

## Surgical closure of atrial septal defect in patients aged 40 years and older: Effect on cardiac function and general clinical outcomes

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### ARTICLE INFORMATION

Received: December 21, 2018

Accepted: February 1, 2019

### Competing interests

The authors declare no competing interests

### Acronyms

**AF:** atrial fibrillation

**ASD:** atrial septal defect

**PAP:** pulmonary artery pressure

**PHT:** pulmonary hypertension

**Qp/Qs:** ratio of pulmonary to systemic blood flow

### ABSTRACT

**Introduction:** Atrial septal defect (ASD) is one of the most common congenital heart diseases in adult patients.

**Objectives:** We evaluated the early and mid-term results of surgical treatment of secundum atrial septal defects in patients with  $\geq 40$  years in terms of cardiac functions and clinical outcomes.

**Method:** Thirty-two patients who had undergone surgical correction for secundum atrial septal defect at the age of 40 years and older were examined. Echocardiographic parameters, cardiac functions and clinical status of all patients were compared before and after the operation to evaluate the efficacy of surgical treatment.

**Results:** The patients were followed for an average of 2,2 years (range 3 months – 3,1 years). There was no mortality in the postoperative period. In the early follow-up, there was no cerebrovascular thromboembolic event, functional capacities of the patients improved. No new atrial fibrillation occurred. Right atrial and ventricle diameters, and pulmonary artery pressures were significantly reduced, while ejection fractions did not change. The need for diuretic therapy was reduced after surgical treatment. No residual intracardiac shunt was detected during follow-up.

**Conclusions:** Surgical closure of atrial septal defects in adult patients over the age of 40 can improve cardiac function by echocardiography and reduce clinical complaints. Even if no intervention is made in such patients, the current complaints are scarce and life-threatening problems are rarely seen in hemodynamic parameters. However, surgical repair should be performed as soon as possible, especially when detected in adult patients.

**Keywords:** Atrial septal defect, Surgery, Adult, Outcome assessment (Health Care)

### *Cierre quirúrgico de comunicación interauricular en pacientes mayores de 40 años de edad: Efecto sobre la función cardíaca y resultados clínicos generales*

### RESUMEN

**Introducción:** La comunicación interauricular (CIA) es una de las cardiopatías congénitas más frecuentes en los pacientes adultos.

**Objetivo:** Se evaluaron los resultados iniciales y a medio plazo del tratamiento quirúrgico de la CIA tipo ostium secundum en pacientes mayores de 40 años de edad en relación con la función cardíaca y los resultados clínicos.

**Método:** Se estudiaron 32 pacientes, mayores de 40 años de edad, a quienes se les realizó corrección quirúrgica de una CIA tipo ostium secundum. Se compararon

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los parámetros ecocardiográficos, de función cardíaca y el estado clínico de todos los pacientes antes y después de la operación para evaluar la eficacia del tratamiento quirúrgico.

**Resultados:** Los pacientes fueron seguidos durante un promedio de 2,2 años (rango 3 meses - 3,1 años). No hubo mortalidad en el postoperatorio. En el seguimiento temprano, no hubo ningún evento tromboembólico cerebrovascular y mejoraron las capacidades funcionales de los pacientes. No ocurrieron nuevas fibrilaciones auriculares. Los diámetros de la aurícula y el ventrículo derechos, y las presiones de la arteria pulmonar se redujeron significativamente, mientras que no se encontró variación en la fracción de eyección. La necesidad de tratamiento diurético se redujo después del tratamiento quirúrgico. No se detectó ningún cortocircuito intracardiaco residual durante el seguimiento.

**Conclusiones:** El cierre quirúrgico de la CIA en pacientes adultos mayores de 40 años puede mejorar la función cardíaca medida por ecocardiografía y reducir los síntomas clínicos. Incluso, si no se utiliza ningún tratamiento en estos pacientes, los síntomas son escasos y rara vez se encuentran alteraciones en los parámetros hemodinámicos con peligro para la vida. Sin embargo, la reparación quirúrgica debe realizarse lo antes posible, especialmente cuando se detecta en pacientes adultos.

**Palabras clave:** Comunicación interauricular, Cirugía, Adulto, Evaluación de resultado (Atención de Salud)

## INTRODUCTION

Atrial septal defect (ASD) is one of the most common congenital heart diseases in adult patients. While it is present in approximately 10% of newborn infants, ASD is responsible for 40% of congenital heart diseases in adult life<sup>1</sup>.

Surgical closure of ostium secundum type atrial septal defects can be safely performed with very low morbidity and mortality even though there is still an existing discussion between surgical indications and treatment options for adult patients with ASD<sup>2,3</sup>. In addition, life-threatening complications such as heart failure, pulmonary hypertension, thromboembolic complications and arrhythmias, which may occur later, with full surgical correction, are prevented<sup>4,5</sup>. Symptoms and pathological hemodynamic problems appear to be minimal in this type of patient and surgical repair should be performed as soon as possible after diagnosis<sup>2,3</sup>.

In this study, we analyzed the early and mid-term effects and results of the surgical treatment of ASD in patients over 40 years of age.

## METHOD

Between August 2009 and November 2018, 32 patients over 40 years of age were diagnosed with ASD

at Atatürk University Faculty of Medicine Department of Cardiovascular Surgery and Erzurum Regional Training and Research Hospital.

Twelve patients (37.5%) hospitalized for surgery consisted of 50 years of age and 4 patients over 60 years of age (12.5%). Twenty one of our patients (65.7%) were male and 11, female (34.3%). The first diagnosis was made by echocardiographic examination in all patients. All of them were above 40 years of age and underwent coronary angiography in addition to cardiac catheterization. No significant changes were observed in the coronary arteries of any of the patients. The ratio of pulmonary to systemic blood flow (Qp/Qs) was determined by oximetry. The study patients had predominant left-to-right inter-atrial shunt with Qp/Qs of at least 1.5:1. In our cases, the mean Qp/Qs rate was between 1.5-2.0, 2.0-3.0, and  $\geq 3.0$  in 9 (28.1%), 19 (59.4%), and 4 (12.5%) patients, respectively.

Additional cardiac pathologies such as severe comorbid disease, previous cardiac surgery, congenital cardiac malformation, rheumatic valve disease, coronary artery disease at diagnosis, mitral or aortic regurgitation, and left ventricular dysfunction were not included in this study. The patients were evaluated clinically and echocardiographically during the follow-up period of 2.2 years.

Patients with pulmonary hypertension (PHT) were included in the study. PHT was defined in 3 categories:

- Mild PHT: pulmonary artery pressure (PAP) below 50 mmHg (n=16, 50%)
- Moderate PHT: PAP between 50 and 75 mmHg (n=12, 37.5%)
- Severe PHT: PAP greater than 75 mmHg (n=4, 12.5%)

Functional capacity (as Class I, II, III, IV according to New York Heart Association [NYHA]), diuretic requirements and rhythm changes were analyzed according to preoperative period in order to evaluate the efficacy of surgical treatment. Eighteen patients (56.3%) were in Class I and II, and 14 were in Class III and IV groups (43.7%). In addition to the right atrium and right ventricular diameters of the patients, PAPs and left ventricular ejection fraction were re-evaluated after the operation and compared with the preoperative results.

All operations were performed under cardiopulmonary bypass and body temperature between 32-36 °C. Twenty seven patients (84.4%) underwent median sternotomy and 5 (15.6%), right thoracotomy. Cold crystalloid cardioplegic solution was given to the aortic root for myocardial protection.

The size of the defect was evaluated after right atriotomy, and tricuspid valve insufficiency was tested. After the defect was closed with primary or patch (pericardial or dacron) (**Figure 1**), patients with advanced tricuspid regurgitation were treated with De Vega annuloplasty.

Early postoperative evaluation was made in the first month after surgery. Later, all patients were followed-up each 3 months to 3.1 years (mean, 2.2 years) by questionnaire or telephone interview with the patient or the referring physician, or both. All patients were advised to appear for clinical and echocardiographic follow-up evaluations at 6- or 8-month intervals, or as soon as possible if either a new symptom appeared or the previous clinical state deteriorated.

### Statistical analysis

Statistical analysis was performed with SPSS 10.0 (SPSS, Chicago, IL, USA). All results are expressed as mean  $\pm$  standard deviation. Kolmogorov-Smirnov test was used for variable data. Paired t tests were used to compare echocardiographic parameters in pre- and postoperative patients. McNemar tests were used to compare diuretic application, rhythm status, and functional capacity of all patients before and after surgery. P value <0.05 was considered significant.

## RESULTS

The analysis included 32 patients who underwent surgical repair of secundum ASD; 11 women (34.3%) and 21 men (65.7%), with a mean age of 46 $\pm$ 9 years



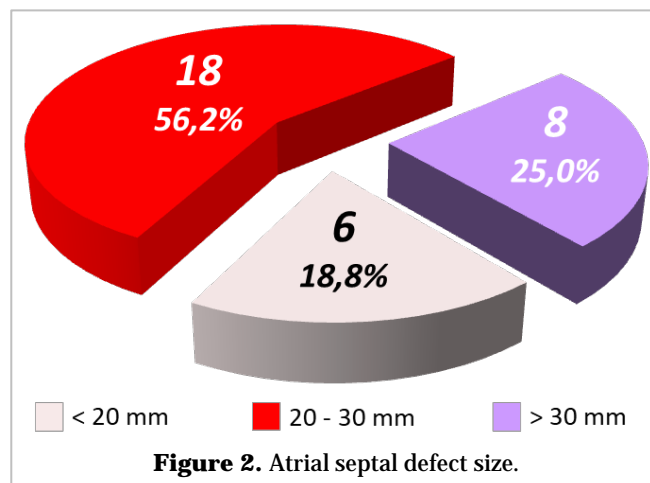
**Figure 1.** Two patients who underwent surgical closure of ASD. Operation images of patients in whom dacron patch (A) and pericardial patch (B) was used.

(range, 40 to 72 years). The ASD diameter was 1.5 to 3.8 cm (mean;  $2.1 \pm 0.8$  cm). Its size distribution is shown in **figure 2**.

ASD was closed with direct suture in 5 patients (9.8%). Pericardial patch (19 patients) or dacron patch (8 patients) were preferred for defect closure in other patients. During the sewing process, continuous sewing technique (with 4/0 or 5/0 prolene material) was used.

All of the patients survived after the operation. The functional capacities of the patients showed a significant improvement after the operation. While the number of patients in Class I and II increased, the number of patients in Class III and IV decreased (**Table**). Twenty-two patients (68.8%) had received diuretic treatment before the operation, whereas only 9 patients (28.1%) received diuretic treatment after the operation. The number of patients using diuretics significantly decreased and this result was statistically significant ( $p < 0.005$ ).

In the preoperative term, 7 patients (21.9%) had atrial fibrillation (AF). Left ventricular ejection fraction was  $< 45\%$  in 9 patients (28.1%), and over 45% in the rest. The right atrial diameters (RADs) were  $< 45$  mm, 45-55 mm, and  $> 55$  mm in 7 (21.9%), 16 (50%), and 9 patients (28.1%), respectively. The right ventricle diameters (RVDs) were  $< 30$  mm, 30-50 mm, and  $> 50$  mm in 6 (18.7%), 20 (62.6%), and 6 patients



(18.7%), respectively. The mean of the RADs and the RVDs were  $48.5 \pm 6.7$  and  $36.9 \pm 8.4$  mm, respectively, before the operation. While the highest RAD was 57 mm, the highest RVD was 46 mm among patients. The values of left ventricular ejection fraction, RAD, RVD, and PAP before and after the operation are shown in **table**. RADs and RVDs were significantly decreased after the operation ( $p < 0.005$ ). The RADs were much smaller than 50 mm in 24 patients. Telecardiography showed significant improvements in pulmonary vascularity and reduction in the size of

**Table.** Comparison of preoperative and postoperative data (echocardiographic variables and clinical parameters).

Parameters	Preoperatively	Postoperatively	P value
Functional capacity (NYHA)			
Class I	8	14	<b>0.005</b>
Class II	10	15	<b>0.005</b>
Class III	9	2	<b>0.005</b>
Class IV	5	1	<b>0.005</b>
Diuretic usage	22	9	<b>0.005</b>
Atrial fibrillation	7	6	0.801
Ejection fraction (%)			
$\leq 45$	9	7	0.522
$> 45$	23	25	0.129
Right atrial diameter (mm)	$48.5 \pm 6.7$	$41.9 \pm 4.1$	<b>0.005</b>
Right ventricle diameter (mm)	$36.9 \pm 8.4$	$30.7 \pm 7.8$	<b>0.005</b>
Pulmonary artery pressure (mmHg)	$47.2 \pm 11.1$	$37.8 \pm 10.9$	<b>0.005</b>

Statistical significance:  $p < 0.05$

the right ventricle. The PAPs were significantly decreased after the operation ( $p < 0.005$ ). PAPs were more than 60 mmHg in only 2 patients. Although the number of patients with left ventricular ejection fraction above 45% increased in the postoperative period compared to preoperatively, this result was not statistically significant ( $p = 0.129$ ).

Preoperative echocardiography revealed moderate or severe tricuspid regurgitation in 15 patients (46.9%). It was trivial in 3 (9.3%) patients. Water computed test was performed preoperatively in patients with moderate and advanced tricuspid regurgitation. De Vega annuloplasty procedure was performed in 11 patients (34.4%) with advanced leakage. Postoperatively, only 2 patients had mild tricuspid regurgitation. Patients with tricuspid annuloplasty by De Vega's method did well during the follow-up period.

One patient (3.1%) had mitral regurgitation related to mitral cleft and mitral valvuloplasty was performed. Another patient (3.1%) had anomalous pulmonary venous connection, which was treated with ASD. Ten patients (31.2%) had aortic regurgitation that was not clinically significant.

The percentage of patients with AF decreased after operation (from 21.8% to 18.7%), but this difference was not significant (**Table**). Although 2 patients recovered normal sinus rhythm after the operation, 1 of them had new AF in the postoperative term. To prevent thromboembolic complications, anticoagulation therapy was started immediately after the re-removal of the thoracic drainage tubes in 5 patients with AF.

#### **Late follow-up**

Twenty-nine patients were followed from 3 months to 3.1 years (mean 2.2 years). Two patients were lost to follow-up after moving to another city in Turkey, and another died in a traffic accident. Twenty-nine patients were class I or II in the mid-term follow-up. Three patients returned to normal sinus rhythm in the second year of follow-up. Late arrhythmias did not develop in any patients. Anticoagulant therapy was continued in patients because of continued AF. Advanced mitral valve regurgitation was detected in 1 patient after the operation. Mitral regurgitation, caused by bileaflet mitral valve prolapse was detected; mitral valve replacement was performed 2 years after the initial operation. Tricuspid regurgitation occurred in 1 patient with De Vega annuloplasty, who was medically treated.

## **DISCUSSION**

Surgical repair interventions for ASD have been successfully performed in many centers for more than 40 years. Perioperative morbidity and mortality rates were 10-20% at the end of the 1950s, these rates decreased to 6% after the 1960s, and up to 0.5% nowadays<sup>6</sup>. This improvement in surgical success and survival rates, and reduction in complications, are due to better operative techniques and better postoperative care. Therefore, the surgical closure of this very common congenital disease has recently been recommended at higher rates, even for older patients. Despite successful and low complication operations, several studies have been published in the last few years that question the policy of routine surgical closure in patients with high PAP<sup>5,7-10</sup>.

Surgical repair is still the main therapy for ASDs. The previous belief that only 50% of patients with unrepaired ASDs survive beyond the age of 40 years and less than 10% reach the age of 60 years, has not been confirmed in many other observational studies<sup>2,6</sup>. Therefore, life expectancy of patients with untreated ASD is generally shortened<sup>1,4,9,11-13</sup>. In particular, when symptoms develop, it has been suggested that patients who are surgically treated have a significant survival advantage –compared to the medical treatment– similar of patients who were operated in their second and third years<sup>7</sup>. Since AF, pulmonary blood flow, right heart overload, arrhythmias and frequency of PHT tend to increase with age, ASD should be operated even if the patient is asymptomatic.

In the late follow-up period, age was found to be an important, meaningful and independent predictor of morbidity and mortality<sup>2</sup>. Murphy reported that patients undergoing surgery after age 40 had a higher risk of postoperative cardiovascular complications and an excellent prognosis in children and young adults<sup>12</sup>. Some of the patients we underwent surgical correction were over 50 or 60 years old. No morbidity or mortality was found in these patients. Our results suggest that surgical closure of ASDs improves symptoms and prevents later complications in these patients. The proportion of patients with NYHA class III-IV decreased from 43,8% to 9,3% postoperatively. This result was found to be consistent with the results in the other published articles<sup>7,14</sup>. These investigators reported that surgical repair of ASDs significantly increased long-term survival in middle-aged and elderly patients.

Studies have shown that the frequency of AF in patients with ASD increases as age increases<sup>1,7,8,12</sup>. In addition, the causes of atrial rhythm disorder were found to be induced by different mechanisms in the preoperative and postoperative periods. Before surgery, the main cause of AF is atrial distension<sup>15</sup>. Although the exact mechanism is not known, AF development in patients after ASD closure may be considered in relation to scarring in the area of ectopic focus or in the area of venous cannulation at the surgical repair site. Right atrial size decreased from 48.5±6.7 to 41.9±4.1 mm in our patients after the operation, and one the patients with AF returned to sinus rhythm, postoperatively. But, this was not statistically significant. Furthermore, in this case, it showed us that the ASD closure should be performed before the occurrence of AF.

Embolization in the postoperative period in patients treated surgically is important for long-term hospitalization, cerebral injury and hospital expenses. This incidence is closely related to the age and the rhythm problems of the patient at the operation stage<sup>15</sup>. AF is a possible cause of an increased incidence of thromboembolic events in patients operated on to correct ASD<sup>14-16</sup>. Because of the high risk of cerebral embolism in elderly patients with chronic AF, we preferred to begin anticoagulant therapy (warfarin) in patients with AF after surgery. We also aimed to reduce the risk of patch-related thromboembolism in small ASD patients by direct suture. Because of the necessity of patching in large defects, we used pericardial patch instead of dacron patch because of thromboembolic predisposition.

Although routine anticoagulant therapy was not recommended after patch closure of ASD<sup>7</sup>, warfarin was administered to patients with chronic AF in the postoperative period and aspirin treatment was started in the other patients. The INR value was kept between 2.5-3.5 in patients treated with warfarin. We suggested that aspirin therapy should be continued for at least 3 months in patients without AF according to the recommendations in the current publications<sup>16-18</sup>. No thromboembolic complication was seen in the postoperative period and follow-up in our patients with AF. This showed that despite being AF, anticoagulant therapy prevented possible embolic events. According to Shah *et al*<sup>9</sup>, the incidence of systemic emboli was reported in ASD patients treated both medically and surgically; therefore, after closure of ASDs, careful monitoring of arrhythmias and anticoagulants were recommended to prevent thromboembolic events.

The associated incidence of tricuspid regurgitation increases with age. In this study, moderate or severe tricuspid regurgitation was detected in 46,9% of the patients. Echocardiographic examination of the tricuspid valve sometimes has a tendency of overestimation. If preoperatively it shows moderate or severe signs of tricuspid regurgitation in patients, water proficiency testing is recommended to decide on tricuspid annuloplasty indication. In addition to ASD closure in these patients, we suggest that a tricuspid annuloplasty is important in decreasing cardiothoracic ratio, improving functional capacity and providing normal sinus rhythm.

PHT is a serious complication that affects the prognosis of ASD. In general, severe PHT associated with ASD is rare. But rarely, it can often develop at an advanced age (between 30 and 40 years of age), progressing rapidly to reverse shunting and causing death<sup>17,18</sup>. It is difficult to predict in which patient with ASD pulmonary vascular disease will develop. In patients with severe PHT, the operation of ASD is very difficult and dangerous. Fiore and colleagues<sup>7</sup> reported that the operative outcome in their series of ASD patients older than 50 years was not influenced by the presence of PHT in the absence of greatly increased vascular resistance. Others have suggested that increases in PAP are not necessarily related to age, and shunt size is not related to severity of symptoms<sup>17,18</sup>. Surgery should indeed be performed in the younger patient and probably before structural changes in the myocardium or pulmonary vasculature have occurred<sup>19</sup>. Despite rare severe PHT in our patients, we suggest that, in patients with PHT, surgeons should be cautious in deciding to operate, irrespective of their age.

The advanced NYHA classification had a pronounced impact on early and late mortality. We found a significant improvement in functional status that the rate of patients with class I and II was increased from 56,2% to 90,6% after surgical treatment (**Table**).

As a result, in addition to the improvement on the NYHA functional class; surgical correction of ASD (for arrhythmia, deterioration of the pulmonary vascular bed and prevention of development of congestive heart failure [growth of the heart cavities]) improves the quality of life of adult patients and prolongs life expectancy, resulting in satisfactory and beneficial results in terms of cardiac functions. Because there is no safe and effective nonsurgical alternative treatment to surgical closure (besides structural interventional procedure with septal closure

devices), we believe that anatomic closure must be performed without delaying the initial treatment for ASD with a Qp/Qs ratio  $\geq 1.5$  and increasing PAP for adults > 40 years old, even these over 60 years of age, who are in NYHA classes III and IV. Patients who are surgically treated should be closely monitored for AF or atrial flutter to prevent or reduce the morbidity and mortality associated with cerebral thromboembolism, and the anticoagulation regimen should be maintained in patients with persistent AF even if the patients were operated.

## CONCLUSIONS

Surgical closure of atrial septal defects in adult patients over the age of 40 can improve cardiac function by echocardiography and reduce clinical complaints. Even if no intervention is made in such patients, the current complaints are scarce and life-threatening problems are rarely seen in hemodynamic parameters. However, surgical repair should be performed as soon as possible, especially when detected in adult patients.

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