

Association of interatrial septal abnormalities with cardiac impulse conduction disorders in adult patients: experience from a tertiary center in Kosovo

Aurora Bakalli,¹ Ejup Pllana,¹ Dardan Koçinaj,¹ Tefik Bekteshi,¹ Gani Dragusha,¹ Masar Gashi,¹ Nebih Musliu,¹ Zaim Gashi²

¹Department of Cardiology, Clinic of Internal Medicine, University Clinical Center of Kosova, Prishtine; ²Department of Gastroenterology, Clinic of Internal Medicine, University Clinical Center of Kosova, Prishtine, Kosovo

Abstract

Interatrial septal disorders, which include: atrial septal defect, patent foramen ovale and atrial septal aneurysm, are frequent congenital anomalies found in adult patients. Early detection of these anomalies is important to prevent their hemodynamic and/or thromboembolic consequences. The aims of this study were: to assess the association between impulse conduction disorders and anomalies of interatrial septum; to determine the prevalence of different types of interatrial septum abnormalities; to assess anatomic, hemodynamic, and clinical consequences of interatrial septal pathologies. Fifty-three adult patients with impulse conduction disorders and patients without ECG changes but with signs of interatrial septal abnormalities, who were referred to our center for echocardiography, were included in a prospective transesophageal echocardiography study. Interatrial septal anomalies were detected in around 85% of the examined patients.

Patent foramen ovale was encountered in 32% of the patients, and in combination with atrial septal aneurysm in an additional 11.3% of cases. Atrial septal aneurysm and atrial septal defect were diagnosed with equal frequency in 20.7% of our study population. Impulse conduction disorders were significantly more suggestive of interatrial septal anomalies than clinical signs and symptoms observed in our patients (84.91% vs 30.19%, $P=0.002$). Right bundle branch block was the most frequent impulse conduction disorder, found in 41 (77.36%) cases. We conclude that interatrial septal anomalies are highly associated with impulse conduction disorders, particularly with right bundle branch block. Impulse conduction disorders are more indicative of interatrial septal abnormalities in earlier stages than can be understood from the patient's clinical condition.

the association between disorders of impulse conduction and congenital anomalies of interatrial septum; to determine the prevalence of different types of interatrial septum abnormalities in patients referred to our echocardiography laboratory; to assess anatomic, hemodynamic, and clinical consequences among different types of interatrial septal pathologies.

Materials and Methods

The study included 53 patients with cardiac impulse conduction disorders of unexplained etiology and patients without ECG changes but with clinical and/or echocardiographic signs of interatrial septal abnormalities who were referred to our center for echocardiography. The prospective study was conducted at the University Clinical Center of Kosova from February 2006 until December 2009. Patients with a known history of interatrial septal abnormalities, patients with autoimmune disease, patients with a documented history of chronic obstructive pulmonary disease and coronary artery disease, as well as patients who could not tolerate transesophageal echocardiography (TEE), were excluded from the study. The study was approved by our institution's ethical committee. Written consent was obtained from all the patients included, and a thorough case history and demographic data were subsequently obtained for each.

A comprehensive physical examination was completed by 2 experienced cardiologists. Patients were categorized in one of the following stages according to clinical signs and symptoms: Stage 1 (presence of murmur, fatigue, dyspnea on physical exertion, absence of other significant signs); Stage 2 (dyspnea, fatigue, absence of cyanosis, usually moderate reduction of pulmonary functional capacity); Stage 3 (rarely congestive heart failure, severe dyspnea, pulmonary hypertension symptoms, upper respiratory tract infections);

Introduction

Embryological development of interatrial septum follows precise stages which allow the continuous passage of oxygenated placental blood from the right atrium to the left. Interatrial septum is programmed to permit this shunt until birth. However, after birth there are certain locations where interatrial septum may be defective.¹ Interatrial septal disorders, which include: atrial septal defect, patent foramen ovale and atrial septal aneurysm, are frequent congenital anomalies found in adult patients. Early detection of these abnormalities is important in order to prevent their hemodynamic and/or thromboembolic consequences. Electrocardiogram (ECG), as an easily accessible and non-invasive diagnostic tool, offers some clues, such as disorders of impulse conduction, which should guide us towards thorough clinical and laboratory investigation for diagnosing interatrial septal abnormalities.

The main aims of this study were: to assess

Correspondence: Aurora Bakalli, Rr. Gazmend Zajmi nr.23. 10000 Prishtine. Kosovo.
Tel. +00.37744151111.
E-mail: abakalli@hotmail.com

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Stage 4 (signs of Eisenmenger complex).²

Routine laboratory tests and chest X-ray were also carried out for every patient included in the study. ECG of all patients were carefully analyzed. Heart rhythm, heart rate, and electrical axis were determined in every patient. Special emphasis was given to assessment of cardiac impulse conduction disorders which include: sinus block, first degree atrio-ventricular block, second degree atrio-ventricular block (Mobitz I and Mobitz II), third degree atrio-ventricular block, atrio-ventricular dissociation, ventricular block (right bundle branch block and left bundle branch block), aberrant conduction, pre-excitation syndromes (Wolff-Parkinson-White and Lown-Ganong-Levine syndromes).

TTE was performed from parasternal, apical and subcostal views. Color-doppler and pulse wave-doppler were applied on interatrial septum to clarify the diagnosis of interatrial septal anomalies. Echocardiographic measurements were obtained according to American Society of Echocardiography recommendations.^{3,4} Aortic root, left atrium, interventricular septum, posterior wall, diastolic and systolic diameters of the left ventricle, right atrial and right ventricle dimensions were obtained. Left ventricular ejection fraction was calculated according to Simpson's rule. Valvular alterations, if present, were noted. Systolic pressure of the pulmonary artery was calculated with the simplified Bernoulli's equation [$RVSP = 4 (TRv)^2 + PRA$; where TRv represents the maximal velocity of tricuspid regurgitation jet, whereas PRA represents an approximate value of right atrial pressure]. In the absence of pulmonary artery stenosis, right ventricular systolic pressure (RVSP) was estimated to be similar to pulmonary artery systolic pressure (PASP); thus this formula was considered to be accurate for quantifying pulmonary hypertension.

TEE was also performed on every patient. Patients received a detailed explanation of the procedure and were told to present themselves under fasting conditions on the day of the procedure. TEE was applied with the patient positioned in the lateral decubitus. Midazolam injection was given in a range from 1.5-5 mg in order to achieve conscious sedation of the patient. Lidocaine spray was applied on hypopharynx for topical anesthesia. TEE projections and measurements were made according to American Society of Echocardiography guidelines.⁴ The procedure was always performed in the presence of at least 2 experienced cardiologists and all the images were archived. Interatrial septum was analyzed in several projections. Color-doppler, pulse wave-doppler and agitated saline as contrast agent were applied with the intention of detecting the eventual presence of interatrial shunting. In cases in which interatrial septum disconti-

nuity was noted, the type of defect and its size were determined. Interatrial defects were categorized as follows: patent foramen ovale (PFO), atrial septal defect (ASD) *ostium secundum* type, ASD *ostium primum* type, ASD *sinus venosus* type, common persistent atrioventricular canal, ASD *sinus coronarius* type.

Interatrial septum was also assessed for atrial aneurysm. Atrial aneurysm (ASA) was defined as interatrial bulging of at least 10 mm from midline. Its excursions and the direction of excursions were also noted with the aim of classifying them according to Olivares-Reyes *et al.* into the following types: ASA type 1R (atrial septum penetrates from midline into the right atrium during the entire cardio-respiratory cycle); ASA type 2L (atrial septum penetrates from midline into the left atrium during the entire cardio-respiratory cycle); ASA type 3RL (the maximal excursion of atrial septum is towards the right atrium, with lesser excursion towards the left atrium); ASA type 4LR (the maximal excursion of atrial septum is towards the left atrium, with lesser excursion towards the right atrium); ASA type 5 (motions of the atrial septum are bidirectional and with equal distance in both atria during the entire cardio-respiratory cycle).

TTE and TEE procedures were performed using Philips iE33 apparatus, in the presence of at least 2 experienced cardiologists.

Statistical analysis

All values were expressed as mean \pm SD or fractions (percentages). Comparison between categorical variables was performed using the χ^2 test. Multivariate analysis was used when more than two variables were compared. Correlation between variables was calculated using Pearson's correlation test. For all tests, a P value less than 0.05 was considered statistically significant. All statistical analyses were performed using statistical software (SSP, version 2.80, 2005).

Results

Fifty-three patients were included in this study. Patients' mean age was 54.35 ± 16.2 years and 56.6% of them were women. Interatrial septal anomalies were detected in around 85% of the examined patients. PFO (Figure 1A) was the most frequent interatrial abnormality found in 32% of the patients, and in combination with ASA (Figure 1B) in an additional 11.3% of the cases. ASA and ASD were detected with equal frequency in our study population (Table 1). Other baseline patient characteristics are presented in Table 1.

Interatrial septal abnormalities were highly associated with cardiac impulse conduction disorders in our patients. Right bundle branch

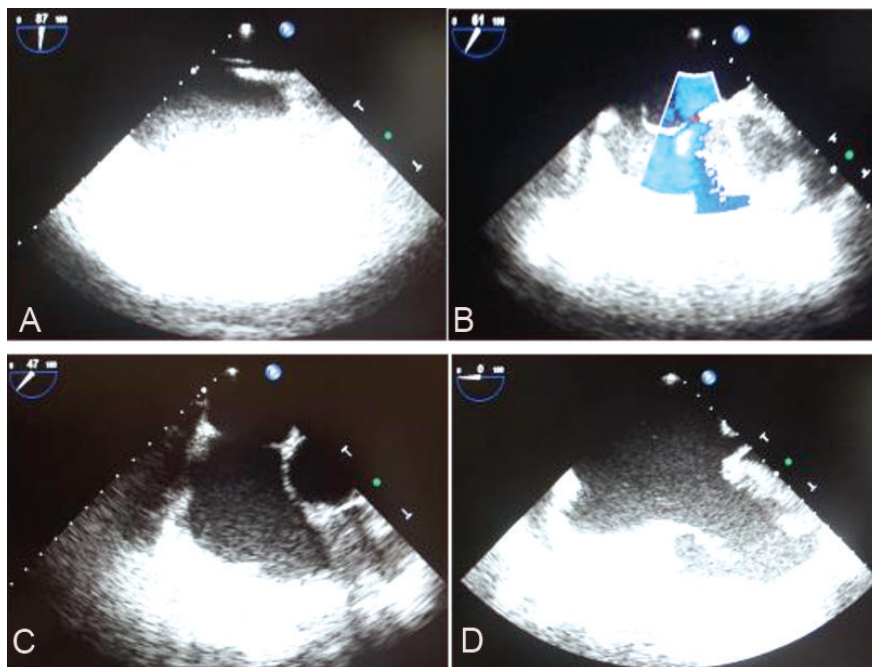


Figure 1. TEE images of interatrial septal abnormalities. (A) PFO in a 30-year old patient with ECG signs of RBBB. (B) ASA type 1R associated with PFO (demonstrated with color-doppler) in a 40-year old patient with RBBB. (C) A large ASD *ostium secundum* type in a 38-year old patient with RBBB. (D) A partial atrio-ventricular canal in a 55-year old patient with ECG signs of LBBB, with absence of entire interatrial septum and incompetent mitral and tricuspid valves resulting in massive regurgitation.

block (RBBB) was present in 9 patients with isolated ASA, and left bundle branch block (LBBB) in one patient with ASA. Twelve out of 17 patients with isolated PFO had ECG signs of RBBB, and one had first degree atrio-ventricular block, whereas 4 of the patients with PFO

Table 1. Patients' baseline characteristics.

Patients (n=53)	
Age	54.35±16.2
Gender	
Females (%)	30/53 (56.6)
Males (%)	23/53 (43.4)
IAS anomalies (%)	45/53 (84.91)
ASA (%)	11/53 (20.75)
ASA and PFO (%)	6/53 (11.32)
PFO (%)	17/53 (32.07)
ASD (%)	11/53 (20.75)
History of stroke (%)	4/53 (7.55)
Heart failure (%)	7/53 (13.21)
Hypertension (%)	26/53 (49.01)
Diabetes mellitus (%)	11/53 (20.75)

Data are presented as ± SD or fractions (%). ASA, atrial septal aneurysm; ASD, atrial septal defect; IAS, interatrial septum; PFO, patent foramen ovale.

Table 2. Basic transthoracic and transesophageal echocardiography characteristics.

Patients (n=53)	
TTE parameters	
Aortic root, mm	33.94±4.41
Left atrium, mm	41.48±7.23
Right atrium, mm	49.51±12.7
Right ventricle, mm	36.01±9.23
IVS, mm	11.09±2.19
Posterior wall, mm	10.43±1.71
LVEDD, mm	50.8±6.28
LVEF, %	58.49±8.74
PASP, mmHg	33.89±17.6
TEE parameters	
LA/LAA thrombus (%)	7/53 (13.21)
RA/RAA thrombus (%)	8/53 (15.09)
LA/LAA SEC (%)	11/53 (20.75)
RA/RAA SEC (%)	12/53 (22.64)

* Data are presented as ±SD or fractions (%); **IVS, interventricular septum; LA, left atrium; LAA, left atrial appendage; LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; PASP, pulmonary artery systolic pressure; RA, right atrium; RAA, right atrial appendage; SEC, spontaneous echo contrast.

Table 3. Comparison of anatomical and hemodynamic consequences of patients with interatrial septal disorders.

	ASA	ASA + PFO	PFO	ASD	P value
Age	57.63±15.2	57±16.2	50.1±19.1	46.45±9.9	0.33
Females (%)	5/11 (45.45)	4/6 (66.67)	10/17 (58.82)	7/11 (63.64)	0.96
RA, mm	48.67±10.7	42±2	40.3±5.3	55.3±17.1	0.07
RV, mm	37.67±12.9	30±7.1	29.87±7.9	43±5.7	0.04
PASP, mmHg	24.81±8.1	35±14.8	23.71±8.5	53.64±17.2	<0.001

Data are presented as ± SD. ASA, atrial septal aneurysm; ASD, atrial septal defect; PASP, pulmonary artery systolic pressure; PFO, patent foramen ovale; RA, right atrium; RV, right ventricle.

combined with ASA had RBBB. Eight of the patients with ASD had RBBB, 2 had LBBB, and one patient did not have signs of impulse conduction disorder but had chronic atrial fibrillation (Figure 2). RBBB was the most frequent impulse conduction disorder encountered in patients with atrial septal pathologies, found in 41 (77.36%) cases. On the other hand, 8 (15.09%) patients with RBBB had no atrial septal anomalies. Subclinical chronic obstructive pulmonary disease may be the reason for the RBBB in 2 of the patients, whereas prior inferior-posterior myocardial infarction was found in one patient. For the remaining 5 patients with RBBB without interatrial anomalies, we were not able to find an explanation for the presence of RBBB. In contrast, from the 8 patients with atrial septal anomalies without signs of impulse conduction disorders, one patient had ASA, 2 patients had a combination of ASA with PFO, 4 patients had PFO, and one patient had ASD.

We were able to diagnose 11 patients with ASD, 7 of whom had ASD *ostium secundum* type (Figure 1C), one had ASD *ostium primum* type, one patient had both ASD *ostium primum* and *secundum* types, one with ASD *sinus venosus* type, and one patient had partial atrio-ventricular canal (Figure 1D). The patient with combination of ASD *ostium primum* and *secundum* types and the patient with partial atrio-ventricular canal had ECG signs of LBBB. Isolated ASA was identified in 11 patients, and in combination with PFO in 6 additional patients. From the 17 patients with ASA, 7 were with ASA type 3RL, 5 with type 1R, 3 with type 4LR, and 2 patients with ASA type 2L.

Basic TTE and TEE parameters obtained in our study population are shown in Table 2. ASD was detected at earlier ages, as compared to the other interatrial septal disorders (Table 3). As expected, ASD had greater anatomical and hemodynamic consequences compared to the other interatrial septal pathologies, although only the size of right ventricle and PASP resulted statistically significantly higher in our study population (Table 3).

Clinical signs and/or symptoms (fatigue, dyspnea, presence of murmur, cyanosis, upper respiratory tract infections, congestive heart failure, clubbing) of interatrial disorders were

observed in only 16 (30.19%) of our patients. There were 4 patients with clinical signs of stage 1, one patient with ASD and 3 patients with PFO. We categorized 7 patients in stage 2, 5 of whom had ASD and 2 patients had PFO combined with ASA. Four patients with ASD had clinical signs of stage 3 and one patient had signs of Eisenmenger complex, thus belonging to stage 4 (Figure 3). Impulse conduction disorders were significantly more indicative of atrial septal anomalies than clinical signs and symptoms observed in our patients (84.91% vs 30.19%, P=0.002). All the patients with atrial septal defect presented with clinical signs and/or symptoms suggestive of the disease. There was an inverse correlation between patient age and the clinical stage of the disease (r=-0.24, P=0.04), which can be explained by the fact that more serious atrial septal abnormalities become symptomatic earlier in comparison to milder forms of interatrial abnormalities, such as PFO and ASA.

Discussion

Early detection of interatrial septal abnormalities is important for prevention of anatomic and hemodynamic consequences, as well as for prevention of thromboembolic events. This is why it is essential to identify indicators that will lead to early diagnosis of these anomalies. Clinical signs, symptoms and ECG serve as guides towards diagnosis of atrial septal defects. ECG offers some clues, such as impulse conduction disorders, which should serve as indications for detailed clinical and laboratory evaluation for identifying atrial septal pathologies. It is well known that complete and incomplete RBBB is the most frequent ECG marker of ASD.⁵⁻¹⁰ ASD may also be associated with other impulse conduction disorders, particularly with prolonged P-R interval.⁶ RBBB might be due to right ventricular volume overload or as a result of true delay of impulse conduction on the right bundle branch^{5,6} whereas prolonged P-R interval may be explained by the atrial enlargement and increased distance for internodal conduction.⁶

While there is plenty of evidence associating ASD and impulse conduction disorders, there are very few data in the medical literature about the relationship of ECG changes to ASA and PFO. Recently, some studies have demonstrated an association between the so-called crochete (M shaped, bifid nodule) pattern in the inferior ECG leads and the presence of PFO.^{11,12} However, controversy remains regarding the correlation of complete or incomplete RBBB to PFO.¹³ We have previously reported the possible association of RBBB to ASA, particularly if combined with other interatrial

anomalies.¹⁴ In a large health screening, Chan *et al.* examined 651,794 school children.¹⁵ The most frequent ECG changes found in these children included premature ventricular beats in 186 cases, followed by RBBB observed in 132 children. Congenital cardiac anomalies were detected in 1,159 school children, where mitral valve prolapse was the most prevalent disorder found in 0.18% of cases, whereas ASD was diagnosed in 0.02% of the children examined. This large cardiac screening resulted in the

detection of a high number of congenital heart anomalies in school children otherwise thought to be healthy.¹⁵

In our study population, patients with interatrial septal anomalies frequently had ECG signs of impulse conduction disorders, particularly RBBB. On the other hand, a small portion of these patients were symptomatic, with the exception of patients with ASD, suggesting that physical examination is reliable only for this group of patients with interatrial septal

abnormalities. In our patients, ECG signs of impulse conduction disorders resulted significantly more frequently associated with atrial septal anomalies than the clinical image.

ASD causes anatomical and hemodynamic burden of the right heart chambers which is also demonstrated in our study. PFO and ASA, on the other hand, were considered to be innocent cardiac disorders. However, recently many authors have held them responsible for occurrence of ischemic strokes in younger patients. Lechat *et al.* found that prevalence of PFO was significantly higher in patients under the age of 55 with a history of stroke than in age-matched healthy subjects.¹⁶ Mas *et al.*, in a prospective study with 598 patients aged from 18 to 55 years with history of cryptogenic stroke found that 36% of these patients had PFO, 1.7% had ASA, and 8.5% of patients had both these anomalies. This study also concluded that patients with history of stroke who had PFO combined with ASA had a higher risk for recurrence of stroke.¹⁷ Other clinical consequences of PFO include also the decompression illnesses,¹⁸ migraine and vascular headaches,¹⁹ and platypnea-orthodeoxia syndrome.²⁰ A relationship between ASA and cerebral ischemic events was first reported in 1987 in a retrospective study by Belkin *et al.*,²¹ and this was confirmed in subsequent multicentric studies.^{22,23} Many authors have suggested that right to left shunting through PFO associated with ASA is the mechanism responsible for occurrence of ischemic stroke.^{22,24,25} Four of our patients with PFO had prior history of stroke. A major limitation of this study is the small number of patients. Another limitation is that we could not perform Magnetic Resonance Imaging or Computed Tomography to ascertain the presence of interatrial septal abnormalities.

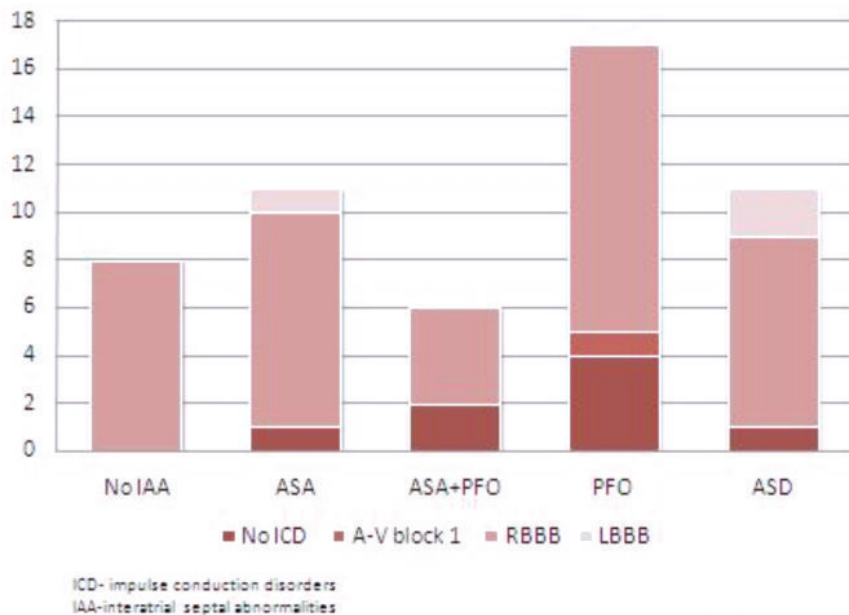


Figure 2. Association of impulse conduction disorders and interatrial septal abnormalities.

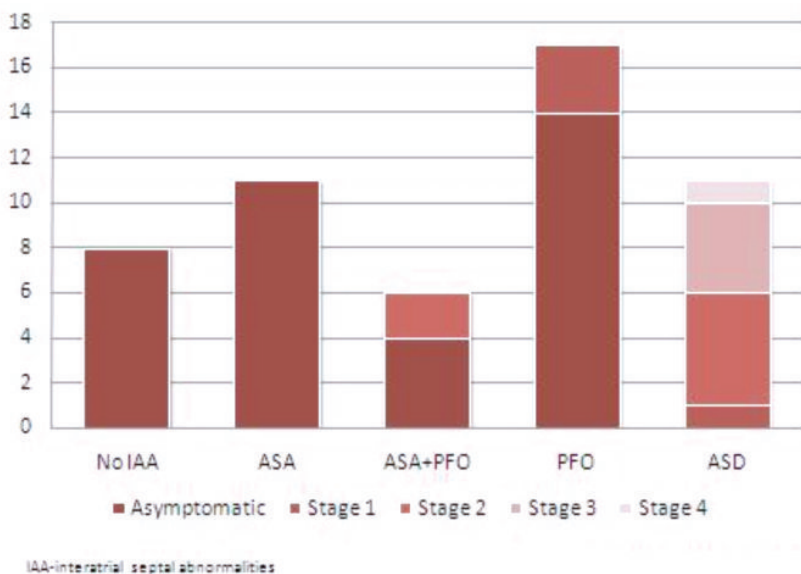


Figure 3. Association of clinical staging and interatrial septal abnormalities.

Conclusions

We conclude that patients with ECG signs of impulse conduction disorders, particularly with RBBB, are highly associated with interatrial septal anomalies. Impulse conduction disorders are more indicative of interatrial septal abnormalities in earlier stages than can be understood from the patient's clinical condition. Thus, presence of ECG signs of impulse conduction disorders should raise the suspicion for interatrial septal pathologies.

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