those without the condition (P <0.001) (Table 2). The prevalence of the PFO was 18.5% in the control group. The persistent left SVC was seen in 34 (18.8%) patients with the SVASD and 1 (0.5%) patient in the control group (P <0.001) (Table 2). The PAPVC was detected in 177 out of the 180 patients with the SVASD by TEE.

The correlations between defect size, right ventricular size, and Qp/Qs were significant in the patients with the SVASD. Increased defect size was associated with increased Qp/Qs and right ventricular size (P <0.001; r = 0.377 and P <0.001; r = 0.386, respectively). Increases in Qp/Qs significantly increased right ventricular size (P <0.001; r = 0.383). Delayed diagnosis of the SVASD significantly increased the pulmonary arterial pressure (P <0.001; r = 0.311). The above mentioned parameters were not collinear (R2 <0.8). In the case group, the body surface area and right ventricular size were significantly higher in men than in women (P <0.001 and P = 0.001, correspondingly) (Table 2).

Table 1. Baseline demographic and echocardiographic characteristics of the case group

| Variable          | Value                          |
|-------------------|--------------------------------|
| Age (y)           | 39.07±14.41 (n=169)            |
| BSA (m^2)         | 1.70±0.19 (n=154)              |
| RV size (cm)      | 4.40±0.68 (n=105)              |
| TAPSE (cm)        | 23.42±5.33 (n=102)             |
| RV S’ (cm/s)      | 13.58±3.35 (n=101)             |
| Qp/Qs             | 2.45±0.65 (n=83)               |
| PAP (mmHg)        | 44.94±19.05 (n=105)            |
| ASD diameter (cm) | 1.64±0.56 (n=100)              |

Table 2. Comparisons of the baseline demographic and echocardiographic characteristics of the case and control groups

| Variable          | Case   | Control  | P     |
|-------------------|--------|----------|-------|
| Gender            |        |          | 0.012 |
| Female            | 106 (58.9) | 92 (46.0) |       |
| Male              | 74 (41.1)  | 108 (54.0) |       |
| Age (y)           | 39.07±14.41 (n=169) | 51.01±15.80 (n=200) | <0.001|
| BSA (m^2)         | 1.70±0.19 (n=154) | 1.74±0.18 (n=156) | 0.071 |
| PFO               |        |          | <0.001|
| Yes               | 81 (45.0)  | 37 (18.5)  |       |
| No                | 99 (55.0)  | 163 (81.5) |       |
| PLSVC             |        |          | <0.001|
| Yes               | 34 (18.9)  | 1 (0.5)    |       |
| No                | 146 (81.1) | 199 (99.5) |       |

Data are presented as the mean±SD or n (%).

n, Number of patients with available data; BSA, Body surface area; RV, Right ventricle; TAPSE, Tricuspid annular plane systolic excursion; S’, Velocity of tricuspid annular systolic motion; PAP, Pulmonary arterial pressure; ASD, Atrial septal defect.
Table 3. Comparisons of the cardiac parameters between male and female patients in the case group*

|              | Female                  | Male                  | P      |
|--------------|-------------------------|-----------------------|--------|
| Age (y)      | 39.88±14.93 (n=101)     | 37.87±13.62 (n=68)    | 0.375  |
| BSA (m2)     | 1.63±0.15 (n=89)        | 1.81±0.19 (n=65)      | <0.001 |
| RV size (cm) | 4.40±0.68 (n=105)       | 4.74±0.65 (n=74)      | 0.001  |
| TAPSE (cm)   | 23.42±5.33 (n=102)      | 24.35±6.26 (n=73)     | 0.291  |
| RV SM (cm/s) | 13.58±3.35 (n=101)      | 14.31±3.44 (n=72)     | 0.169  |
| PAP (mm Hg)  | 44.94±19.05 (n=105)     | 41.78±15.88 (n=73)    | 0.246  |
| Qp/Qs        | 2.45±0.65 (n=83)        | 2.59±0.75 (n=59)      | 0.241  |
| ASD diameter (cm) | 1.64±0.56 (n=100) | 1.74±0.54 (n=65) | 0.266 |
| PFO          |                         |                       | 0.260  |
| Yes          | 44 (41.5)               | 37 (50.0)             |        |
| No           | 62 (58.5)               | 37 (50.0)             |        |
| PAPVC        |                         |                       | 0.999  |
| Yes          | 104 (98.1)              | 73 (98.6)             |        |
| No           | 2 (1.9)                 | 1 (1.4)               |        |
| PLSVC        |                         |                       | 0.249  |
| Yes          | 23 (21.7)               | 11 (14.9)             |        |
| No           | 83 (78.3)               | 63 (85.1)             |        |

*Data are presented as the mean±SD or n (%).

Discussion

The present study is the first investigation of its kind to investigate the presence of the PFO in patients with the superior type of SVASD (Figure 5). We noticed the existence of the PFO in most of our patients with the SVASD during TEE (which is performed routinely in patients with the SVASD). We, hence, retrospectively reviewed all the reports of the superior type of SVASD diagnosed by TEE in this center within the preceding 11 years to assess the existence of the PFO. The purpose of this study was to evaluate the presence of the PFO in patients with the SVASD and to highlight the importance of the preoperative detection of the PFO in patients with the SVASD. The ASD accounts for about 6% to 10% of all congenital heart diseases. With an incidence of 1 child per 1500 live births, the ASD is deemed the most common acyanotic congenital heart defect. While females constitute 65% to 75% of patients with the secundum ASD, there is no gender difference in patients with the sinus venosus ASD and the ostium primum ASD.9

The superior type of SVASD constitutes about 5% to 10% of all ASDs, and the SVC type is more common than the IVC type. The main factor in the SVASD diagnosis is the overriding of the SVC or the IVC on the intact muscular rim of the fossa ovalis, which makes the connection between the 2 atria. In the superior type of SVASD, there is a defect in the atrial wall between the SVC and the right pulmonary veins. As a result, the right pulmonary veins drain into the SVC and the right atrium.16-18

The PFO, often considered to be a normal anatomical variant, is quite common and exists in more than 20% to 25% of adults.19 In the current study, the prevalence of the PFO in the control group (18.9%) is relatively lower than that reported in previous studies. Autopsy studies have found the PFO in at least 1 out of every 4 patients. Younger adults with cryptogenic stroke are more likely to have the PFO than patients with other types of stroke. In adults, TEE is considered the gold standard for the diagnosis of the PFO. TTE with agitated saline contrast injection can be used as a
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Conclusion

The ASD is the most prevalent acyanotic congenital heart disease. The superior type of SVASD is a type of ASD generally associated with other congenital heart anomalies, particularly the PAPVC. Given that surgery is needed for SVASD repair, all the associated anomalies should be mentioned in the patient’s echocardiography report. Due to the high rate of the association between the PAPVC and the SVASD, most physicians often look for the PAPVC when TEE is performed. Although surgeons fully examine the septum during surgery, sometimes only focusing on the SVASD and the PAPVC may mask the presence of the PFO.

This study was the first to highlight the coexistence of the PFO and the left persistent SVC in patients with the superior type of SVASD. The association between the PFO and the SVASD is unclear. However, physiological, genetic or fetal factors may play an important role in the association between the PFO and congenital heart anomalies such as the SVASD.

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References

1. Naqvi N, McCarthy KP, Ho SY. Anatomy of the atrial septum and interatrial communications. J Thorac Dis 2018;10(Suppl 24):S2837-S2847.
2. Windecker S, Wahl A, Nedelchev K, Arnold M, Schwerzmann M, Seiler C, Mattle HP, Meier B. Comparison of medical treatment with percutaneous closure of patent foramen ovale in patients with cryptogenic stroke. J Am Coll Cardiol 2004;44:750-758.
3. Turc G, Calvet D, Guérin P, Stroussi M, Chatellier G, Mas JL; CLOSE Investigators. Closure, anticoagulation, or antiplatelet therapy for cryptogenic stroke with patent foramen ovale: systematic review of randomized trials, sequential meta-analysis, and new insights from the CLOSE study. J Am Heart Assoc 2018;7:e008356.
4. Kutty S, Sengupta PP, Khandheria BK. Patent foramen ovale: the known and the to be known. J Am Coll Cardiol 2012;59:1665-1671.
5. Morton SU, Brodsky D. Fetal Physiology and the Transition to Extruterine Life. Clin Perinatol 2016;43:395-407.
6. Chubb H, Whitaker J, Williams SE, Head CE, Chung NA, Wright MJ, O’Neill M. Pathophysiology and management of arrhythmias associated with atrial septal defect and patent foramen ovale. Arrhythm Electrophysiol Rev 2014;3:168-172.
7. Falanga G, Carej S, Oreo G, Khandheria BK, Zito C. How to understand patent foramen ovale clinical significance: Part I. J Cardiovasc Echogr 2014;24:114-121.
8. Lynch JJ, Schuchard GH, Gross CM, Wann LS. Prevalence of right-to-left atrial shunting in a healthy population: detection by Valsalva maneuver contrast echocardiography. Am J Cardiol 1984;53:1478-1480.
9. Webb G, Gatzoulis MA. Atrial septal defects in the adult: recent progress and overview. Circulation 2006;114:1645-1653.
10. Attenhofer Jost CH, Connolly HM, Danielson GK, Bailey KR, Schaff HV, Shen WK, Warness CA, Seward JB, Puga FJ, Tajik AJ. Sinus venous atrial septal defect: long-term postoperative outcome for 115 patients. Circulation 2005;112:1953-1958.
11. Pascoe RD, Oh JK, Warness CA, Danielson GK, Tajik AJ, Seward JB. Diagnosis of sinus venous atrial septal defect with
transesophageal echocardiography. Circulation 1996;94:1049-1055.
12. Donovan MS, Kassop D, Liotta RA, Hulten EA. Sinus venosus atrial septal defect as a cause of palpitations and dyspnea in an adult: a diagnostic imaging challenge. Case Rep Med 2015;2015:128462.
13. Kafka H, Mohiaddin RH. Cardiac MRI and pulmonary MR angiography of sinus venosus defect and partial anomalous pulmonary venous connection in cause of right undiagnosed ventricular enlargement. AJR Am J Roentgenol 2009;192:259-266.
14. Kivistö S, Hänninen H, Holmström M. Partial anomalous pulmonary venous return and atrial septal defect in adult patients detected with 128-slice multidetector computed tomography. J Cardiothorac Surg 2011;6:126.
15. Hoey ET, Lewis G, Yusuf S. Multidetector CT assessment of partial anomalous pulmonary venous return in association with sinus venosus type atrial septal defect. Quant Imaging Med Surg 2014;4:433-434.
16. Kessel-Schaefer A, Linka A, Pretre R, Buser P. Inferior sinus venosus defect associated with incomplete cor triatriatum dexter and patent foramen ovale. Eur J Echocardiogr 2006;7:239-242.
17. Sojak V, Sagat M, Balazova E, Siman J. Outcomes after surgical repair of sinus venosus atrial septal defect in children. Bratisl Lek Listy 2008;109:215-219.
18. al Zaghal AM, Li J, Anderson RH, Lincoln C, Shore D, Rigby ML. Anatomical criteria for the diagnosis of sinus venosus defects. Heart 1997;78:298-304.
19. Silvestry FE, Cohen MS, Armsby LB, Burkle NJ, Fleishman CE, Hijazi ZM, Lang RM, Rome JJ, Wang Y; American Society of Echocardiography; Society for Cardiac Angiography and Interventions. Guidelines for the echocardiographic assessment of atrial septal defect and patent foramen ovale: from the American Society of Echocardiography and Society for Cardiac Angiography and Interventions. J Am Soc Echocardiogr 2015;28:910-958.
20. Hubail Z, Lemler M, Ramaciotti C, Moore J, Ikemba C. Diagnosing a patent foramen ovale in children: is transesophageal echocardiography necessary? Stroke 2011;42:98-101.
21. González-Alujas T, Evangelista A, Santamarina E, Rubiera M, Gómez-Bosch Z, Rodríguez-Palomares JF, Avegliano G, Molina C, Atvarez-Sabin J, García-Dorado D. Diagnosis and quantification of patent foramen ovale. Which is the reference technique? Simultaneous study with transcranial Doppler, transthoracic and transesophageal echocardiography. Rev Esp Cardiol 2011;64:133-139.
22. Yamashita E, Murata T, Goto E, Fujiwara T, Sasaki T, Minami K, Nakamura K, Kumagai K, Naito S, Kario K, Oshima S. Inferior vena cava compression as a novel maneuver to detect patent foramen ovale: a transesophageal echocardiographic study. J Am Soc Echocardiogr 2017;30:292-299.
23. Homma S, Sacco RL. Patent foramen ovale and stroke. Circulation 2005;112:1063-1072.
24. Sharma RK, Houston BA, Lima JA, Cameron DE, Tedford RJ. Never too old for congenital heart disease: sinus venosus atrial septal defect with anomalous pulmonary venous return in an octogenarian. Pulm Circ 2015;5:587-589.
25. Anuwatworn A, Gedela M, Bendaly E, Prescott-Focht JA, Yee J, Clark R, Jonsson O. Sinus venous atrial septal defect complicated by Eisenmenger syndrome and the role of vasodilator therapy. Case Rep Cardiol 2016;2016:368923.
26. Ghosh S, Ghosh AK, Ghosh SK. Patent foramen ovale and atrial septal aneurysm in cryptogenic stroke. Postgrad Med J 2007;83:173-177.
27. Mügge A, Daniel WG, Angermann C, Spes C, Khandheria BK, Kronzon I, Freedberg RS, Keren A, Deenning K, Engberding R. Atrial septal aneurysm in adult patients. A multicenter study using transthoracic and transesophageal echocardiography. Circulation 1995;91:2785-2792.