

# Who Falls Through the Gap? Revisiting the Pulmonary Hypertension Nomenclature in Atrial Septal Defect Closure

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## ABSTRACT

**Background:** The incidence of atrial septal defect is 1.6 per 1,000 live births accounting for 8-10% of all congenital heart defects. For the majority of patients the clinical course is often benign. However, pulmonary arterial hypertension is known to complicate 9 to 35% of patients with a secundum type atrial septal defect. The purpose of the study is to apply the new definition of pulmonary hypertension to our cohort of atrial septal defect interventional closures. **Objectives:** We aim to see whether children with atrial septal defect who have a mean pulmonary artery pressure of <20 mmHg have differences in body habitus and outcomes compared with the children with mean pulmonary artery pressure of 21-25mmHg and children with mean pulmonary arterial pressure of >25 mmHg. **Methods:** The data collection took place from January to March 2022. A retrospective search was carried out at the archives of the hemodynamic laboratory of a large pediatric hospital in Athens, Greece, carrying out a large number of catheterizations for congenital heart disease. **Results:** In total, we retrieved 78 children, 30 boys and 48 girls with a diagnosis of atrial septal defect. In 17 cases the mean PAP was not documented so the remaining 61 children were stratified according to their mean PAP as mean PAP <20 mmHg, mean PAP >20mmHg but less than 25 mmHg and more than 25 mmHg. **Conclusions:** There was no difference in height, weight, BMI, BMI centile, sex age, hospital stay between the groups of no pulmonary hypertension, pulmonary hypertension and pulmonary pressures between 20-25 mmHg.

**Keywords:** atrial septal defect closure, pulmonary hypertension, congenital heart disease

## INTRODUCTION

The incidence of atrial septal defects is around 1.6/1,000 live births, accounting for 8-10% of all congenital septal defects [1]. The clinical consequence of these defects is related to the anatomic location, size, and associated cardiac anomalies. For the majority of patients, the clinical course is often benign [2]. However, pulmonary arterial hypertension is known to

complicate 9 to 35% of patients with a secundum type atrial septal defect [3]. Closure of the atrial septal defect decreased both pulmonary hypertension and mean pulmonary artery pressure in adults [4]. Traditionally, pulmonary hypertension has been defined as mean pulmonary artery pressure of at least 25 mmHg. During the 6th World Symposium on Pulmonary Hypertension, the task force members suggested that this definition be changed to mean pulmonary artery pressure of more than 20mmHg [5].

The management of atrial septal defect is indicated for right-sided chamber enlargement and is usually carried out by transcatheter device implantation and less commonly by surgical repair [6]. The purpose of this study is to apply the new definition of pulmonary hypertension as mean pulmonary arterial pressure of 20 mmHg to our cohort of atrial septal defect interventional closures. We aim to compare whether patients who fall into the category of 20-25 mmHg of pulmonary arterial pressure have different characteristics such as age, sex and body habitus, or face more complications than the ones who have lower than 20mmHg or higher than 25 mmHg pulmonary arterial pressures.

## MATERIALS AND METHODS

This is a retrospective search in the archives of a large pediatric hospital. The data collection took place from January to March 2022. From 2011-2019, 752 catheterizations for congenital heart disease were performed in children from 1 day old to 19 years old. Height and weight were recorded to the first

decimal place. Children under 2 years old were excluded as the centers for diseases control definition does not calculate the body mass index in less than 2 years old. Body mass index was calculated from the somatometric data from the formula height/squared body weight. Subsequently, the body mass index centile was calculated according to the appropriate criteria for age and sex. "Underweight" were defined as children whose Body mass index was below the 5th centile for age and sex, "healthy weight" when the percentile was from the 5th until the 85th centile, "overweight" when the centile was above the 85th but less than the 95th centile and "obese" when the body mass index was above the 95th centile. In 7 children the height was not recorded and was removed. Also, 12 children suffered from a chromosomal syndrome such as Down's and Williams' syndrome and were excluded as well, leaving 378 catheterizations. Of the 378 catheterizations, the atrial septal defect cases were a total of 78. The children were further divided into 3 categories: preschool children 2-5 years old, school children 6-12 years old and adolescents 13-19 years old. The study was approved by the Ethics Committee of the Hospital (protocol number 13293/18/06/2020).

## RESULTS

There were 78 cases of atrial septal defect, 30 boys and 48 girls. In 17 cases the mean PAP was not documented. Accordingly, the remaining 61 children with documented mean PAP were further divided into three categories according to the mean PAP (Table 1).

	mPAP<20 mmHG	mPAP<20 mmHG%	mPAP 21-25 mmHG	mPAP 21-25 mmHG%	mPAP>25 mmHG	mPAP>25 mmHG%
<b>Males</b>	10	37.04	7	33.33	6	46.5
<b>Females</b>	17	62.96	20	66.67	7	53.85
<b>Age</b>	10.07		9.15		10.54	
<b>SD</b>	3.34		3.27		3.36	
<b>BMI CENTILE</b>	55.93		51.67		59.31	
<b>SD</b>	31.66		37.31		35.49	
<b>Underweight</b>	2	3.7	4	14.81	1	7.69
<b>Healthy weight</b>	19	70.35	14	52.85	8	61.54
<b>Overweight</b>	4	14.81	4	14.81	2	15.38
<b>With obesity</b>	3	11.1	5	16.66	2	15.38
<b>n</b>	27		27		13	

### Mean PAP less than 20 mmHg

There were 21 children whose mean pulmonary artery pressure was less than 20mmHg. Nine of them were boys (42.86%) and 12 (57.14%) were girls. Their mean age was 9.9 years (SD 3.24 years). One child was a preschooler (4.75%), 15 were school age children (71.43%) and 5 were adolescents (23.81%). The mean body mass index centile was 54.19 (SD 33.19). There were 17 successful interventional catheterizations and 4 were deferred. One child was underweight (4.76%), 15 had normal weight (71.43%) while 3 were overweight (14.29%) and 2 were obese (9.52%). The mean admission was 3.01 days long (SD 2.99 days) and there were two instances of bleeding complications.

### Mean PAP more than 20 mmHg but less than 25mmHg

There were 23 children in the group, 6 male and 17 female. Their mean age was 9.17 years of age (SD 3.05). Two of the children were of preschool age (8.7%), 19 were of school age (82.61%) and two were adolescents (8.7%). Their mean body mass index centile was 55.04 (SD 36.26). In 18 instances the catheterizations were successful and in 5 instances, the defect could not be closed interventionally. There were 3 underweight children (13.04%), 12 of healthy weight (52.17%), 4 were overweight (17.39%) and 4 were obese (17.39%). There was 1 complication. The days of admission were 3.3 days (SD 3.14 days).

### Mean PAP more than 25 mmHg

There were 17 children, 9 males and 8 females. Their age was 10.2 years (SD 3.6). Two of the children were preschoolers (11.76%), 12 were of school age (76.55%) and 3 were adolescents (17.65%). Two of the children were underweight (11.76%), 10 had a healthy weight (58.82%), 2 were overweight (11.76%) and 3 were with obesity (17.65%). Their mean days of admission were 4.29 days (SD 5.32).

The Kruskal-Wallis H test showed that there was no statistically significant difference in age in years  $\chi^2(2)=1.01$ , Body Mass Index  $\chi^2(2)=0.14$ ,  $p=0.933$ , BMI centile  $\chi^2(2)=0.06$ ,  $p=0.97$ . More, there was no statistically significant difference between age type (preschool, school, adolescents),  $\chi^2(2)=1.73$ ,  $p=0.422$ , body type  $\chi^2(2)=0.01$ ,  $p=0.952$ , or days of admission  $\chi^2(2)=0.15$ ,  $p=0.93$ .

## DISCUSSION AND CONCLUSION

The prevalence of pulmonary arterial hypertension in atria septal defects ranges from 24-62% in adults [1-4]. In pediatrics, Risk factors such as very premature birth, very low birth weight, congenital, and chromosomal abnormalities, neonatal pulmonary disease and need for ventilation support, as well as pulmonary hypertension, were associated with very early atrial septal defect closure [4]. Our results did not show any significant difference in age, BMI centile, body habitus, complication rate or length of stay between the various groups of no pulmonary hypertension, pulmonary hypertension and mean PAP between 20-25 mmHg.

In adult studies, obesity is a well-known risk factor for the development of pulmonary hypertension. Systemic and local inflammation, insulin resistance and oxidative stress have been implicated in the pathogenesis of pulmonary hypertension [7-9]. Childhood and adolescent obesity has negative impact on the structure and function of the heart. More, obesity compromised pulmonary function and contributed to sleep apnea [10]. A larger cohort study is needed to elucidate the true prevalence of pulmonary hypertension in the presence of an atrial septal defect as well as the optimal management.

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### CONFLICT OF INTEREST

There is no conflict of interest.

### ETHICAL APPROVAL

The article was approved by the Hospital Ethics Committee. The manuscript has been read and approved by all the authors, that the requirements for authorship as stated earlier in this document have been met, and that each author believes that the manuscript represents honest work, if that information is not provided in another form.

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