

Iatrogenic atrial septal defect post radiofrequency ablation in patients with left atrial SVT: Predictors and outcomes

Defecto iatrogénico del tabique auricular posablación por radiofrecuencia en pacientes con TSV auricular izquierda: predictores y resultados

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Abstract

Iatrogenic atrial septal defect (IASD), post Catheter ablation during electrophysiological study simply can be assess with Echocardiography nowadays ablation consider the main line in the managements of patients with various type of arrhythmia. This study aims to determine the outcomes of Iatrogenic Atrial Septal Defect (IASD) six months post radiofrequency ablation (RF) procedure of left atrial arrhythmia using non-invasive Transthoracic Echocardiography (TTE) parameters (LVEF, E/e` and ASD size) with sheath size as predictors of atrial septal defect closure.

Patients and methods: A prospective study was conducted in Iraqi Centre for Heart Diseases included 47 patients post Electrophysiology procedure and ablation of left atrial SVT were selected after non complicated transeptal puncture using two size of sheath in three type of arrhythmia and follow up done simply with Transthoracic echocardiography (TTE) was used to evaluate the atrial septal defect (ASD) (from May 2019-May 2020) in Iraqi centre for heart diseases.

Results: After Electrophysiology study, results of this study were analysed and collected according to duration of procedure, sheath size and number that used in septostomy, size of IASD and Echocardiographic parameters. The mean age of the patients (36.28 ± 10.34 years), males

were 23 (48.9%) while females were 24 (51.1%), without structural heart diseases and good LV function with mean EF ($64.68 \pm 5.23\%$) . Iatrogenic atrial septal defects (IASDs) were detected by TTE in all patients with range from (2-5) mm with mean of (3.47 ± 0.92), performed by Transseptal puncture (TSP), either with single 8 French sheath in 24 (51.06%) patients or single 12 French sheath in 17 (36.17%) patients while 6 (12.77%) patients the defect was performed by double transeptal sheath. spontaneous closure occur in 35(74%) patients within first three months with clear significant association between size of ASD that related to the sheath size and duration of procedure ($P < 0.0001$). We notice that some Echocardiographic parameters were also associated with IASD without any clinical complications and/ or deterioration.

Conclusions: post catheter ablation number and size of sheath and duration of ablation consider as a predictor to closure of residual atrial septal defect post atrial septostomy and can simply assess with non-invasive Transthoracic Echocardiography parameters such (Atrial septal defect size and body surface area) during initial six months follow up.

Keywords: Iatrogenic atrial septal defect, Transseptal puncture, Radiofrequency ablation, transthoracic echocardiography

La comunicación interauricular iatrogénica (IASD), post ablación con catéter durante el estudio electrofisiológico simplemente se puede evaluar con Ecocardiografía, hoy en día la ablación se considera la línea principal en el manejo de pacientes con diversos tipos de arritmias. Este estudio tiene como objetivo determinar los resultados del defecto del tabique auricular iatrogénico (IASD) seis meses después del procedimiento de ablación por radiofrecuencia (RF) de la arritmia auricular izquierda utilizando parámetros de ecocardiografía transtorácica (ETT) no invasiva (FEVI, E / e' y tamaño de la CIA) con tamaño de la vaina como predictores del cierre de la comunicación interauricular.

Pacientes y métodos: Se realizó un estudio prospectivo en el Centro Iraquí de Enfermedades Cardíacas que incluyó a 47 pacientes después del procedimiento de electrofisiología y se seleccionaron la ablación de la TSV de la aurícula izquierda después de una punción transeptal no complicada utilizando dos tamaños de vaina en tres tipos de arritmia y seguimiento realizado simplemente con La ecocardiografía transtorácica (ETT) se utilizó para evaluar la comunicación interauricular (ASD) (de mayo de 2019 a mayo de 2020) en el centro iraquí de enfermedades cardíacas.

Resultados: Después del estudio de electrofisiología, los resultados de este estudio fueron analizados y recolectados de acuerdo con la duración del procedimiento, el tamaño de la vaina y el número que se utilizó en la septostomía, el tamaño de la IASD y los parámetros ecocardiográficos. La edad media de los pacientes ($36,28 \pm 10,34$ años), los varones 23 (48,9%) y las mujeres 24 (51,1%), sin cardiopatías estructurales y buena función del VI con FE media ($64,68 \pm 5,23\%$). Se detectaron defectos del tabique auricular iatrogénico (IASD) por ETT en todos los pacientes con rango de (2-5) mm con media de ($3,47 \pm 0,92$), realizado por punción transeptal (TSP), ya sea con una única vaina de 8 French en 24 (51,06 %) pacientes o simple 12 vaina francesa en 17 (36,17%) pacientes mientras que en 6 (12,77%) pacientes el defecto se realizó mediante doble vaina transeptal. El cierre espontáneo ocurre en 35 (74%) pacientes dentro de los primeros tres meses con una clara asociación significativa entre el tamaño de la CIA que se relaciona con el tamaño de la vaina y la duración del procedimiento ($P < 0,0001$). Observamos que algunos parámetros ecocardiográficos también se asociaron con IASD sin ninguna complicación clínica y / o deterioro.

Conclusiones: el número y el tamaño de la vaina después de la ablación con catéter y la duración de la ablación se consideran un factor predictivo del cierre de la comunicación interauricular residual posterior a la septostomía auricular y pueden evaluarse simplemente con parámetros de ecocardiografía transtorácica no invasiva como (tama-

ño de la comunicación interauricular y área de superficie corporal) durante el seguimiento inicial de seis meses.

Palabras clave: comunicación interauricular iatrogénica, punción transeptal, ablación por radiofrecuencia, ecocardiografía transtorácica

Introduction

Transseptal puncture (TSP) has been increasingly and commonly required over the past two decades of the left atrium (LA) catheterization, in order to perform ablation of different types of arrhythmias¹, mostly for ablation of LA tachycardia's and pulmonary vein isolation (PVI) in patients with atrial fibrillation (AF)². Furthermore, the transseptal approach has always been an alternative method to the transaortic technique for ablation of left-sided accessory pathways or occasionally for performing ablation of left ventricular tachycardia¹. TSP remains a challenging and demanding procedural step in accessing the LA and has its inherent risks and safety concerns, with its major complication being cardiac perforation and development of cardiac tamponade³.

Iatrogenic atrial septal defect (IASD) consider an important issue of TSP and subsequent use of large-bore sheaths through the septum relates to persistent or iatrogenic atrial septal defects which have been reported to be detected in the majority (87%) of patients in the immediate post-procedural period, but with significantly decreasing percentage (7%) over the ensuing 12 months⁴.

The interatrial septum develops embryologically from fusion of the septum primum and septum secundum in early gestation⁵. The fossa ovalis represents the membranous remnant of a closed foramen ovale. Where the thinned septum primum, and thicker, muscular septum secundum fuse forms the limbus, a raised margin surrounding the fossa ovalis⁵

The most important step during the TSP procedure appears to be the correct landing of the transseptal sheath/needle assembly into the fossa ovalis and the avoidance of inadvertent puncture of adjacent structures, particularly the aorta. Several landmarks may be used with fluoroscopic guidance alone utilizing different (AP/LAO/RAO) fluoroscopic views or in difficult or demanding situations guidance is best provided with echo imaging. Upon puncturing the inter-atrial septum, it is imperative to ensure that the needle has entered the left atrium (LA) before attempting to advance the dilator and then the sheath over it into the LA. Pressure recording from the LA, withdrawing arterial blood, and contrast injection (and observing its downward course toward the left ventricle), all via the needle, can provide such confirmation^{6,7}.

Both TTE and TEE can be used to detect IASD and define the shunt degree. TEE is more accurate to study IASD

morphology and size⁸. The lack of long-term follow up in patients undergoing transcatheter procedures requiring TSP limits the understanding of IASDs natural history. Current evidence supports IASD closure if patients develop symptoms (i.e. worsening heart failure, refractory hypoxemia, cryptogenic stroke or other paradoxical embolic phenomena)⁹.

Transseptal puncture (TSP) is one of the most challenging steps in catheter ablation of atrial fibrillation (AF). Single TSP reduces the risk associated with the puncture, double transseptal access simplifies the procedure in terms of immediate visualization of signals in the pulmonary vein, as well as avoidance of multiple changes of ablation and multipolar catheter through the single sheath¹⁰.

Two-dimensional (2D) transthoracic echocardiography (TTE) is a simple, non-invasive approach that has high sensitivity and specificity for detection of ASD. Echocardiography is very useful after AF ablation for detection and monitoring for early and late related complications, and also for LA reverse remodelling assessment in patients with stable sinus rhythm. It has been demonstrated that restoration and maintenance of sinus rhythm after catheter ablation is associated with a decrease in LA volumes (reverse structural LA remodelling), with subsequent improvement of LA function. Using the new tissue Doppler derived parameters, it was shown that in parallel with the improvement in LA function, both left ventricle systolic and diastolic function improved in the patients who maintained sinus rhythm¹¹.

In Current study we determine the outcomes of iatrogenic Atrial Septal Defect (IASD) in six months post radiofrequency ablation (RF) procedure of left atrial arrhythmia using non-invasive Transthoracic Echocardiography (TTE) parameters (LVEF, E/e' and ASD size), with sheath size and study duration as predictors of atrial septal defect closure.

nection. With Doppler studies by (GE Vivid E9 ultrasound) machine with 5 MHz phased array probe in subject lying in supine and left lateral decubitus position.

- The LV ejection fraction was measured by M-mode in PLAX view.
- LA antero-posterior dimension was measured by 2-D in PLAX view.
- Trans mitral Doppler flow was obtained by PW Doppler on the tip of mitral valve leaflet from apical four-chamber view and peak early filling velocity (E) wave was measured.
- Pulse tissue Doppler imaging was obtained from medial and lateral mitral annulus and early diastolic annulus velocity (E') was measured.
- The size of inter atrial septal defect was measured in subcostal view by using colour Doppler and the direction of inter atrial defect flow was also assessed.

Transseptal puncture procedural data:

The data were collected from procedure report including sheath size, sheath number and duration of procedure.

Statistical Analysis

The collected data were entered to EXCEL program (Microsoft) then analysed using SPSS for Windows software (version 23, Inc., Chicago, IL, USA 2018). Continuous data were expressed as mean and standard deviation values (Mean \pm standard deviation). Categorical data were expressed in frequencies, percentages, minimum and maximum. Comparisons between two means in groups were performed with using independent sample t-test and one way ANOVA test was used to test the significance of difference between more than two means variables.

Multivariate logistic regression analysis was used to identify the risk factors predicting the success and failure of ASD. The adjusted relationships between AS closure and studied variables were assessed with odds ratios and their 95%. Significance testing was 2-sided with the significance level set at $P < 0.05$.

A prospective study was conducted in Iraqi Centre for Heart Diseases included patients post Electrophysiology procedure and ablation of left atrial SVT were selected according to inclusion and exclusion criteria and referred to Echocardiographic unit from single Electrophysiologist, during period from May 2019 to May 2020. Written informed consent was given to all patients included in this study (Post left atrial SVT ablation procedure. Aging more than 15 years old). While our study excluded those with LV systolic dysfunction, Structural heart disease, Poor image quality and CHA₂DS₂-VASc score > 1 .

Pre and post ablation with septostomy procedure, standard Echocardiography was performed under ECG con-

After Electrophysiology study, results of this study were analysed and collected according to duration of procedure, sheath size and number that used in septostomy, size of IASD and Echocardiographic parameters. The total patients enrolled in this study were 47 patients included 23(48.9%) males (mean age 35.13 ± 8.93 years) and 24(51.1%) female (mean age 37.38 ± 11.62 years) (Table 1), those patients underwent radiofrequency ablation of left atrial SVT with single-puncture of interatrial septum. They were categorized according to type of catheter approach as in (Table 2).

Regarding the baseline echo parameters as seen in (Table 3) which reveal that an iatrogenic ASD was detected by colour Doppler in the 47 patients with a diameter range from (2–5 mm), also there was a left to right shunting through the defect.

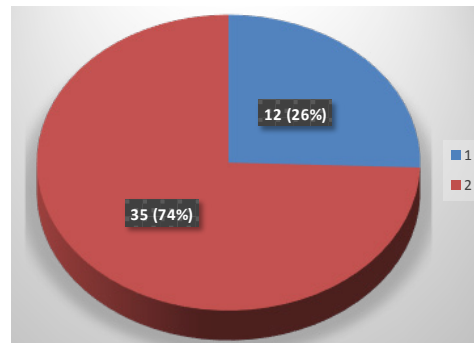
Procedural data:

The duration of procedure was significantly longer in patients who underwent pulmonary vein isolation for AF (procedure mean time was 97.0 ± 28.1 minutes), While patients who underwent left sided accessory pathway radiofrequency ablation with (procedure mean time was 3.49 ± 2.48 minutes).

Transthoracic echocardiography at baseline, 3 and 6 months follow up:

An iatrogenic ASD was found in the first day after procedure in all 47 patients, then after 3 months follow up we noticed that 35(74%) patients developed spontaneous closure of the ASD and the rest 12(26%) patients had

Figure 1: Percentage and frequency closure of ASD at 3 months follow up



At initial baseline follow up, we noticed that the size of ASD was significantly related to type of arrhythmias ($P < 0.0001$), 9(19%) of total sample had AF and 38(80.8%) of them had left sided accessory pathway, according to the type of arrhythmia the size of ASD was larger in AF patients than WPW who had accessory pathway as seen in (Table 4).

As well as, that the size of ASD related significantly to the size of catheter that used in the procedure ($P < 0.0001$), in patients who underwent RF ablation with (8f) catheter had smaller ASD size while those who had the procedure by using (12f) catheter was larger in size as seen in (Table 4)

Table 1: Baseline demographic character of studied group.

No (%)	Age (years)			BSA (m ²)			
	(Mean \pm SD)	Min	Max	(Mean \pm SD)	Min	Max	
Male	23 (48.9)	35.13 (8.93)	17	53	1.91 (0.16)	1.60	2.20
Female	24 (51.1)	37.38 (11.62)	19	57	1.80 (0.15)	1.60	2.10
Total	47 (100)	36.28 (10.34)	17	57	1.86 (0.16)	1.60	2.20

Table 2: Distribution of types of arrhythmia according to size and number of sheath

Type of Arrhythmia	Single sheath		Double sheath	Total
	8f No (%)	12f No (%)	No (%)	
WPW	24 (63.15)	14 (36.84)	0 (0.00)	38
AF	0 (0.00)	3 (33.33)	6 (66.66)	9
Total	24 (51.06)	17 (36.17)	6 (12.77)	47

*AF atrial fibrillation, WPW wolf-Parkinson-white syndrome

Table 3: Baseline Echo parameter

Echo parameters	(Mean \pm SD)	Min	Max
LVEF(%)	64.68 (5.23)	56	77
LVIDd	47.13 (5.31)	40	74
IVSd	8.81 (1.33)	7	12
PWd	8.62 (1.21)	7	12
E wave	73.23 (12.99)	45	97
A wave	59.43 (8.54)	30	74
E/A ratio	1.25 (0.36)	0.7	3
e'lateral	12.23 (2.49)	7	19
E/e' ratio	6.45 (1.80)	4	12
IASD size	3.47 (0.92)	2	5

*LVEF left ventricle ejection fraction, LVIDd left ventricle internal dimension in diastole, IVSd interventricular septum in diastole, PWd posterior wall in diastole, IASD iatrogenic atrial septal defect.

Moreover, the ASD size was highly related and significantly associated with the duration of the procedure ($p < 0.0001$), we found that patients with (2 mm) ASD size had (2.97 ± 0.78 minutes mean duration of procedure) and those with (5 mm) ASD size had (mean duration of 112.50 ± 13.89 minutes) (Table 5).

In our study we classified the patients according to number of catheter that used for ablation, when a comparison done regarding size of ASD, we found the smaller size of ASD associated with single catheter while the larger size associated with double catheter approach (Table 6).

And regarding the type of arrhythmia, we noticed that

patients with left sided accessory pathway underwent ablation by a single catheter, while patients with AF had ablation with double catheter approach (Table 6)

When comparing according to no. of sheath (single vs double) in relation to periodic echo follow up (initial, 3 and 6 months) regarding closure of ASD, we found that at initial Echo all the patients had ASD while at 3 months follow up, 35(74%) patients with spontaneous closure of ASD had single sheath approach and 6% of the patients with double sheath approach had persistent ASD, On other hand, at 6 month follow up reveal that 100% of all ASD had been spontaneously closed (Table 7).

Table 4: Association between types of arrhythmia according to size of ASD

Type of arrhythmia		ASD Size				total	P value
		2mm	3mm	4mm	5mm		
Type of arrhythmia	WPW	6 (15.78)	21(55.26)	11(28.95)	0 (0.00)	38	0.0001
	AF	0 (0.00)	0 (0.00)	1 (11.11)	8 (88.89)	9	
	TOTAL	6 (12.77)	21(44.68)	12(25.53)	8 (17.02)	47	
Size of sheath	8F	6 (25.00)	18(75.00)	0 (0.00)	0 (0.00)	24	0.0001
	12F	0 (0.00)	3 (17.65)	12(70.59)	2 (11.76)	17	
	8F & 12F	0 (0.00)	0 (0.00)	0 (0.00)	6 (100.0)	6	
	TOTAL	6 (12.77)	21(44.68)	12(25.53)	8 (17.02)	47	

AF atrial fibrillation, WPW wolf-Parkinson-white syndrome

Table 5: Association between ASD size and duration of procedure

Size of ASD	No	Duration of procedure (in minutes)			P value
		Mean \pm SD	Min	Max	
2mm	6	2.97 (0.78)	2.00	4.33	0.0001
3mm	21	3.04 (0.52)	2.00	4.00	
4mm	12	13.75 (14.71)	6.6	90.00	
5mm	8	112.50 (13.89)	90	120.00	
Total	47	33.88 (12.84)	2.00	120.00	

Table 6: Distribution of number and size of sheath according to size of ASD and type of arrhythmia

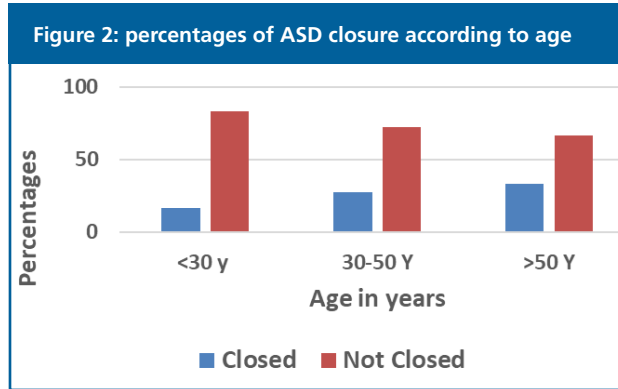
Variables	Single		Double No (%)	Total	p-value
	8f No (%)	12f No (%)			
Size of ASD					0.0001
2-3mm	24 (88.89)	3 (11.11)	0 (0.00)	27	
4-5mm	0 (00.00)	14 (70.00)	6 (30.00)	20	
Type of arrhythmia					0.0001
WPW	24 (63.15)	14 (36.84)	0 (00.00)	38	
AF	0 (00.00)	3 (33.33)	6 (66.66)	9	
Total	24 (51.06)	17 (36.17)	6 (12.77)	47	

Table 7: Distribution of studied group according to the size of sheath and size of ASD in baseline, 3, and 6 months follow-up

Follow up of ASD closure	Single sheath		Double sheath No (%)	Total	p-value
	8f No (%)	12f No (%)			
1 st follow up					NA*
Not closed	24 (51.06)	17 (36.17)	6 (12.77)	47	
Closed ASD	0 (0.00)	0 (0.00)	0 (0.00)	0	
2 nd follow up					0.0001
Not closed	0 (0.00)	6 (50.00)	6 (50.00)	12	
Closed ASD	24 (68.57)	11 (31.43)	0 (0.00)	35	
3 rd follow up					NA*
Not closed	0 (0.00)	0 (0.00)	0 (0.00)	0	
Closed ASD	24 (51.06)	17 (36.17)	6 (12.77)	47	
Total	24 (51.06)	17 (36.17)	6 (12.77)	47	

*NA= Non Applicable.

At 3 months follow up of those patients, we found that the closure of ASD was associated with increasing in their ages (P-value 0.048) (Figure 2)



In addition to that, there was no significant differences regarding the gender and BSA of patients in association with ASD closure

The logistic regression analysis of different variables as shown in (Table 7) reveal that each of the following BSA, LVEF, type of catheter, ASD size and troponin level where could be consider independent predictors for ASD closure after 3 months follow up.

Table 7: Logistic Regression Table; Predictors for delay closure of ASD after 3 month follow up

Predictors	Coefficient	Odds ratio	P value	Confidence interval	
				Lower	upper
Age	0.06	1.06	0.056	0.89	1.30
Gender	- 5.01	0.21	0.157	0.01	5.23
BSA	- 14.87	1.89	0.023	1.21	3.84
LVEF	- 2.136	1.67	0.045	1.08	5.45
Sheath size	-3.246	1.94	0.034	1.02	4.26
LAV1 1 st	0.021	0.98	0.460	0.02	7.89
ASD Size	- 15.36	2.01	0.001	1.81	4.25
Duration	14.25	1.10	0.698	0.45	8.25

Discussion

Transseptal technique for left atrial supraventricular tachycardia (SVT) ablation is an increasingly frequent procedure. The generation of an iatrogenic atrial septal defect is an unavoidable consequence and is not to be considered a complication. Little is known about the course and the potential clinical outcome after this procedure.

Our findings suggest that this technique leads to traumatic dilatation of the artificial interatrial gap, accompanied by a significant risk for iatrogenic interatrial defects for 12/47 (26%) of patients with persistent atrial septal defect at 3 month follow up, while 35/47 (74%) of patients undergoes spontaneous closure of the defect.

These findings are not agreed with Rillig A et al⁽¹⁹⁾ who have found that 96.3% of patients had spontaneously closed ASD at 3 months follow up after PVI.

While At Obel et al²⁰ detailed an IASD incidence of 6.5% in patients who having experienced pulmonary vein isolation (PVI) procedure after a longer follow-up period.

At Anselmino et al²¹ also found a rate of 5.6% of patients displayed an IASD after radiofrequency ablation at a median follow up of 12 months.

The wide range of variety concerning the occurrence of ASD that seen in these reported studies might derive from their various inclusion criteria. They were not excluding preprocedural PFO or ASD, evaluating the postprocedural ASD with transoesophageal echocardiography and different approach of the procedure was utilized either single or double puncture during radiofrequency or cryoablation.

In our study, Transthoracic Echocardiography with colour Doppler was used to assess iatrogenic ASD which is less invasive method during follow up, the mean size of the defect detected was (3.47±0.92) with left to right shunt and no significant hemodynamic consequences.

While many Studies that used transthoracic echocardiography (TTE) for the follow up of iatrogenic ASD conducted lower rates of persistent defects compared with those that used TEE22. However, the TEE examination is more invasive and may not be a feasible surveillance test for many patients.

In addition our study found that the size of ASD was larger in patients who underwent PVI of AF and the prevalence of persistent iatrogenic ASD (at maximum follow up of 6 months) strongly associated with the size of the transeptal sheath. This due to the procedure requires active manipulation of an ablation catheter (8-12 Fr) and a mapping catheter (8Fr) across the septum. This could be achieved with a single transeptal puncture with double transeptal sheath or by performing two separated transeptal punctures. Our study findings in consistent with Rillig A et al¹⁹ who have raised concern among electrophysiologists with respect to the non-negligible prevalence of persistent iatrogenic ASD following cryoablation PVI or by using double catheter single TS puncture technique. While not agreed with Nagy Z et al²³ who found that iatrogenic ASD independent of the ablation method and it is a frequent phenomenon after cryoablation procedure at the 3-month follow up.

In other hand, our study revealed that the duration of ablation was longer (19.1%) who had AF and underwent PVI with mean duration of 97±28.6 minutes and the ASD was larger in size when compared with patients who underwent ablation of left-sided atrial accessory pathway.

While Hammerstigle et al²⁴ reported almost similar findings regarding the mean procedural time during PVI is considered longer compared with other catheter-based interventions with transeptal approach, and extensive intraprocedural catheter manipulation is necessary to complete PVI. These procedural characteristics seem to advance the development of persistent ASD. Moreover Obel

et al²⁰ discussed that prolonged duration of transeptal instrumentation during PVI and the extensive catheter manipulation are risk factors for the occurrence of ASD.

In addition our finding demonstrated that the age of patients was associated with the closure of ASD which means that with increasing the age of the patients was associated with persistent ASD at 3 months follow up, which mean with long standing arrhythmia and fibrosis may lead to delay the closure of the defect.

Our study reported that the body surface area (BSA) and gender of patients did not have significant influence on the closure of ASD.

These findings are with agreement with Nagy Z et al²³ regarding the age of patients they found that the age was a significant predictor of persistent ASD at the 3-month follow up, older patients had higher prevalence of having IASD at 3 months, but not consist with our finding regarding that patients who presented with IASD at 3 m An explanation for that, when a univariate analysis of age, size, number of sheath and duration of ablation significantly associated with ASD closure while BSA was not associated due to the small sample studied group of patients were within close range of BSA.

On the other hand, by a multivariate analysis of each BSA, LVEF, type of catheter and initial baseline size of ASD were predictors of ASD persistence at 3 months follow up.

Conclusions

umber and size of sheath, duration of ablation consider as a predictor to closure of residual atrial septal defect post atrial septostomy and can simply assess with non-invasive Transthoracic Echocardiography parameters such (Atrial septal defect size and body surface area) during initial six months follow up.

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