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Age and Defect Size as Predictors of Pulmonary Hypertension in Secundum Atrial Septal Defect: A Retrospective Study from the Himalayan Region

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Abstract

Background and aims: Atrial septal defect is a common congenital heart disease. Most patients are asymptomatic. The incidence and progression of pulmonary hypertension in these defects have important clinical implications. We sought to establish the role of age and defect size as predictors of pulmonary hypertension.

Methods: Hospital discharge summaries of patients who underwent surgical defect closure by a single unit of Shahid Gangalal National Heart Center between 2018 and 2023 were retrospectively reviewed. Baseline variables and echocardiography data were analyzed using SPSS. Pulmonary artery systolic pressure of > 50 mmHg in echocardiography was used to define pulmonary hypertension. A p-value of <.05 was considered significant.

Results: A total of 407 patients underwent atrial septal defect closure during that period, with a mean age being 22.1±12.5 (3-55) years and one-third (32.2%) being males. The majority (84.6%) were in NYHA I or II functional class. Mean pulmonary artery systolic pressure was 47.0±11.8 (24-113)mmHg. Mean indexed defect size was 2.2±0.8 (1.1-6.0) cm/m2. Age had a positive correlation of 0.38 with pulmonary artery systolic pressure (p <.001). Interestingly, indexed defect size had a negative correlation of .15 with pulmonary artery systolic pressure (p=.002). Multiple regression showed only age as the significant factor predicting pulmonary hypertension with a standardized beta of .357 (p<.001). Receiver operating characteristic curve analysis showed an area under the curve of. 733, p<.001 for age and pulmonary artery systolic pressure.

Conclusions: Patients' age and not the indexed size of the defect dictate the development of pulmonary artery hypertension in patients with secundum atrial septal defects.

Keywords: age, atrial septal defect, pulmonary artery hypertension

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Introduction

Atrial septal defect (ASD) is a common congenital heart disease accounting for 6–10% of all congenital heart diseases, and it has a prevalence of 2 to 3.89 per 1000 children.[1] Pulmonary arterial hypertension (PAH) is seen in 6% to 35% of patients with ASD secundum.[2-7] Pulmonary hypertension in ASD is due to the left-to-right shunt through the defect which results in right ventricular volume overload and pulmonary overcirculation.[8] Long standing pulmonary hypertension in a case of ASD might result into Eisenmenger's syndrome and no longer be operable. Moreover, we are not sure about the rate of progression of pulmonary hypertension; and there is clinical uncertainty regarding the relative influence of age versus defect size on the development of PAH. Our study aims to determine whether patient age or indexed atrial septal defect size is the primary predictor of pulmonary arterial hypertension in patients with secundum-type atrial septal defects.

Methods

We designed a retrospective cohort study analyzing hospital discharge summaries of patients who had undergone surgical ASD closure for secundum type ASD by a single team of Department of Cardiac Surgery at Shahid Gangalal National Heart Center between 2018 and 2023. There are two teams in the department, both would be operating on similar types of cases. Because of the ease of data availability, we included the cases from only one team. Patients with primum type of defect, sinus venosus type of defect, and patients with associated other cardiac anomalies were excluded. All patients who underwent secundum type ASD closure were included. None of the patients had to be excluded due to missing data. Baseline variables (age, sex, body surface area (BSA), New York Heart Association (NYHA) functional class) and echocardiographic variables (type of the defect, size of the defect as ASD diameter, and pulmonary artery systolic pressure (PASP)) were recorded. PASP of >50mmHg was defined as significant pulmonary hypertension. Primary outcome was the presence of pulmonary hypertension (PASP>50mmHg). Echocardiography was done for all patients by cardiologists preoperatively and PASP was calculated by calculating tricuspid regurgitation velocity in all patients.

All data were stored anonymously. Due to the retrospective nature of the study, consent for participation was not taken. Ethical approval was obtained from the Institutional Review Committee of our center (Ref no: SGNHC/IRC: 13-2024). Data were analyzed using SPSS version 29. Data were expressed as mean±SD (range), percentage; wherever appropriate. Pearson's correlation, multiple regressions, ROC curve analysis, and chi-square test were the statistical tests we applied during data analysis. Multiple regressions were done by putting PASP as dependent variable, and age and indexed defect size as independent variables. ROC curve was constructed by putting PASP >50mmHg as state variable and patient age as test variable. A p value of <.05 was considered as significant.

Results

A total of 407 patients underwent ASD closure for ASD secundum between 2018 and 2023. We operated on a small baby as small as 3 years old to an adult as old as 55 years old. Most of the patients were in NYHA I or II functional class. The mean absolute size of the defect was 2.5±0.6 (1.0-4.5)cm, and indexed size of the defect was 2.2±0.8 (1.1-6.0)cm/m2. Pulmonary artery systolic pressure was 47.0±11.8 (24-113)mmHg. Significant pulmonary hypertension (PASP >50mmHg) was present in 33.2 % (n=135). The results have been summarized in table 1.

We further looked on the same variables comparing patients with and without significant pulmonary hypertension. Patients with significant pulmonary hypertension tended to be older, increasingly females; and had larger BSA, larger absolute ASD diameter, and smaller indexed ASD diameter. However, both the groups had similar NYHA functional status. (Table 1).

Table 1: Baseline characteristics of patients.

Variables	Overall patients (n=407)	Patients with PASP >50mmHg (n=135)	Patients with PASP <50mmHg (n=272)	P value
Age (mean±SD, range), years	22.1±12.5 (3-55)	28.6±11.4	18.8±11.7	.000
Sex (male), n(%)	131 (32.7)	32 (23.4)	99 (36.4)	0.01
Body surface area (BSA), m2	1.22±0.32 (0.35-1.82)	1.38±0.19	1.15±0.35	.000
NYHA status n(%) I II III IV	 104 (25.6) 240 (59) 56 (13.8) 7 (1.7)	 40 (29.6) 71 (52.6) 21 (15.6) 3 (2.2)	 64 (23.5) 169 (62.1) 35 (12.9) 4 (1.5)	0.324
PASP (mean±SD, range), mmHg	47.0±11.8 (24-113)	59.9±11.1	40.6±5.0	.000
ASD diameter (mean±SD, range),cm	2.5±0.6 (1.0-4.5)	2.7±0.7	2.4±0.6	.000
Indexed ASD diameter(mean±SD, range), cm/m2	2.2±0.8 (1.1-6.0)	2.0±0.6	2.3±0.9	.000

Age had a positive correlation of 0.38 with PASP (p <.001), indicating that older age is associated with higher PASP (Figure 1). Indexed ASD size had a negative correlation of 0.15 with PASP (p=.002) (Figure 2). Multiple regression analysis showed only age as the factor which predicts PASP with standardized beta of .357 (p<.001). Indexed ASD size did not predict PASP and had standardized beta of -.016 (p=.799).

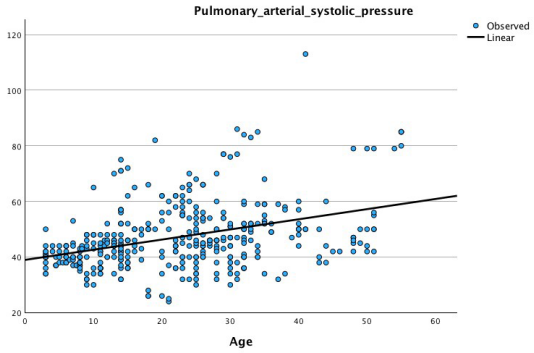

Figure 1. *Correlation between age of the patients and PASP. This has a positive correlation of 0.38 (p<.001).*

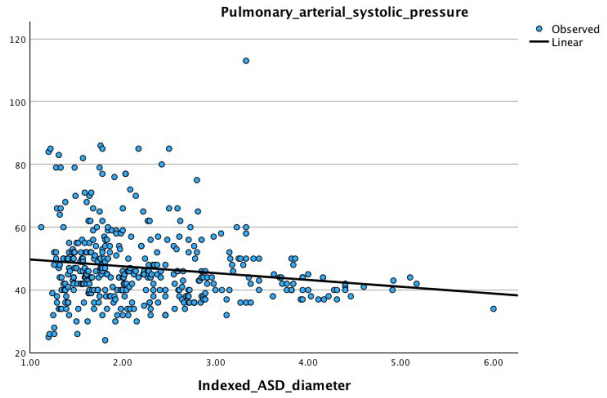

Figure 2. *Correlation between indexed ASD diameter and PASP. This has a negative correlation of 0.15 (p=.002).*

As we had defined PASP of >50mmHg as significant pulmonary artery hypertension, we further looked into the age and PASP by calculating ROC curve. ROC curve analysis showed area under the curve (AUC) of .733, p<.001 (Figure 3). Age cut off of 5.7 years revealed sensitivity of 99.3% with specificity of 9.02% predicting significant pulmonary artery hypertension. At the age of 13.5 years, it has sensitivity of 96.3% with specificity of 41.9%., and at the age of 15.5 years, it has sensitivity of 86.7% with specificity of 52.6%.

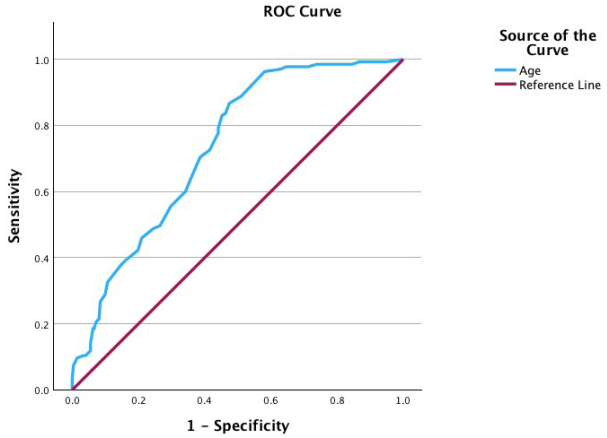

Figure 3. *ROC curve showing depicting the age and PASP. Area under the curve (AUC) was .733, p<.001.*

Discussion

Atrial septal defect closure is one of the most common surgical procedures in cardiac surgery, although a significant number of these patients undergo catheter based closure recently. When to operate after the initial diagnosis is a big concern for us. So, we aimed to find out if the age of the patients or the size of the defect predicts the development of pulmonary hypertension.

We showed that age is the only factor that predicts pulmonary hypertension; it had a positive correlation of 0.38. Indexed ASD size showed a weak negative correlation.

Our hypothesis was that the size of ASD has a role in predicting pulmonary artery hypertension. Because the size of the defect is an absolute number, we decided to index it by dividing by BSA for the purpose of analysis. Indexed ASD size did not predict the development of pulmonary artery hypertension, and to our surprise, it had a small degree of negative correlation with PASP. We are not exactly sure about this finding, however, one possible explanation would be that some of our cases we operated on were as small as 3 years old, and they had a large defect of 2cm, which resulted in a maximal indexed ASD size of 6cm/m2. However, those small kids had their PASP in the range of 40s. Also, we did not consider the geographical location of our patients. Because Nepal is a country where people live in plains, mountains, and the Himalayas, high altitude might have something to do with the development of pulmonary hypertension.

Similar to our findings, other authors have shown that the risk of PAH with ASD increases with age; however, the size of the defect has a loose association with the development of the PAH.[3,9] In adult patients, Vogel and colleagues[3] showed that patients with sinus venosus defect had pulmonary artery hypertension developed at an early age as opposed to patients with ASD secundum. Because our patients were only of secundum type and we included patients of all ages, we cannot compare our data with theirs as it is.

We used echocardiographic parameters to define pulmonary artery hypertension by measuring tricuspid regurgitation velocity, which gave us a clue about PASP. This method is non-invasive and easily reproducible, although some argue that cardiac catheterization is required to quantify PASP.[10]

Using age as a cutoff point to predict pulmonary artery hypertension, we showed that it has a sensitivity of 99.3% at the age of 5.7 years with a very low level of specificity; At the age of 13.5 years, it has a sensitivity of 96.3% with a specificity of 41.9%. To further increase the specificity of the test, age needs to be further increased to 15.5 years, at which point, it has a specificity of 52.6% but at the expense of sensitivity (86.7%). Because a good screening test should have very high sensitivity irrespective of specificity, an age cut-off of 5.7 years could be utilized to predict pulmonary hypertension. We believe that after the diagnosis, when a child is more than 5.7 years old, we could plan surgery to prevent further progression of pulmonary artery hypertension. Furthermore, if someone is diagnosed at an older age than this, at the age of 15 years, almost 86% of patients have already developed significant PAH, so intervention before this age is probably beneficial.

Limitations

Being a retrospective study, it has several limitations inherent to its design. However, this is a study from a Himalayan country, and due to its unique geographical location, this might be an interesting paper to begin with. Our focus was only on the age and size of the defect, so we did not analyze other variables further to see if they had a role to play. We defined pulmonary artery hypertension as systolic PA pressure of > 50 mmHg, which is an arguable value because some other authors would define pulmonary artery hypertension using the mean pulmonary artery pressure value. Also, the size of the defect was measured by different referring cardiologists, and their techniques of measuring the size of the defects might be different. We included patients with secundum-type defects only, so the results cannot be generalized for patients with sinus venosus and other types of atrial septal defects. However, our important message is that age is the factor that predicts pulmonary artery hypertension, and the size of the defect does not predict pulmonary artery hypertension, contrary to the perceived belief. Because we encounter a large number of patients with ASD in our cardiology OPD, carefully designed randomized studies could further be done to support/refute our findings in future studies.

Conclusion

Age of the patients predicts the development of significant pulmonary artery hypertension in patients with secundum-type atrial septal defects; however, indexed ASD size has a weak negative correlation with pulmonary artery hypertension.

References

1. Silvestry FE, Cohen MS, Armsby LB, Burkule NJ, Fleishman CE, Hijazi ZM, et al., 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. Journal of the American Society of Echocardiography 2015;28(8):910-958. DOI: https://doi.org/10.1016/j.echo.2015.05.015.
2. Engelfriet PM, Duffels MGJ, Möller T, Eric Boersma E, Tijssen JGP, Thaulow E, et al., Pulmonary arterial hypertension in adults born with a heart septal defect: the Euro Heart Survey on adult congenital heart disease. Heart 2007;93:682-687. DOI: https://doi.org/10.1136/hrt.2006.098848
3. Vogel M, Berger F, Kramer A, Alexi-Meshkishvili V, Lange PE. Incidence of secondary pulmonary hypertension in adults with atrial septal or sinus venosus defects. Heart 1999;82:30-3. DOI: https://doi.org/10.1136/hrt.82.1.30
4. de Lezo JS, Medina A, Romero M, Pan M, Segura J, Caballero E, et al. Effectiveness of percutaneous device occlusion for atrial septal defect in adult patients with pulmonary hypertension. Am Heart J 2002;144:877-80. DOI: https://doi.org/10.1067/mhj.2002.126121
5. Yong G, Khairy P, De Guise P, Dore A, Marcotte F, Mercier L-A, et al. Pulmonary arterial hypertension in patients with transcatheter closure of secundum atrial septal defects: a longitudinal study. Circ Cardiovasc Interv 2009;2:455-62. DOI: https://doi.org/10.1161/CIRCINTERVENTIONS.108.826560
6. Steele PM, Fuster V, Cohen M, Ritter DG, McGoon DC, et al. Isolated atrial septal defect with pulmonary vascular obstructive disease-long-term follow-up and prediction of outcome after surgical correction. Circulation 1987;76:1037-42. DOI: https://doi.org/10.1161/01.CIR.76.5.1037.
7. van der Linde D, Konings EEM, Slager MA, Witsenburg M, Helbing WA, Takkenberg JJM, et al. Birth prevalence of congenital heart disease worldwide: a systematic review and metaanalysis. J Am Coll Cardiol. 2011;58(21):2241–47. DOI: https://doi.org/10.1016/j.jacc.2011.08.025.
8. Moons P, Bovijn L, Budts W, Belmans A, Gewillig M. Temporal trends in survival to adulthood among patients born with congenital heart disease from 1970 to 1992 in Belgium. Circulation. 2010;122(22):2264-72. DOI: https://doi.org/10.1161/CIRCULATIONAHA.110.946343.
9. Therrien J, Rambihar S, Newman B, Siminovitch K, Langleben D, Webb G, et al. Eisenmenger syndrome and atrial septal defect: nature or nurture? Can J Cardiol 2006;22:1133–1136. DOI: https://doi.org/10.1016/S0828-282X(06)70950-3.
10. Post MC. Association between pulmonary hypertension and an atrial septal defect. Netherlands Heart Journal 2013;21:331-32. DOI: 10.1007/s12471-013-0432-9.