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# "Can the Size of the Atrial Septal Defect in the Newborn Predict Spontaneous Closure?"

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**Abstract**

**Background:** Atrial septal defect (ASD) is a common congenital anomaly that may close spontaneously in neonates. Predicting spontaneous closure can guide early clinical decisions. This study aims to identify echocardiographic predictors of spontaneous ASD closure.

**Methods:** A retrospective analysis of echocardiographic data from 302 neonates diagnosed with ASD or patent foramen ovale (PFO) during the neonatal period was conducted. ASD diameter and septum-to-ASD ratio were measured at the first echocardiogram. Patients were followed up with a second echocardiogram after more than three months to assess for spontaneous closure.

**Results:** Of the 302 patients, 72 (33%) exhibited spontaneous closure. There was no significant difference in the mean age at the first exam between patients with and without spontaneous closure. However, smaller ASD diameter and higher septum-to-ASD ratio at initial presentation were statistically significant associated with spontaneous closure.

**Conclusions:** Echocardiographic parameters, specifically ASD diameter and septum-to-ASD ratio, are valuable predictors of spontaneous closure in neonatal ASDs. These findings can assist in the early identification of neonates likely to benefit from cardiologic follow-up, enhancing management in pediatric cardiology.

**Keywords:** Neonatal Echocardiography; Atrial Septal Defect; Pediatric Echocardiography; Neonatal Cardiology.

**Abbreviations:** ASD: Atrial septal defect; CI: Confidence interval; DA: Ductus arteriosus; IAS: Interatrial septum; LA: Left atrium; N-SC: Non-Spontaneous ASD Closure; PFO= Patent foramen ovale; PVR: Pulmonary vascular resistance; RA: Right atrium; RV: Right ventricle; SC: Spontaneous ASD Closure; TTE: Transthoracic Echocardiogram.

## Introduction

The transthoracic echocardiogram (TTE) is a widely used imaging diagnostic tool in the clinical management of cardiovascular conditions in the neonatal population, playing a crucial role in clinical decision-making by providing valuable information regarding congenital or acquired conditions. Among the various parameters evaluated through TTE, the analysis of the ASD stands out, as it plays a vital role in fetal circulation by connecting the right atrium (RA) and the left atrium (LA) and allowing shunting from the RA to the rest of the body.

During the fetal period, circulation operates under a different regime than postnatally, wherein the ASD and the ductus arteriosus (DA) work to divert a large portion of pulmonary flow to the rest of the body (systemic output), playing a fundamental role in maintaining cardiac output. After birth, there is a progressive decrease in pulmonary vascular resistance (PVR), and all the flow passing through the lungs also goes through the systemic circulation, which should function without the need for shunts.

While the DA is expected to close spontaneously within the first few hours of life, the ASD generally closes within the first two years. However, in a significant portion of the population (approximately 25 to 30%), the ASD may not close spontaneously, potentially leading to varied clinical repercussions. These clinical repercussions are attributed to the shunting of systemic flow to the pulmonary circulation due to the presence of the communication and the physiological low PVR, resulting in pulmonary over circulation. The magnitude of these repercussions is closely related to factors such as the size of the defect, the patient's hemodynamic status, PVR, and the compliance of the right ventricle (RV). In certain cases, the persistence of a significant ASD may require therapeutic interventions, either surgical or percutaneous. It is important to note that, although small communications may close spontaneously, studies have shown that even larger ASDs, with diameters of up to 8 mm, have a chance of spontaneous closure [1–4].

In this context, the precise evaluation of ASD using TTE is invaluable not only for providing critical information for clinical decision-making but also for guiding the selection of the most appropriate treatment for each patient. A thorough understanding of these aspects is essential for enhancing clinical outcomes in new-borns with interatrial communication.

## Objective

The aim of this study is to determine if the size of the ASD in the neonatal period can predict spontaneous closure.

## Methods

Between January 2015 and July 2021, the echocardiograms of 1873 neonates born at the Albert Einstein Hospital, initially diagnosed with ASD or PFO were retrospectively reviewed. Included in the study were 302 patients who had ASD or PFO as their initial diagnosis and who underwent a second TTE in our service more than 3 months after the first examination, with the aim of evaluating spontaneous closure. Collected demographic data included age at the time of examination and birth weight. Patients with complex congenital heart diseases or other comorbidities with cardiovascular impact were excluded from the study.

TEE were conducted by a team of echo cardiographers with more than three years of experience, utilizing Philips CX 50, Philips Affinity 70, and EPIC CVx systems (Philips Medical Systems), equipped with S12 8-MHz or S8 4-MHz transducers. All examinations adhered to standard echocardiographic protocols. The interatrial septum (IAS) analysis was performed from the subcostal position, with measurements of the IAS diameter and ASDs captured at the end of diastole (Figure 1). The septum-to-ASD ratio was calculated in each case. These measurements, as well as the atrial septal diameters for ASDs, were remotely assessed by a single, experienced examiner who was blinded to clinical data. In cases of multiple defects, the diameters were aggregated to compute the septum-to-ASD ratio.

Comparisons between continuous variables were conducted using the Mann-Whitney U test. Neonates were categorized into two groups: those with spontaneous ASD closure (SC) and those without (N-SC), based on the outcomes of the follow-up echocardiogram. Standard tests were employed to ascertain the sensitivity and specificity of predictive factors for spontaneous closure, observed three months post-initial TTE. A linear regression model was applied to analyse the ASD diameter and septum-to-ASD ratio, aiming to delineate differences between the groups with a 95% confidence interval (CI). Results were reported as mean ± standard deviation (SD) or percentages, with statistical significance set at $p \leq 0.05$.

## Results

A total of 1,873 medical records were evaluated. Among these, 302 patients were diagnosed with either ASD or PFO during their initial neonatal TTE and underwent a follow-up examination more than three months later, qualifying them for inclusion in this study.

Of these, 215 were diagnosed with ASD, with 72 (33%) demonstrating spontaneous closure. No statistically significant difference was observed in the mean age at the time of the first examination between the groups; the SC group had an average of 6.25 ± 16.17 days of life (DOL), compared to 4.81 ± 8.74 DOL in the N-EC group (p=0.519). However, a statistically significant difference was noted in the age (days) at the time of the second TTE between the FeE and NFeE groups (466.81 ± 365 vs. 273.91 ± 359; $p < 0.001$).

The measurement of the ASD (mm) showed no statistical difference between the SC group and N-SC group (17.8 ± 4.94 vs. 17.56 ± 4.28; p=0.666). Echocardiographic parameters that demonstrated statistically significant differences in predicting spontaneous closure were the ASD diameter (mm) at the first TTE (2.89 ± 1.03 vs. 3.58 ± 1.57mm; $p < 0.008$; OR = 0.69 [0.54-0.88]) and the septum-to-ASD ratio (6.68 ± 2.64 vs. 5.75 ± 2.78; $p < 0.005$; OR = 1.14 [1.02-1.27]) as can be seen in Table 1. The ROC curve analysis for predicting spontaneous closure using septum/ASD ratio indicated an Optimal Cutoff Point of 4.78, with an area under the curve (AUC) of 0.62, a sensitivity of 80.6%, and a specificity of 45.6% (Figure 2).

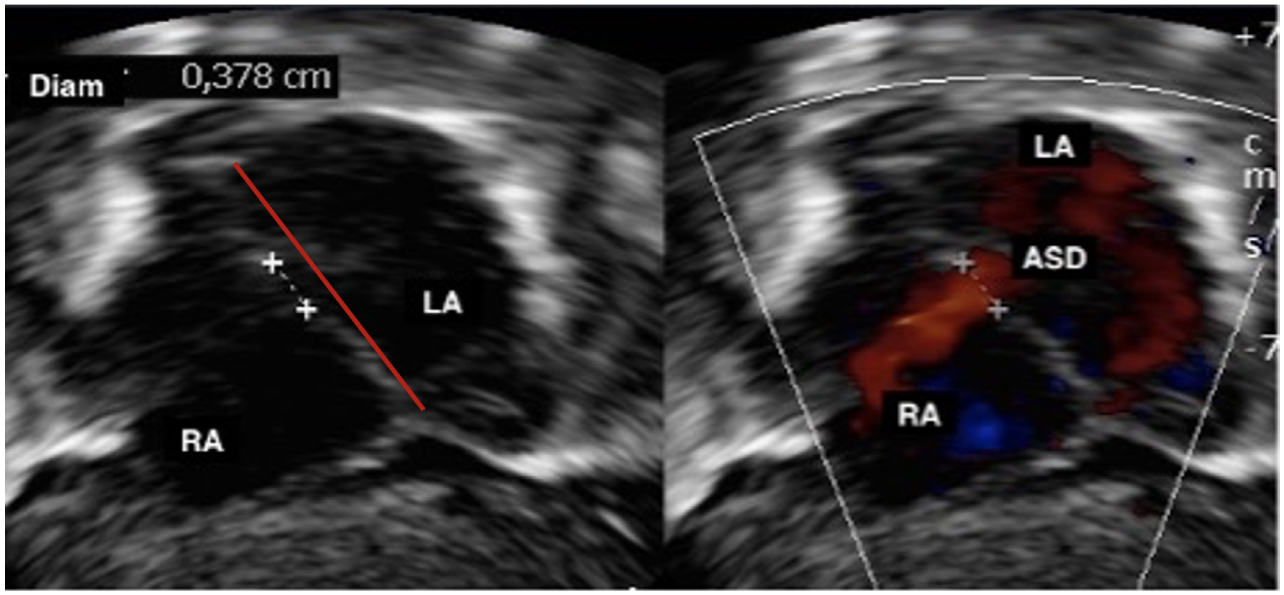


**Figure 1:** two-dimensional echocardiogram in the subcostal view showing ASD. Red line: septum diameter. Dashed line: ASD diameter.

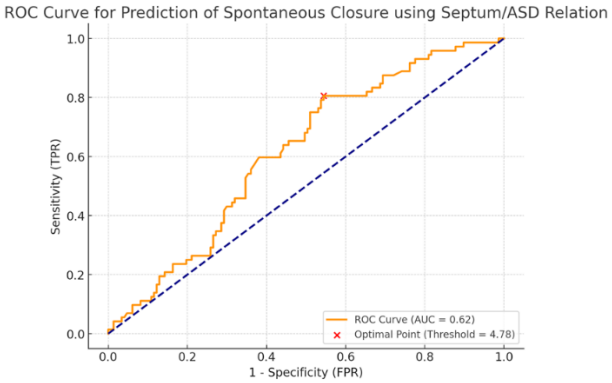


**Figure 2:** ROC curve for atrial septal defect diameter. Septum-to-ASD ratio vs. spontaneous closure.

| | | | | | | | | | Logistic Regression | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | OR | CI (95%) | |
| Variable | Spontaneous Closure | Mean | SD | p25 | Median | p75 | N | p-value | | 95% CI - Lower | 95% CI - Upper |
| ASD diameter | No | 3.58 | 1.77 | 2.40 | 3.00 | 4.50 | 143 | 0.008 | 1.00 | | |
| | Yes | 2.89 | 1.03 | 2.30 | 2.60 | 3.50 | 72 | | 0.69 | 0.54 | 0.88 |
| | Total | 3.35 | 1.59 | 2.30 | 2.90 | 4.00 | 215 | | | | |
| septum diameter | No | 17.56 | 4.28 | 14.40 | 18.00 | 20.40 | 143 | 0.666 | 1.00 | | |
| | Yes | 17.80 | 4.94 | 13.88 | 18.05 | 21.53 | 72 | | 1.01 | 0.95 | 1.08 |
| | Total | 17.64 | 4.50 | 14.10 | 18.00 | 21.00 | 215 | | | | |
| septum/ASD ratio | No | 5.74 | 2.58 | 4.98 | 1.44 | 17.47 | 143 | 0.004 | 1.00 | | |
| | Yes | 6.68 | 2.64 | 6.24 | 2.43 | 18.70 | 72 | | 1.14 | 1.02 | 1.27 |
| | Total | 6.05 | 2.63 | 5.50 | 1.44 | 18.70 | 215 | | | | |
| Mann-Whitney Test | | | | | | | | | | | |

**Table 1:** Comparison of variables measured in the first echocardiogram of patients who did or did not undergo spontaneous closure of the atrial septal defect (ASD) in the second echocardiogram.

## Discussion

This study evaluated a cohort of neonatal patients from a quaternary hospital to determine whether the ASD diameter at the initial neonatal echocardiogram could predict spontaneous closure. Only 33% of patients in our cohort experienced spontaneous ASD closure, which is lower than rates typically reported in the literature (56-79%) [5,6]. This discrepancy may be partly due to the relatively early timing of the second echocardiogram, conducted on average 11.1 months after the initial exam, potentially limiting the opportunity to observe later spontaneous closures that might occur over a more extended follow-up period.

In fetal circulation, the presence of an ASD is physiologically essential, enabling right-to-left shunting of blood to maintain systemic output and oxygenation despite the high pulmonary vascular resistance (PVR) characteristic of intrauterine life. Postnatally, with a significant drop in PVR and the redirection of blood flow through the lungs, the premium septum generally functions as a valve, facilitating spontaneous closure of the ASD or PFO within the early years of life. This closure plays a critical role in the complete separation of systemic and pulmonary circulations, ensuring balanced cardiac output without imposing excessive strain on either side of the heart [6].

In the presence of a larger ASD, the defect persists, exposing the right atrium to increased blood volume. Over time, this leads to dilation of the right heart chambers due to sustained volume overload. Echocardiography, therefore, serves as an invaluable diagnostic tool, providing insights into the cardiovascular adaptation of neonates. Early echocardiographic assessment allows clinicians to detect structural and functional abnormalities, guiding decision-making and ensuring timely interventions that may mitigate long-term complications.

Our study identified significant differences in both the ASD diameter and the septum-to-ASD ratio between patients with and without spontaneous closure. Specifically, a smaller initial ASD diameter and a higher septum-to-ASD ratio were associated with a greater likelihood of spontaneous closure. The mean ASD diameter in the spontaneous closure group (SC) was 2.89 ± 1.03 mm compared to 3.58 ± 1.57 mm in the non-closure group (N-SC) ($p < 0.008$, OR = 0.69 [0.54-0.88]). Additionally, the SC group exhibited a mean septum-to-ASD ratio of 6.68 ± 2.64, significantly higher than the 5.75 ± 2.78 observed in the N-SC group ($p < 0.005$, OR = 1.14 [1.02-1.27]). Thus, the data suggest that smaller ASD sizes and greater septum diameter relative to ASD diameter may predict spontaneous closure.

The ROC analysis of the septum/ASD ratio further reinforces these findings, with an optimal threshold of 4.78 yielding a sensitivity of 80.6% and specificity of 45.6%. While the model's specificity remains moderate, the high sensitivity implies that the septum/ASD ratio can be a useful predictor in identifying cases likely to experience spontaneous closure4. This finding aligns with previous studies, which indicate that defect size correlates with the likelihood of closure; smaller defects tend to close spontaneously more often. Our results underscore the importance of these early echocardiographic parameters as predictors of spontaneous ASD closure outcomes, potentially aiding clinicians in prognosis and management.

Interestingly, the measurement of total atrial septal diameter showed no statistical difference between the groups, consistent with the expectation that total septal size does not influence the likelihood of closure, as it is unrelated to defect size or shunt dynamics.

A primary limitation of our study is the relatively small sample size, largely due to the requirement for a follow-up echocardiogram. Given that patients are not always followed up in the same facility or may not receive subsequent echocardiographic evaluations, the dataset was constrained. Additionally, to minimize interobserver variability, all defect diameter measurements were performed by

a single experienced pediatric echo cardiographer with over five years of clinical experience. However, the retrospective nature of the study and the involvement of various examiners in acquiring the initial echocardiographic images may introduce inherent variability in image quality and measurement. Further prospective studies with larger cohorts and standardized follow-up protocols would help validate these findings and establish clearer guidelines for ASD prognosis.

## Conclusion

This study explored the relationship between the size of the ASD during the neonatal period and the likelihood of its spontaneous closure, leveraging early TTE as a diagnostic tool. Our findings indicate that smaller ASD diameters and higher septum-to-ASD ratios are associated with a greater likelihood of spontaneous defect closure. These results emphasize the value of these echocardiographic parameters as predictors of spontaneous ASD outcomes.

Despite its limitations, this study contributes to our understanding of the factors influencing spontaneous ASD closure, highlighting the significance of defect size as a prognostic indicator. These results can guide clinical practice by enabling the early identification of patients more likely to retain the ASD, thus informing potential clinical follow-up strategies.

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