MJMR, Vol. 35, No. 3, 2024, pages (22-28).

Open Access
ISSN: 2682-4558

Research Article

Patent Foramen Ovale in patients with Aortic Root Dilatation

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DOI: 10.21608/MJMR.2024.303597.1745

Abstract

Background: Aortic root dilatation and patent foramen ovale (PFO) are two separate medical conditions; altered geometry due to aortic root dilatation may lead to hinder the complete closure of the foramen ovale.However, the relationship between both is not well-established and requires further research. **Aim:** was to explore the relation between PFO & aortic root dilatation. **Methods:** This case-control study was carried out in the Department of Cardiology, Minia University Hospital, during the period from May 2022 to May 2024; the study including 210 participants they were classified into two groups: Group I including 120 participants who had dilated aortic root and Group II including 90 participants as a control group. All the participants were subjected to: Transthoracic echocardiography and Transesophageal echocardiography. Measurement of maximum diameter at different levels of aortic root was taken. All aortic diameters were indexed to patient's body surface area. Multiplane TEE was used to identify PFO shunt either spontaneously, under valsalva or agitated saline injection. PFO shunt degree was classified as small, moderate or large. **Results:** This study showed non statistically significant increase number of PFO 12 (10%) in group I compared to 6 (6.7 %) in group II (p=0.694). PFO was clearly visualized in 3 participants, using valsalva maneuver in 6 participants and using contrast study in 9 participants. 12 PFO shunt were small and 6 were moderate in degree. **Conclusion:** Based on the results of this study, we observed increased number and percentage of PFO in patients with aortic root dilatation. This may support the possibility of changing the anatomical conformation of inter atrial septum by aortic root dilatation.

Keywords: patent foramen ovale, aortic root dilatation.

Introduction

Aortic root dilatation and patent foramen ovale (PFO) are two separate medical conditions; altered geometry due to aortic root dilatation may lead to hinder the complete closure of the foramen ovale. However, the relationship between both is not well-established and requires further research. [1]

Methods

Population study

The current observational case-control study was conducted in the cardiology department of El-Minya University Hospital from May 2022 to May 2024.The Ethics and Research Committee of the Faculty of Medicine at Minia University approved the study protocol, it was in accordance with the declaration of Helsinki ethical principles of medical studies including Human subjects 2013. (*Approval no. 134:11/2021*).

Inclusion criteria:

The current study included 210 participants. They were classified into two groups:

1. Group I (n=120) included participants, who had dilated aortic root diameter.
2. Group II (n=90) included participants, who had normal aortic root diameter.

Exclusion criteria:

Participants with any of the following were excluded from the study: presence of chest disease associated with pulmonary hypertension as interstitial lung disease, chronic obstructive pulm-onary disease, obstructive sleep apnea, kyphoscoliosis, scleroderma, cystic fibrosis, obesity, hypoventilation syndrome and cardiac diseases associated with increase right sided pressure as severe mitral stenosis, severe tricuspid regurgitation, pulmonary stenosis, atrial septal defect, complete atrioventricular septal defect, ventricular septal defect, primary or secondary pulmonary hypertension and left ventricular systolic dysfunction.

Transthoracic echocardiography (TTE):

* Two-dimensional Transthoracic Echocardio-graphy was performed by two experienced cardiologists according to the current recommendations.
* Commercially available echocardiogram systems (*Philips healthcare, IE 33* with a 2.5–3.5 MHz transducer) were employed to image patients in the left lateral decubitus position.
* Through the use of echocardiography, pictures of the proximal aortic root were captured along the parasternal long axis. The patient's right shoulder was the target of the transducer's notch as it was positioned at the third or fourth intercostal space to capture these pictures. When taking aortic measures from individuals with a dilated aorta, it is necessary to move the transducer to a higher position, closer to the second intercostal gap.[2-3]
* Aortic root measurements were carried perpendicular to the long axis of the aorta. Defining the diameter of aortic root as the maximum distance between the two leading margins of the anterior and posterior walls of the aortic root at end diastole. [4]
*****At the aortic annulus (AAd), Sinotubular Junction (STJd), Ascending thoracic aorta (AScAd), and aortic root at Sinus of Valsalva (sVd), measurements of maximum different levels of aorta were obtained. Every aortic diameter was matched to the body surface area of the subject.[5]

Transesophageal echocardiography (TEE):

* A transesophageal echocardiogram (TEE) was conducted utilizing a high-quality ultrasound machine that is commercially accessible (Philips Healthcare, IE33).
* All patients were subjected to multiplane TEE and examined in the right lateral decubitus position.
* We positioned the transducer in order to get a mid-esophageal Aortic Valve Short-Axis View. The mid-esophageal AoV short-axis view was acquired by positioning the ultrasound probe in the mid-esophagus at average depth of 12-14 cm. The multiplane angle was set at an average of 30°, with incremental adjustments in the transducer angle to scan the specific areas of interest. Additional views were recorded at angles of 45°, 60°, and 75°. This sequence of transducer angles allowed a gradual examination of the interatrial septum (IAS) starting with the aortic valve (AoV) short-axis view and transitioning to the modified bicaval tricuspid valve view. The AoV short-axis image was acquired to display the septum. This perspective enabled visualization of the convergence of septum primum and septum secundum in the presence of a patent foramen ovale (PFO).
* The two-dimensional pictures were optimized and then color Doppler mapping was performed. The color Doppler scale was approximately decreased to about 35-40 cm/sec in order to detect the slow velocity of blood across a tiny opening (fenestration), specifically a patent foramen ovale (PFO). [6]
* We used TEE to identify the shunt**,** spontaneous or under Valsalva maneuver as small, moderate and severe.

Performing a contrast study:

We instructed the patient to cease inhalation or exhalation during the middle of their breathing cycle, close their mouth and nostrils, and exert pressure or strain ‘bear down’. The right heart has decreased in size due to a decrease in venous return. Consequently, actions such as the Valsalva maneuver result in the right atrial pressure surpassing the left atrial pressure upon release. This is essential to recognize a patent foramen ovale (PFO) that may only open during certain phases of the cardiac cycle when the anticipated pressure between the atria is reversed. As the patient received an injection of Agitated saline (about 10 to 20 ml of saline 0.9%), they were instructed to get the strain released. Observing the atrial septum bulge into the left atrium upon relaxation of the Valsalva maneuver was considered optimal. This indicated a temporary rise in right atrial pressure over left atrial pressure. If the Valsalva exercises had negative results or were not fully executed, saline injections were administered with an alternative method of provocation. A quick and forceful inhalation or cough causes the diaphragm to move upwards, resulting in an increase in the flow of blood returning to the heart, which may cause the patent foramen ovale (PFO) to open. [7]

Agitated saline solution:

Diagnosis of PFO was made both during rest and during the Valsalva maneuver. The agitated saline solution was prepared by mixing 9 mL of NaCl 0.9% and 1 mL of air in a total volume of 10 mL. This solution was then injected quickly into the antecubital vein of all patients using two syringes connected to a three-way stopcock and a tap.[8]

Diagnostic criteria of PFO with TEE:

1. On 2-dimensional imaging, there is no defect in the continuity of the atrial septum.
2. ⩾ 1 distinct microbubble becomes seen in the left atrium within three cardiac cycles after the right atrium is made opaque during contrast transesophageal echocardiography (TEE).

* The degree (size) of shunting was classified as small if less than 5 contrast bubbles emerged, moderate-sized shunt if 5-25 contrast bubbles appeared, and large size if more than 25 contrast bubbles showed in the left atrium.[9]

TEE and aortic measurements:

* A third echocardiographer, who is uninformed of the previous transthoracic echocardiography (TTE) data, conducted all measurements of the aortic root. The aortic root diameter was assessed using long axis view (120°- 150°) at the level of the sinuses of Valsalva, measuring the maximum transverse dimension.[3]
* Measurements were taken at a right angle to the main direction of the aorta using the leading-edge method.[3]
* Measurement of aortic annulus was done at the end of the heart's contraction phase (end-systole), while the diameters of the Valsalva sinuses (VS) and the proximal aorta were measured at the end of the heart's relaxation phase (end-diastole), as advised.[3]

The dilatation of the aortic root was determined by measuring the diameter of the Valsalva sinuses of the proximal aorta, taking into account the patient's age and adjusting it based on the patient's body surface area using the following equations: [10] [11]

- < 20 yrs old $SOVd = 1.02 + 0.98 \times BSA$
- 20-39 yrs old $SOV\,d = 0.97 + 1.12 \times BSA$
- > 40 yrs old $SOVd = 1.92 + 0.74 \times BSA$

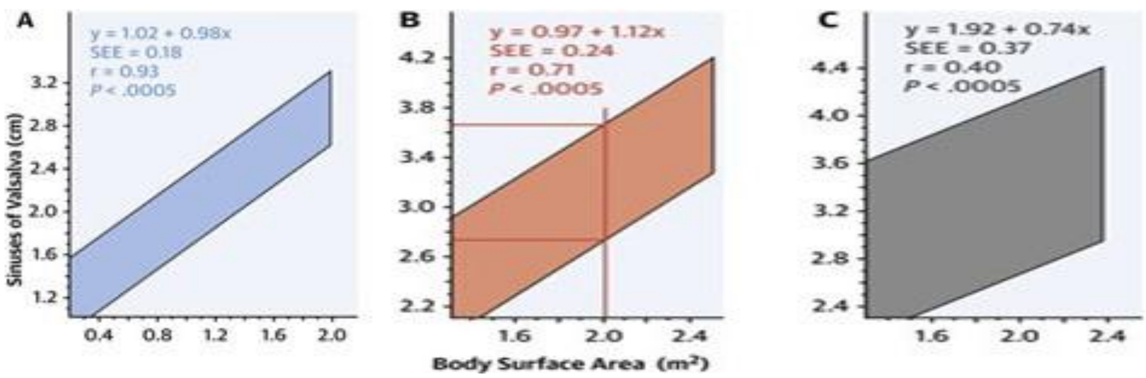

Fig. (1): Aortic root diameter(vertical axis)in relation to BSA(horozintal axis)

Statistical analysis

The IBM SPSS 28.0 statistical program software (IBM; Armonk, New York, USA) was employed to calculate the data analysis. Quantitative data were presented as Mean ± Standard Deviation (SD), while categorized data were presented as both numbers and percentages. The independent sample t-test for parametric data was used for comparison between two independent groups. The Chi-square test or Fisher's exact test were used to compare categorical variables. A p-value less than 0.05 was considered significant.

The spearman's correlation coefficient r was utilized to conduct correlation studies. The correlation coefficient is a numerical value that runs from 0 to 1. The strength of correlation is categorized as weak (r=0-0.24), fair (r=0.25-0.49), moderate (r=0.5-0.74), or strong (r=0.75-1). Regression analysis was used to detect the effect of independent risk factors (age, sex, smoking, Hypertension, endothelial dysfunction) on dependent variable aortic root dilatation.

Results

Table (1): Demographic and baseline characteristics of the study population.

	Group I (n=120)	**Group II (n=90)**	**p value**
Age (Ys), (Mean ± SD)	57±13	52±13	0.099
Males, n (%)	99 (82%)	60 (67%)	0.126
Diabetes Mellitus, n (%)	42 (35%)	18 (20%)	0.169
Hypertensive, n (%)	78 (65%)	42 (47%)	0.125
Smoking status, n (%)			
Current smoker	51 (42%)	21 (23%)	0.167
Ex-smoker	12 (10%)	6 (7%)	
Weight (kg), (Mean ± SD)	76.40±10.79	79.67±9.66	0.188
Height (cm), (Mean ± SD)	164.5±6.7	166.9±7.4	0.164
BMI, (Mean ± SD)	28.15±3.05	28.49±2.38	0.600
BSA (Mosteller), (Mean ± SD)	1.86±0.15	1.91±0.14	0.233

BMI: Body Mass Index— **BSA:** Body Surface Area

There were no statistically significant differences between both groups regarding their age, Risk factors (Smoking , Hypertension & Diabetes mellitus), Sex and body Surface area (Tab1).

Table (2): TTE and TEE characteristics of the study population.

	Group I (n=120)	**Group II (n=90)**	**p value**
TTE			
-Lt ventricular hypertrophy, n(%)	57 (47.5%)	24 (26.7%)	0.076
-Max SoV (Nomogram), (Mean ± SD)	3.27±0.17	3.21±0.23	0.243
TEE			
-PFO, n (%)	12 (10%)	6 (6.7%)	0.694
-AoR Diameter cm(TEE),(Mean ± SD)	4.12±0.65	2.87±0.47	**<0.001**

TTE: Transthoracic Echocardiography— **TEE:** Transesophageal Echocardiography— **AoR:** Aortic Root— **PFO:** Patent Foramen Ovale— **Max SoV:** Maximum Sinus of Valsalva

Interobserver variability showed 0.825 agreement between measures.

PFO was visualized using TEE in 18 participants. 12 participants were in Group I and 6 participants were in Group II. PFO was clearly visualized in 3 participants, using valsalva maneuver in 6 participants and using contrast study in 9 participants.12 PFO shunt were small and 6 were moderate in degree. Group I had more number of patients with Left ventricular hypertrophy 57 (47.5%) vs. 24 (26.7%), p=0.076. However, the difference didn't reach statistically significant value (p=0.076) (Tab 2).

Table 3: Correlation between aortic root diameter using transesophageal echocardiography (TEE) and other variables.

	AoR Diameter cm (TEE)	
	Rho	**p**
Age (y)	0.332	**0.005**
BMI	0.067	0.583
BSA Mosteller	-0.071	0.560

AoR: Aortic Root— **BMI:** Body Mass Index— **BSA:** Body Surface Area

Table 3 shows significant positive fair correlation is shown between age and aortic root diameter (rho= 0.332, p=0.005).

Table 4: Binary logistic regression analysis for predicting presence of aortic root dilatation.

Variable	**Univariate analysis**	
	cOR (95% CI)	**p value**
Age (y)	1.03 (0.99-1.07)	0.101
Male	2.36 (0.77-7.18)	0.131
Smoking status		
Current smoker	2.68 (0.91-7.88)	0.072
Ex-smoker	2.21 (0.36-13.47)	0.390
BMI	0.96 (0.80-1.14)	0.607
BSA Mosteller	0.14 (0.01-3.45)	0.228
Hypertension	2.12 (0.81-5.59)	0.127
Diabetes Mellitus	2.15 (0.71-6.51)	0.174
PFO	1.56 (0.27-9.11)	0.624

N.B. Dependent variable aortic root dilatation, CI confidence interval, NE not estimated R2= 0.411
BMI: Body Mass Index— **BSA:** Body Surface Area— **PFO:** Patent Foramen Ovale

Univariate binary logistic regression analysis was performed to detect variables predicting the presence of aortic root dilatation. ***Table 4*** summarizes the results of regression analyses. Variables did not show significant correlations with aortic root dilatation in univariate analysis

Discussion

Our results revealed non statistically significant increased number of PFO 12(10%) in aortic root dilatation group compared to 6(6.7%) in normal aortic root dimension group and this may raise the possibility of changing the anatomical conformation of IAS by aortic root dilatation. Yet, we don't reach a statistically significant value that may raise the need for large scale study.

Beyls et al., 2020, examined the dilatation of the aortic root in 315 consecutive individuals who had a stroke of unknown cause. The researchers discovered that the presence of PFO was more often seen in the group with aortic root dilation compared to the group with normal aortic root dimensions (47/68 (69%) vs. 120/247 (49%), p=0.004). The study showed that individuals with PFO had larger aorta dimensions compared to those without PFO, particularly in terms of the diameter of the Valsalva sinuses. Furthermore, the analysis using multivariate logistic regression revealed that aortic root dilatation was significantly and independently linked to the presence of PFO. [12]

In a study conducted by Keenan et al., in 2012, it was found that patients with PFO-related cryptogenic strokes had a significantly larger aortic diameter at the sinuses of Valsalva level (34 ± 4 mm) compared to healthy controls (31 ± 3 mm) (P < 0.01). The size difference between the two groups was approximately 10%. The study included forty-seven patients who presented with cryptogenic cerebrovascular accidents (CVA) that were most likely caused by PFO (confirmed by contrast study), and they were compared to forty-seven healthy controls. [1]

The difference in findings in our research may be ascribed to the choice of individuals who were diagnosed with cryptogenic cerebrovascular accident (CVA) and were considered most likely to have a patent foramen ovale (PFO) based on prior retrospective studies.

The first meta-analysis conducted by Farooq et al., in 2024 included 510 publications from Pub-Med that focused on patients with platypnea-orthodeoxia syndrome. The researchers examined a total of 191 case reports. Out of these, 93 cases did not show any aortic root disease or had no mention of it. The remaining 98 cases, accounting for 51.3% of the total, had a high occurrence of concurrent aortic root disorders. Out of the total number of patients, 82 (83.7%) were diagnosed with aortic root aneurysm, which constituted the largest proportion. Among the remaining patients, nine (9.2%) had aortic root elongation and seven (7.1%) had a twisted aorta. An important component of this research is the previously indicated lack of accurate reporting of aortic root size in many of the evaluated studies. It is very probable that many of the studies that did not disclose the aortic root size had significant underlying aortic root diseases. [13]

In our research, we observed positive fair correlation (rho=-0.332, p=0.005) between age and aortic root diameter. In order to identify variables that predict the presence of aortic root dilatation, the research employed both univariate and multivariate binary logistic regression analysis. There were no significant associations found between variables and aortic root dilatation in both univariate and multivariate analyses.

Conclusions

Based on the results of this study, we observed increased number and percentage of PFO in patients with aortic root dilatation. This may support the possibility of changing the anatomical conformation of inter atrial septum by aortic root dilatation.

Study limitations:

The main limitation of our study was a relatively small sample size, so our results need to be confirmed by a larger scale study. Using two dimensional transthoracic echocardiography limit identification of tortious or elongating aorta.

Funding:

This work was funded& sponsored by authors.

Conflict of interest:

None of the authors has any conflict of interest to report.

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