

Correlation of electrocardiogram parameters and hemodynamic outcomes in patients with isolated secundum atrial septal defects

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ABSTRACT

- Objective** : The characteristic rSR' pattern in lead V1 on electrocardiogram (ECG) has been described in association with atrial septal defect (ASD) and right ventricular dilation. We aimed to determine if temporal ECG changes can guide a more discriminate and cost-effective screening during follow-up of isolated secundum ASD.
- Methods** : Our study population included all pediatric patients followed at the Stollery Children's Hospital with a secundum ASD, not associated with other significant heart disease, between 2004 and 2010. We collected clinical as well as serial echocardiographic and ECG data.
- Results** : We identified 141 patients with ASD, 95% were asymptomatic and 88% referred for a murmur. Moderate-to-large (>5 mm) ASDs were present in 52%. The prevalence of an rSR' pattern was 26% in the overall cohort and 54% in the large ASD group. During median follow-up of 28.7 months, 37 patients underwent surgical or transcatheter closure. Among patients with rSR' on ECG, 78% had moderate-to-large ASD size. In that group, the presence versus the absence of rSR' correlated with lower positive predictive value (PPV) for spontaneous closure (7% vs. 36%; $P = 0.01$) and higher PPV for device or surgical closure (71% vs. 38%; $P = 0.02$).
- Conclusion** : We observed a lower prevalence of rSR' pattern in patients with isolated ASD than previously reported. However, an rSR' pattern had incremental value in predicting the need for surgical or device intervention for closure in moderate-large groups. This can be used to tailor patient echocardiographic screening and caregiver counseling.
- Keywords** : Echocardiography, electrocardiogram, RSR' pattern, secundum atrial septal defect

INTRODUCTION

An isolated atrial septal defect (ASD) is the second most common congenital heart disease. Secundum defects are the most common subtypes of ASDs, accounting for approximately 70% of all cases.^[1,2] The majority of ASDs are diagnosed in the first 2 years of life.^[3,4] While a certain proportion of ASDs becomes insignificant, larger ASDs may result in a notable left-to-right shunt and right-sided

heart failure.^[3-8] Patients with large ASDs are often asymptomatic until at least the 3rd or 4th year of life. Some patients may not develop symptoms for years despite significant right ventricular (RV) dilation.^[9] Follow-up of asymptomatic patients with an ASD requires interval echocardiograms to assess for RV dilation and signs of a hemodynamically significant left-to-right shunt.^[10,11]

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The rSR' pattern in precordial leads V1 or V2 on electrocardiogram (ECG) is a described pattern in patients with hemodynamically significant ASDs, with a reported prevalence of 43%–78% [Figure 1].^[12-17] This pattern is rarely described in normal patients as well. This rSR' pattern is hypothesized to correlate with RV enlargement rather than a conduction disturbance.^[15,18-23] However, the natural history of the progressive ECG changes in patients with ASDs has not been studied. Specifically, the temporal relationship between the degree of RV dilation assessed on echocardiography and the development of rSR' pattern on ECG has not been explored.

We hypothesized that identifying a temporal relationship between the development of the rSR' pattern on ECG and significant RV dilation on echocardiogram, as well as the need for surgical or catheter intervention, would serve as a screening tool for patients with potentially hemodynamically significant ASDs. Specifically, identifying a temporal correlation would allow for cost-effective serial ECG screening and more discriminate echocardiographic screening triggered by the development of an rSR' on ECG.

We sought to determine the prevalence of the rSR' on ECG in a consecutive cohort of all patients with isolated secundum ASDs followed at a single institution. We aimed to explore the temporal correlation between the development of ECG changes and that of RV dilation on echocardiogram, along with clinical symptoms and management strategies.

METHODS

Study design and patients

Between 2004 and 2010, we identified 151 consecutive patients followed at the Stollery Children's Hospital, meeting the following inclusion criteria: (1) Isolated secundum ASD diagnosed on echocardiogram within the first 2 years of life; (2) patients followed for a minimum duration of 6 months. Exclusion criteria included any patient with a patent foramen ovale or any patient with associated congenital heart diseases, except for hemodynamically insignificant patent ductus arteriosus, small restrictive muscular ventricular septal defect (VSD), and mild pulmonary

artery stenosis (gradient <25 mmHg). Ten patients were excluded due to missing charts and data. We retrospectively reviewed the charts on the eligible 141 patients with ASDs. The study was approved by the Ethics Committee.

Data collection

We collected demographic information including gender, date of birth, cardiac and noncardiac diagnoses, dates of first and last follow-up, and if applicable, date and indication of operative or transcatheter ASD closure. Detailed ECG parameters and measurements were all reviewed before being recorded. For each patient, all ECGs were reviewed in a chronological fashion to identify the first documented rSR' pattern (in leads V1/2). If identified, the most contemporaneous echocardiogram, performed within 6 months of the abnormal ECG, was reviewed, and the ASD size and RV end-diastolic diameter z-score were recorded. In patients with no rSR' pattern throughout follow-up, the first reported ECG and echocardiogram were used. RV diameters are routinely obtained on m-mode, in the parasternal long-axis views and measured offline. Weight and height are routinely obtained at the time of the echocardiogram, for z-score calculations. If the patient underwent ASD closure, information from the last preoperative evaluation and ECG was collected. Patients were grouped based on their ASD size into small (<5 mm), moderate (5–8 mm), and large (>8 mm) subgroups. Standard lead placement, paper speed, and voltage scale were used for all ECGs. The ECG was manually and separately interpreted by MR and JA.

Statistical analysis

Continuous variables were summarized as median with interquartile range (IQR), and categorical variables were described by frequency distributions. Chi-square or Fisher's exact test (if cell counts <5) was done to compare categorical variables across groups. The Kruskal-Wallis test (more than two groups) was used to compare continuous variables. The prevalence of rSR' pattern and positive predictive value (PPV) of rSR' to predict outcome (i.e., spontaneous closure or intervention closure) across categories of ASD were calculated and presented with 95% confidence intervals (CIs). QRS morphology was divided into three categories: rSR' or QR, RSr', and RS or R. For comparative data analysis,

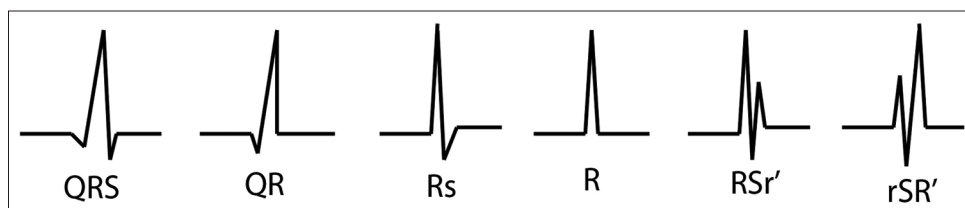


Figure 1: QRS morphology

Table 1: Characteristics of patients across their categories of atrial septal defect size (n=141)

Characteristics	ASD size			P
	<5 mm (n=68)	5-8 mm (n=45)	>8 mm (n=28)	
Age at initial presentation (months)*	2.0 (0.8-3.7)	3.6 (2.2-6.9)	6.3 (2.4-10.3)	0.0004
Gender (female)	37 (54.4)	27 (60.0)	20 (71.4)	-
Asymptomatic	67 (98.5)	42 (93.3)	26 (92.9)	-
Follow-up duration (months)	23.8 (14.4-42.3)	34.3 (21.1-45.2)	32.1 (25.6-41.5)	0.1
ECG findings	-	-	-	-
QRS complex	-	-	-	-
Axis*	83.0 (63.5-99.0)	89.0 (75.0-108.0)	90.0 (79.5-126.5)	0.1
Duration*	66.0 (59.0-75.0)	70.0 (64.0-77.0)	72.0 (69.0-80.0)	0.03
QRS morphology	-	-	-	-
rSR' or QR	8.0 (11.8)	13.0 (28.8)	15.0 (53.6)	0.001
RSr'	15 (22.1)	7.0 (15.6)	-	-
RS or R	45.0 (66.2)	25.0 (55.6)	13.0 (46.4)	-
R amplitude*	0.8 (0.6-1.3)	0.8 (0.4-1.3)	0.4 (0.3-1.0)	0.03
R' amplitude (all patients)*	0.0 (0.0-0.2)	0.0 (0.0-0.7)	0.7 (0.0-1.0)	0.005
R' amplitude (only rSR')*	0.6 (0.3-0.9)	1.3 (0.9-1.4)	1.0 (0.7-1.6)	0.03
Echo findings	-	-	-	-
z score >2	16.0 (23.5)	34.0 (75.6)	25.0 (89.3)	<0.0001
Outcomes	-	-	-	-
Remained same	21 (30.9)	16 (35.6)	2 (7.1)	<0.0001
Spontaneous closure	47 (69.1)	16 (35.6)	2 (7.1)	-
Intervention closure	-	13 (28.9)	24 (85.7)	-

*Presented as median with IQR. ASD: Atrial septal defect, ECG: Electrocardiogram, Echo: Echocardiogram, IQR: Interquartile range

we combined the latter two groups. Two-sided $P < 0.05$ was considered statistically significant. Correlation coefficients were calculated using the Spearman method. All analyses were performed using SAS statistical software (Version 9.4 SAS Institute, Cary, NC, USA).

RESULTS

Patients' characteristics

Data for 141 eligible patients were reviewed, 60% of whom were female. Median (IQR) ages at first and last cardiology assessment were 2.7 (1.4–6.9) and 34.7 (21.3–49.9) months, respectively. The median age at initial presentation was higher at 6.3 months in patients with large ASD compared to 3.6 and 2.0 months in moderate and small ASD, respectively [$P = 0.0004$, Table 1]. Hemodynamically insignificant cardiac diagnoses were present in 40 (28%) patients, most commonly a small VSD (10%), mild pulmonary valve stenosis (9%), or a small patent ductus arteriosus (3%). Noncardiac syndromes were present in 28 (20%) patients, including trisomy 21 in 13 (9%). The great majority of patients was asymptomatic on presentation (95%) and was referred because of a systolic murmur (88%). The distribution of patients with small (<5 mm), moderate (5–8 mm), and large (>8 mm) ASD was 48%, 32%, and 20%, respectively.

QRS morphology and atrial septal defect size

A summary of findings is presented in Table 1. Follow-up duration was a median (IQR) of 28.7 months (17.0–42.5) and ranged from 6.0 to 91.5 months, with none of the patients lost to follow-up. On ECG analysis, all patients were in sinus rhythm, and there was no large

P wave amplitude (>3 mm) in lead II. The median (IQR) PR interval was 112 (102–124) msec. Only three patients had prolonged QRS interval (>100 ms). The QR ECG pattern was seen in only one patient at first follow-up, who had a small size ASD, and in four patients on last follow-up, three of whom had a small size ASD and one had a moderate size ASD.

The overall prevalence of rSR' pattern was 26% (36/141), decreasing to 16% on ECG at last follow-up as rSR' resolved in 14 patients. In patients with small ASD, the prevalence was 12% (95% CI: 5%–22%) (8/68). On follow-up, rSR' resolved in three patients. Two of the five patients with a persistent rSR' pattern had shorter follow-up periods of <20 months. In patients with moderate ASD, the prevalence was 29% (95% CI: 16.0%–44.0%) (13/45), and on follow-up, rSR' resolved in eight patients. In patients with large ASDs, the prevalence was 54% (95% CI: 34.0%–72.0%) (15/28), and on follow-up, rSR' resolved in three patients. Of the 36 patients with an rSR' pattern, 28 (78%) had moderate-to-large ASDs.

The median age at first ECG with a documented rSR' was 9.5 (IQR 5.2–23.5) months: 7.0 (IQR 3.7–15.3) months for small ASD, 7.7 (IQR 5.2–15.6) months for moderate ASD, and 19.6 (IQR 8.4–27.2) months for large ASD patients ($P = 0.07$). Of all patients with an rSR', 51% had that pattern documented on their initial ECG or within 6 months of initial presentation. This ratio was similar between subgroups being 50% for small, 62% for moderate, and 43% for large ASD.

Echocardiographic parameters demonstrated no difference in age, gender distribution, or median follow-up duration across the different ASD size groups

[Table 1]. A RV end-diastolic diameter z-score >2 was found in 80% of patients with moderate-to-large ASD versus 23% of those with small ASD ($P < 0.001$).

QRS morphology and clinical outcomes

In the overall patient cohort, 65 (46%) patients experienced ASD spontaneous closure as documented on echocardiogram. In patients with small ASDs, 69% experienced spontaneous closure while the remaining had no change in ASD size. Patients with moderate and large size ASD experienced spontaneous closure in 36% and 7%, respectively. Among patients with moderate-to-large ASD, 37 (26%) underwent intervention for ASD closure, 18 surgically and 19 by transcatheter. Median (IQR) age at intervention was 44 (32.9–53.9) months. Main indications for intervention were for significant hemodynamic changes on echocardiogram in 84% and signs and symptoms of heart failure in 16%.

Among all patients with no rSR', 57% had a small ASD, whereas among patients with an rSR', 78% had moderate-to-large ASD size. In patients with a small ASD, the PPV for spontaneous ASD closure or remaining the same was 100% whether an rSR' pattern was absent or present. None of the patients with small ASD underwent intervention for ASD closure. In patients with moderate-to-large ASD size, the PPV for spontaneous closure was 36% (95% CI: 21.9%–51.2%) if an rSR' pattern was absent and 7% (95% CI: 0.9%–23.5%) if an rSR' pattern was present ($P = 0.006$). The PPV for intervention for ASD closure in those patients was 38% (95%CI: 23.8%–53.5%) versus 71% (95% CI: 51.3%–86.8%) if rSR' was absent versus present ($P = 0.008$). For the subgroup with large (>8 mm) ASD size, only one spontaneous closure occurred in a patient with no rSR' and none in those with an rSR'. The PPV for intervention for ASD closure was 77% (95% CI: 46.2%–95.0%) versus 93% (95% CI: 68.1%–99.8%) if rSR' was absent or present ($P = 0.3$). Table 2 provides a summary of all PPV grouped by the presence of rSR' pattern, ASD size, and

clinical outcomes. A subgroup analysis of only those patients over the age of 4 years at last follow-up did not reveal significant difference in the PPV.

In terms of other ECG parameters, there was no correlation between the patient's outcome and R amplitude, R' amplitude, QR pattern, QRS duration, or axis. There was no correlation between QRS duration and RV end-diastolic diameter z-score ($r = 0.06, P = 0.5$); however, there was a modest correlation between R' amplitude and RV end-diastolic diameter z-score ($r = 0.4, P = 0.006$).

DISCUSSION

In this study, we evaluated the natural history of ECG parameters in a consecutive cohort of patients with ASDs not associated with other significant congenital heart disease. We identified a lower prevalence of rSR' in the overall cohort and the subgroups. There was no correlation between QRS duration and the RV z-score on echocardiogram; however, in patients with an R', there was a significant correlation of R' amplitude with the RV end-diastolic diameter z-score, suggesting that R' amplitude may be the more relevant ECG representation of the underlying RV morphological changes. The median age at initial presentation was significantly higher at approximately 6 months in the large ASD group compared to 2–4 months in the small-moderate group. In addition, the age at first ECG with an rSR' pattern was also significantly older in the large ASD group. However, the rSR' pattern was present on initial ECG in a similar proportion between all three study groups and 51% for the overall cohort, the remaining developed upon follow-up.

The prevalence of the rSR' pattern was low in both the overall cohort (26%) and the moderate-to-large ASD size group (38%). This is in contrast to prior studies reporting higher prevalence rates. Cohen *et al.* reported an overall rSR' prevalence of 43%, with prevalence rates of 40%, 58.1%, and 62.1% in patients with small (<5 mm), moderate (5–9 mm), and large (>10 mm) ASD size, respectively.^[14] They reported similar median age of patients to our study (at last follow-up), however, used different ASD size ranges. The remaining studies included either smaller patient cohorts of 20–47 patients with an older mean age of 7.7 years^[12,13,17] and/or included a select patient population referred for ASD closure.^[13,14,17] In the study by Schiller *et al.*, the reported RSR' prevalence combined RSR', rSR', and QR patterns in lead V1.^[24]

The second main finding in this study was the correlations between the presence or absence of rSR' on ECG and the hemodynamic outcome of moderate-to-large ASDs. In the combined group of patients with moderate-to-large ASDs, the presence versus absence of an rSR' pattern

Table 2: Positive predictive values of rSR' pattern according to clinical outcomes and atrial septal defect size (n=141)

Clinical outcomes	rSR' present	PPV (95% CI)		
		<5 mm (n=68), %	>5 mm (n=73), %	>8 mm (n=28), %
Spontaneous closure	Yes	75 (35-97)	7 (1-24)	None
	No	68 (55-80)	36 (22-51)	8 (0.2-36)
Spontaneous closure and remained the same	Yes	100 (63-100)	29 (13-49)	7 (0.2-32)
	No	100 (94-100)	62 (47-76)	23 (5-54)
Intervention for ASD closure	Yes	None	71 (51-87)	93 (68-100)
	No	None	38 (24-54)	77 (46-95)

ASD: Atrial septal defect, CI: Confidence interval, PPV: Positive predictive value

correlated with a very low PPV for spontaneous closure (7% vs. 36%; $P=0.01$) and a higher PPV for the requirement of device or surgical closure (71% vs. 38%; $P=0.02$), respectively. In the subgroup of patients with large ASDs, only one patient experienced spontaneous closure and did not have an rSR' pattern on ECG. The presence of an rSR' in that group showed a higher proportion requiring surgical closure (PPV of 93% vs. 77%; $P=0.3$) although not statistically significant. Hence, in moderate-to-large ASDs, spontaneous closure can occur in about a third when rSR' is absent while unlikely when it is present. In addition, the development of an rSR' pattern can aid in early parent counseling about the higher likelihood of requiring surgical closure and the importance of ongoing serial echocardiographic follow-up.

In small ASDs, whether an rSR' was present or absent, all ASDs showed a clinically equivalent outcome of either spontaneous closure or remaining the same. This is in keeping with existing knowledge about the high rate of spontaneous closure in small ASDs. The specific rate of spontaneous closure was not different in patients with or without rSR' (75% vs. 68%; $P=1.0$). Therefore, in patients with small ASDs, the outcome is determined by the ASD size, and the presence of an rSR' pattern does not indicate the need for ongoing follow-up with routine echocardiograms.

CONCLUSION

This retrospective study evaluating ECG characteristics in patients with isolated secundum ASDs identified lower prevalence rates of rSR' pattern and older age at clinical and rSR' presentation in patients with large ASD. The presence of an rSR' pattern on ECG had no impact on the clinical course of patients with small ASD. However, the development of an rSR' pattern had an incremental value in predicting the need for surgical or device intervention for closure in both moderate and large size ASD groups. Increase in the frequency and timing of screening echocardiography, as well as parent counseling, can be tailored based on these ECG findings in patients with potentially hemodynamically significant ASDs.

Limitations

This study is limited by the retrospective nature of its design and is subject to missing or incomplete data. Furthermore, RV end-diastolic diameter by m-mode as a surrogate for RV size is subject to suboptimal accuracy and low reproducibility. Outcome ascertainment in patients with an isolated ASD is probably incomplete as some may still require surgical closure at an older age and would not have been captured during this study's time frame. The low rSR' prevalence may be related to the limited follow-up duration in some patients. Finally, our study also included a more homogenous but relatively young patient population at initial assessment.

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Conflicts of interest

There are no conflicts of interest.

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