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Role of Doppler echocardiography for assessing right ventricular cardiac output in patients with atrial septal defect

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Abstract

Background: Although Doppler echocardiography is routinely used to assess left ventricle cardiac output, there are limited data about the feasibility of Doppler echocardiography for right ventricular (RV) cardiac output assessment in patients with left-to-right shunt. The purpose of the study was to determine the correlation between Doppler-derived and Fick-derived RV cardiac index (CI), and the interobserver correlation in Doppler-derived RV CI assessment.

Methods: Retrospective study of patients (age ≥18 years) with unrepaired atrial septal defect who underwent cardiac catheterization and echocardiography (within 3 days), 2004-2017. RV CI was calculated using the hydraulic orifice formula: [.785 × (right ventricle outflow tract diameter)^2 × right ventricular outflow tract (RVOT) time velocity integral × heart rate]/body surface area.

Results: A total of 128 patients (age 52 ± 17 years; female 88 [69%]) met the inclusion criteria. There was a modest correlation between Doppler-derived and Fick-derived RV CI (r = .57, P < .001), and the mean difference between Doppler-derived and Fick-derived RV CI was −.3 (95% confidence interval of agreement, −.8 to +.9) L/min/m^2. There was also a modest correlation between Doppler-derived RV CI from observer #1 and observer #2 (r = .62, P < .001), and the mean difference between Doppler-derived RV CI from observer #1 and observer #2 was −.2 (95% confidence interval of agreement, −.9 to +.6).

Conclusions: The current study demonstrated a modest correlation between Doppler-derived and Fick-derived RV cardiac output, and a modest interobserver correlation in Doppler-derived RV cardiac output assessment. Further studies are required to validate these results and to explore other potential applications such as in patients with chronic pulmonary regurgitation.

KEYWORDS
atrial septal defect, cardiac output, Doppler echocardiography, right ventricle

Abbreviations: CI, cardiac index; ICC, intraclass correlation; LV, left ventricle; LVOT, left ventricular outflow tract; Qp:Qs, ratio of pulmonary to systemic blood flow; RV, right ventricle; RVOT, right ventricular outflow tract; TVI, time velocity integral.

1 | INTRODUCTION

Transthoracic echocardiogram is the primary imaging modality for structural heart disease.[1-3] It is portable, easy to operate, noninvasive, and does not pose any risk to the patient, hence making it the ideal test of longitudinal monitoring. Doppler echocardiography is routinely used for the assessment of left ventricular (LV) stroke volume and cardiac output in clinical practice.[1-3] LV cardiac output is often used as a surrogate for right ventricular (RV) cardiac output, thereby avoiding the need to directly measure RV cardiac output.

In the setting of venous or intracardiac left-to-right shunt, LV and RV cardiac output become discordant because of isolated increase in RV stroke volume.[1-3] As a result, the LV cardiac output cannot be used as surrogate for RV cardiac output in such disease conditions.[4,5] Echocardiography is not currently used for the assessment of RV cardiac output in the setting of left-to-right shunt because of limited data about the feasibility of measuring RV stroke volume by echocardiography.[1-3] Other imaging modalities such as cardiac magnetic resonance imaging and cardiac computed tomography scan are used to assess RV stroke volume and cardiac output in such situations.[4,5] Unlike Doppler echocardiography, these cross-sectional imaging modalities are not readily available and do have some other limitations.[4,5] We hypothesized that Doppler-derived cardiac output measurements correlated with Fick-derived cardiac output measurements. The purpose of this study was to determine if Doppler-derived cardiac output measurements correlated with Fick-derived cardiac output (gold standard) measurements.

The primary study objective was to determine the correlation between RV cardiac output and Qp: Qs measured by Doppler echocardiography and invasive hemodynamic assessment based on the Fick's principle (gold standard). The secondary study objective was to determine interobserver correlation in the assessment of Doppler-derived RV cardiac output.

2 | METHODS

2.1 | Patient selection

This is a retrospective study of adult patients (age ≥18 years) with unrepaired atrial septal defect (excluding patent foramen ovale) who underwent cardiac catheterization for clinical indications (quantification of left-to-right shunt, assessment of pulmonary vascular resistance, and transcatheter closure of atrial septal defect) at Mayo Clinic Rochester from January 1, 2004 to December 31, 2017. Only the patients that had both transthoracic echocardiogram and cardiac catheterization performed within 3 days, and patients with less than or equal to mild pulmonary regurgitation (in order to avoid spurious increase in Doppler-derived RV stroke volume) were included in the study. The Mayo Clinic Institutional Review Board approved this study and waived informed consent for patients that provided search authorization. The electronic health records were extensively reviewed in these patients.

2.2 | Invasive and noninvasive data acquisition

2.2.1 | Cardiac catheterization

All cardiac catheterizations were performed for clinical indications under mild sedation. The techniques for performing cardiac catheterization in patients with congenital heart disease have been described.[6,7] In this cohort, cardiac index (CI) was calculated based on the Fick's principle using assumed oxygen consumption.[8,9] Hemodynamic data were manually abstracted from catheterization reports; reported values represent an average of 6-8 consecutive beats, according to heart rate.

2.2.2 | Echocardiography

We reviewed all digital echocardiographic images and performed offline tracing of left ventricular outflow tract (LVOT) diameter and time velocity integral (TVI). All measurements and calculations for LV stroke volume and cardiac output were performed as stipulated by the American Society of Echocardiography guidelines.[1] LVOT diameter was measured using 2D echocardiogram from the parasternal long-axis window while LVOT TVI was measured using pulsed wave Doppler from the apical window. LV stroke volume was calculated as .785 × (LVOT diameter)^2 × LVOT TVI.[1] Doppler data were accepted if the angle of insonation was <20 degrees. Cardiac output was calculated as stroke volume × heart rate. We used the heart rate recorded on the TVI pulsed wave Doppler clip for the calculation of cardiac output. LV CI was calculated by dividing the cardiac output by the body surface area. Although the correlation between Doppler- and Fick-derived LV CI assessments has been demonstrated in previous studies, we performed the assessment in this study just as a calibration to show that our technique is similar to previous studies and that this technique can be applied to the right side.

The right ventricle outflow tract (RVOT) diameter and TVI were measured from both the parasternal long-axis and the parasternal short-axis windows (Figure 1). Using the same principle of the hydraulic orifice formula (flow rate = cross-sectional area × flow velocity), we calculated RV stroke volume as .785 × (RVOT diameter)^2 × RVOT TVI.[1] RV cardiac output was calculated as stroke volume × heart rate, and RV CI was calculated by dividing the cardiac output by the body surface area. One of the investigators (ACE) measured RVOT diameter and TVI in all patients, and also repeated these measurements (blinded) in 25 of the patients in order to assess intraobserver agreement. A highly experienced sonographer (R.P), who was blinded to the measurements of the investigator, also measured the RVOT diameter and TVI in all patients, in order to assess interobserver agreement.

2.3 | Statistical analysis

Data were presented as mean ± standard deviation or counts (%), and between-group comparisons were performed using paired t-test and Fisher's exact test. Normality was assessed using Shapiro-Wilk test.

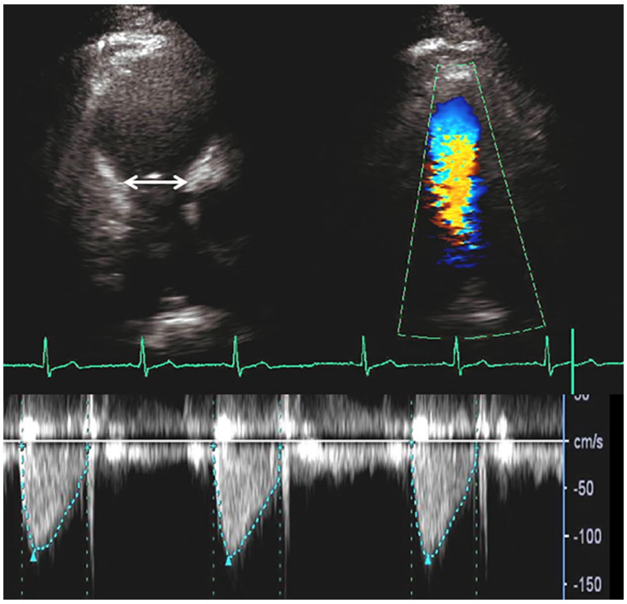

FIGURE 1 Images from parasternal short-axis window showing two-dimensional (top left), color Doppler (top right), and pulsed wave Doppler (bottom) of the right ventricular outflow tract. White arrow shows the site of measurement of RVOT diameter from the two-dimensional, and the sample volume for pulsed wave Doppler was obtained from the same point

Intraobserver and interobserver variability for RVOT diameter, RVOT TVI, and RV CI was assessed using the intraclass correlation (ICC) and 95% confidence interval. Bland-Altman and linear regression were used to assess the agreement between Doppler-derived and Fick-derived CI, and the agreement between Doppler-derived RV CI between observers. In order to assess the predictive value Doppler-derived RV CI, we defined nonsignificant shunt as Fick-derived Qp:Qs < 1.5:1. Logistic regression was used to assess the ability of Doppler echocardiography to discriminate (reliably identify) patients with nonsignificant shunt. All statistical analyses were performed with JMP software (version 13.0; SAS Institute Inc, Cary, NC).

3 | RESULTS

Out of 151 patients (126 secundum atrial septal defect and 25 sinus venosus atrial septal defects) that met the inclusion criteria for the study, 128 (83%) had echocardiographic images of adequate quality to perform offline measurements of RVOT diameter and TVI. Of the 23 excluded patients, 17 were excluded because they did not have adequate RVOT pulsed wave Doppler signals, and 6 were excluded because they did not have adequate 2D images of the RVOT to allow for accurate measurement of RVOT diameter. There were no significant differences in the baseline clinical characteristics of the study cohort compared to the patients that were excluded (Table S1). The average size of defect measure from subcostal or parasternal window was 16 ± 7 mm, and 96 patients underwent closure of atrial septal defect. All patients had left-right shunt by color Doppler. The mean age at the time of the study was 52 ± 17 years, and 88 (69%) were females. Table 1 shows the baseline clinical and echocardiographic data of the study cohort.

3.1 | Echocardiography

The RVOT diameter and TVI were measured from the parasternal short-axis view in all 128 patients. On the other hand, only 106 (83%) had adequate images for RVOT diameter and TVI measurements from the parasternal long-axis view. The RVOT dimensions and hemodynamic indices are shown in Table 1. There was no significant difference between RVOT diameter obtained from the short axis vs the long axis (2.6 ± .4 vs 2.5 ± .7 cm, $P = .412$), and the ICC was .91 (95% CI .85 to .96). Similarly, there was no significant difference between RVOT TVI obtained from the short axis vs the long axis (28 ± 4 vs 29 ± 5 cm, $P = .508$), and the ICC was .93 (95% CI .89 to .97).

Observer #2 (R.P) who was blinded to the measurements obtained by observer #1 (ACE) performed measurements of RVOT diameter and TVI from the parasternal long-axis and short-axis windows. The between-observer ICC for RVOT diameter was .89 (95% confidence interval .81 to .97) and .88 (95% confidence interval .82 to .94) for parasternal short-axis view and long-axis windows, respectively. The between-observer ICC for RVOT TVI was .92 (95% confidence interval .85 to .96) and .90 (95% confidence interval .83 to .95) for parasternal short-axis view and long-axis windows, respectively. The intraobserver ICC for RVOT diameter was .94 (95% confidence interval .90 to .98) and .93 (95% confidence interval .88 to .97) for parasternal short-axis view and long-axis windows, respectively. The intraobserver ICC for RVOT TVI was .95 (95% confidence interval .91 to .98) and .92 (95% confidence interval .89 to .96) for parasternal short-axis view and long-axis windows, respectively.

3.2 | Doppler-Fick correlation

The invasive hemodynamic data of the study cohort are shown in Table 2. The mean interval between echocardiogram and cardiac catheterization was 39 ± 18 hours. There was a modest correlation between Doppler-derived RV CI and Fick-derived RV CI ($r = .57$, $P < .001$), and the mean difference between Doppler-derived RV CI and Fick-derived RV CI was −.3 L/min/m^2 (95% confidence interval of agreement, −.8 to +.9), Figure 2. Just for reference, we assessed correlation between Doppler-derived and Fick-derived LV CI, and correlation coefficient was $r = .71$, $P < .001$. The mean difference between Doppler-derived and Fick-derived LV CI was −.2 L/min/m^2 (95% confidence interval of agreement, −.7 to +.6). There was no significant difference in the degree of correlation of Doppler-derived and Fick-derived cardiac output for the LV compared to that of the RV (p interaction = .162). There is no significant difference in the mean Doppler-derived and Fick-derived ratio of pulmonary to systemic blood flow (Qp:Qs) (1.6 ± .6 vs 1.7 ± .3, $P = .218$), and there was a modest correlation between Qp:Qs assessment from both methods ($r = .52$, $P = .011$), Table 3. There was no significant difference between the Doppler-derived RV CI in patients that were

TABLE 1 Clinical and echocardiographic data

	n = 128
Age, years	52 ± 17
Female	88 (69%)
Body mass index, kg/m^2	27 ± 5
Body surface area, m^2	1.9 ± .3
Hypertension	51 (40%)
Hyperlipidemia	33 (26%)
Coronary artery disease	10 (8%)
Diabetes mellitus	12 (9%)
Atrial fibrillation	28 (21%)
Atrial flutter/tachycardia	12 (9%)
Echocardiography[a]	
RVOT hemodynamics	
RVOT diameter, cm (PLAX) [n = 128]	2.5 ± .7
RVOT TVI, cm (PLAX) [n = 114]	29 ± 5
RVOT diameter, cm (PSAX) [n = 126]	2.6 ± .4
RVOT TVI, cm (PSAX) [n = 119]	28 ± 4
Pulmonary valve peak velocity, m/s	1.2 ± .4
Mean gradient, mm Hg	9 ± 4
Mild pulmonary regurgitation	24 (19%)
Trivial pulmonary regurgitation	104 (81%)
Heart rate, bpm	71 ± 12
LVOT hemodynamics	
LVOT diameter, cm	2.2 ± .3
LVOT TVI, cm	21 ± 4
Aortic valve peak velocity, m/s	1.3 ± .3
Aortic valve mean gradient, mm Hg	6 ± 2
≥Moderate RV enlargement	81 (62%)
≥Moderate RV systolic dysfunction	11 (8%)
≥Moderate tricuspid regurgitation	26 (20%)
Tricuspid regurgitation velocity, m/s	2.9 ± .6
Medial E/e′	10 ± 4
Lateral E/e′	7 ± 3
LV ejection fraction, %	63 ± 8

Abbreviations: E/e′, ratio of mitral inflow early filling velocity to tissue Doppler early velocity; LV, left ventricle; LVOT, left ventricle outflow tract; PLAX, parasternal long axis; PSAX, parasternal short axis; RV, right ventricle; RVOT, right ventricle outflow tract; sig, significant; w/o, without.
[a]The assessment of severity of regurgitation, RV enlargement, and systolic dysfunction was based on qualitative assessment.

in sinus rhythm (n = 116) vs patients that had atrial arrhythmia the time of echocardiogram (n = 12); 3.7 ± 1.2 L/min/m^2 (Qp:Qs 1.6:1) vs 3.6 ± .9 L/min/m^2 (Qp:Qs 1.7:1), P = .217.

The RV CI was also calculated using the RVOT indices from the parasternal short-axis window obtained by observer #2. There was a modest correlation between Doppler-derived RV CI from observer #1 and observer #2 (r = .62, P < .001), and the mean difference between Doppler-derived RV CI from observer #1 and observer #2 was −.2 L/min/m^2 (95% confidence interval of agreement, −.9 to +.6), Figure 3. The intraobserver ICC and interobserver ICC for RV CI was .81 (95% confidence interval .73 to .90) and .74 (95% confidence interval .61 to .83), respectively.

Out of the 128 patients in the study, 76 (59%) who underwent ASD closure (transcatheter 63, and surgical 13) had postintervention echocardiograms of sufficient image quality for the assessment of RV CI. Both the LV CI and RV CI were assessed in these patients, and the RV CI was 2.6 ± .8 L/min/m^2 while the LV CI was 2.7 ± .3 L/min/m^2. The Doppler-derived Qp:Qs was .97:1.

TABLE 2 Cardiac catheterization data

	n = 128
Heart rate, bpm	68 ± 7
Right atrial pressure, mm Hg	9 ± 3
Right ventricular systolic pressure, mm Hg	40 ± 17
Right ventricular end-diastolic pressure, mm Hg	11 ± 4
Pulmonary artery systolic pressure, mm Hg	40 ± 16
Pulmonary artery mean pressure, mm Hg	25 ± 12
Pulmonary artery diastolic pressure, mm Hg	14 ± 6
Pulmonary artery wedge pressure, mm Hg	11 ± 4
Left ventricular end-diastolic pressure	13 ± 4
Left atrial pressure, mm Hg	11 ± 3
Transpulmonary gradient, mm Hg	13 ± 8
Aortic systolic pressure, mm Hg	103 ± 19
Mixed venous saturation, %	81 ± 7
Main pulmonary artery saturation, %	91 ± 6
Pulmonary vein saturation, % [N = 64]	98 ± 1
Systemic arterial saturation	98 ± 1
Right ventricular cardiac index, L/min/m^2	3.9 ± 1.1
Left ventricular cardiac index, L/min/m^2	2.7 ± .6
Qp:Qs	1.7 ± .3
Pulmonary vascular resistance index, WU × m^2	3.9 ± 1.3

Abbreviation: Qp:Qs, ratio pulmonary blood flow to systemic blood flow.

3.3 | Predictive value of Doppler-derived RV CI

Of the 128 patients, 37 (29%) had Fick-derived Qp:Qs < 1.5:1, and we defined this group as having nonsignificant shunt. Among these 37 patients, 32 (86%) also had Doppler-derived Qp:Qs < 1.5:1. Doppler echocardiography was able to discriminate (reliably identify) patients with nonsignificant shunt (Fick-derived Qp:Qs < 1.5:1) with a sensitivity of 73% and specificity of 81%, and area under the curve .705.

4 | DISCUSSION

In this study, we demonstrated the feasibility of assessing RV cardiac output in the setting of left-to-right shunt using Doppler echocardiography. The study showed a modest correlation between

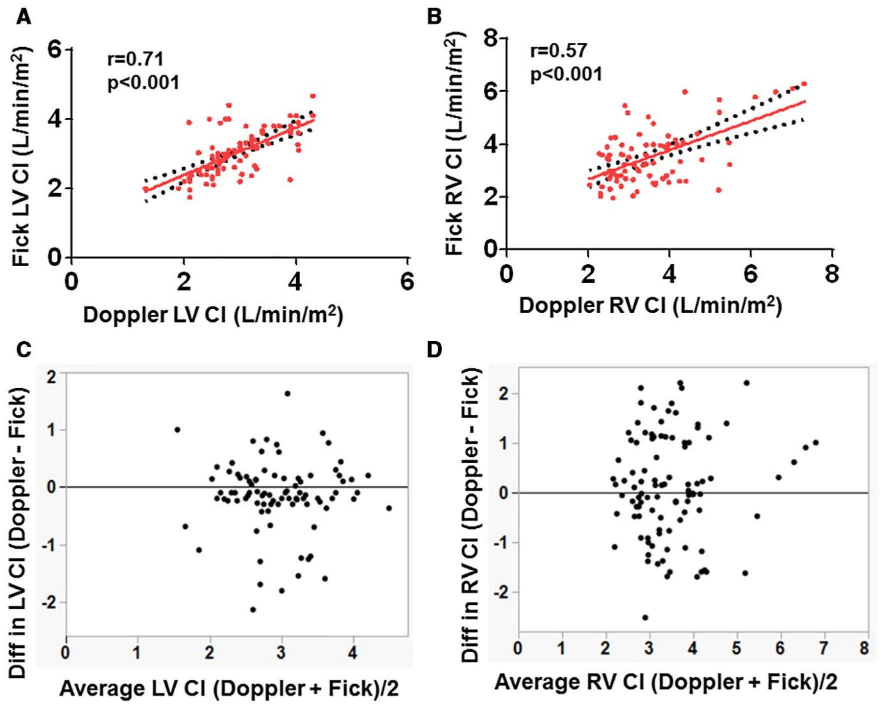

FIGURE 2 A, Linear correlation of Fick-derived vs Doppler-derived left ventricular (LV) cardiac index (CI). B, Linear correlation of Fick-derived vs Doppler-derived right ventricular (RV) CI. C, Bland-Altman plot showing the mean difference between Fick-derived and Doppler-derived LV CI. The mean difference was −.2 (95% confidence interval of agreement, −.7 to +.6). D, Bland-Altman plot showing the mean difference between Fick-derived and Doppler-derived RV CI. The mean difference was −.3 (95% confidence interval of agreement, −.8 to +.9)

TABLE 3 Echo-Cath correlation data

	Fick	Doppler
Heart rate, bpm	68 ± 7	71 ± 4
Aortic systolic blood pressure, mm Hg	103 ± 19	112 ± 16
Aortic diastolic blood pressure, mm Hg	74 ± 13	79 ± 11
Right ventricular cardiac index, L/min/m^2	3.9 ± 1.1	3.7 ± 1.4
r, *P* value	.57, *P* < .001	
Left ventricular cardiac index, L/min/m^2	2.7 ± .6	2.6 ± .9
r, *P* value	.71, *P* < .001	
Qp:Qs	1.7 ± .3	1.6 ± .6
r, *P* value	.52, *P* = .011	

Abbreviation: Qp:Qs, ratio pulmonary blood flow to systemic blood flow.

Doppler-derived and Fick-derived RV cardiac output and Qp:Qs. Just for comparison, we also assessed the correlation between Doppler-derived and Fick-derived LV cardiac output. There was no significant difference in the degree of correlation of Doppler-derived and Fick-derived cardiac output for the LV compared to that of the RV. Additionally, there was modest intraobserver and interobserver agreement for Doppler RV CI as shown by an intraobserver ICC and interobserver ICC of .81 (95% confidence interval .73 to .90) and .74 (95% confidence interval .61 to .83), respectively.

Although the assessment of LV (pump) function is almost universally based on the measurement of ejection fraction, this index of LV function is highly load-dependent and sometimes is not an accurate reflection of systemic cardiac output which is the important variable from the standpoint of meeting the body's metabolic demands.[1-3] The LV cardiac output, on the other hand, represents a composite measure of preload, afterload, contractility, and heart rate which are key determinants of hemodynamic performance.[10,11] The role of Doppler echocardiography for the assessment of LV cardiac output is well established based on data from several clinical studies.[10-12] It is now routinely used in clinical practice as a diagnostic and prognostic marker in disease conditions associated with low cardiac output such as in the heart failure population.[1-3,13]

The Doppler-derived LV cardiac output is often used as a surrogate for RV cardiac output because both values are identical for an *"in-series"* circulatory system. In disease conditions, the result in isolated RV volume overload, the LV and RV cardiac output becomes discordant, thereby violating the underlying assumptions that allow us to use the values of LV and RV cardiac output interchangeably.[14] As a result of this, the assessment RV cardiac output in disease conditions such as venous or intracardiac left-to-right shunt and pulmonary regurgitation requires cross-sectional imaging or invasive hemodynamic studies.[4,5,7] Although these procedures are routinely performed with high safety profile, they lack the advantages of transthoracic echocardiography which include being readily available, easy to operate, no risk to the patient, and lower cost.[15] Some of the challenges of using Doppler echocardiography to directly measure RV cardiac output revolve around the difficulty of accurately measuring the RVOT diameter and obtaining Doppler alignment for RVOT TVI. The current study demonstrated that Doppler-derived RV cardiac output had a modest correlation with the gold standard of invasive hemodynamics. More importantly, we demonstrated that the performance of Doppler-derived cardiac output, measured in terms of degree of correlation with the gold standard of invasive hemodynamics, was not different for the LV and RV. This finding strongly argues against the concerns that the complex RVOT anatomy may not lend itself to the geometric assumptions of the hydraulic orifice formula and the continuity equation.[10-12]

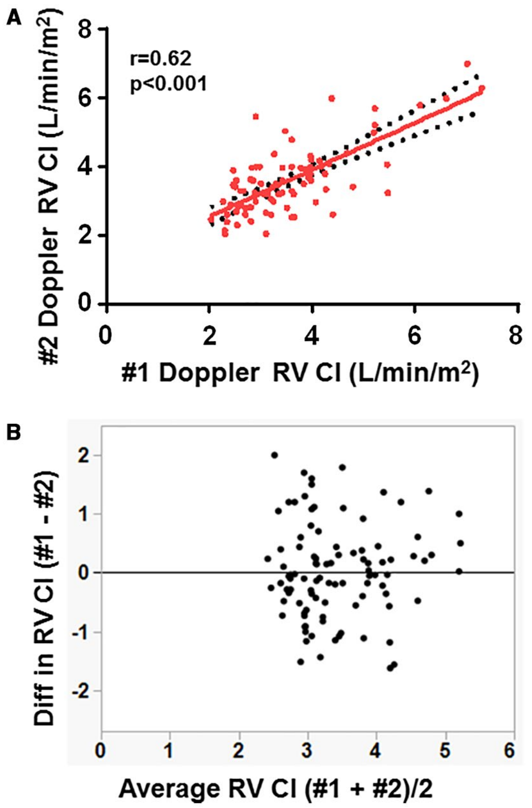

FIGURE 3 A, Linear correlation of Doppler-derived right ventricular (RV) cardiac index (CI) between observer #1 and observer #2. B, Bland-Altman plot showing the mean difference between Doppler-derived RV CI between observer #1 and observer #2. The mean difference was −.2 (95% confidence interval of agreement, −.9 to +.6)

4.1 | Clinical application and future direction

One of the criteria for intervention in patients with RV volume overload due to atrial septal defect is a Qp:Qs > 1.5:1.[3,16] The assessment of Qp:Qs requires either invasive hemodynamic studies or cross-sectional imaging.[4,5,7] This study demonstrates the concept that echocardiography-derived measurements of QP:QS correlate with invasive hemodynamic assessment. However, further study is needed to identify the ideal echocardiography-derived QP:QS threshold to defer sending patients for cardiac catheterization. The implications of deferring a hemodynamically significant shunt are great, and this measure should be optimized to improve sensitivity to identify a significant shunt.

4.2 | Limitations

This is a retrospective single-center study and is therefore prone to selection and ascertainment bias. The Doppler and invasive hemodynamic assessments were not performed simultaneously, and this raises a concern about temporal changes in loading conditions affecting the internal validity of the results. We mitigated against this problem by assessing not just RV cardiac output, but also LV cardiac output and Qp:Qs. Although changes in loading conditions due to fasting and sedation required for cardiac catheterization will affect the absolute value of RV cardiac output, it will also likely cause a proportional change in LV cardiac output, and therefore the Qp:Qs will be unchanged. And lastly, we excluded patients with significant pulmonary regurgitation from the study and this limits the generalizability of our results to this important population.

4.3 | Conclusions

In this study of 128 patients with atrial septal defect, we demonstrated a modest correlation between Doppler-derived RV cardiac output and the gold standard of invasive hemodynamic assessment that is based on the Fick's principle. We also showed that it was feasible to obtain the adequate RVOT indices required for RV cardiac output assessment in 83% of patients undergoing routine echocardiography. Finally, the study showed a modest interobserver correlation in the assessment of Doppler-derived RV cardiac output making it a good metric for longitudinal monitoring. Further studies are required to validate the results of this study and also to assess the feasibility of calculating RV cardiac output in patients with chronic pulmonary regurgitation.

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CONFLICT OF INTEREST

None.

AUTHOR CONTRIBUTIONS

Study design: Yogeswaran, Kanade, Mejia, Egbe
Data collection: Yogeswaran, Kanade, Mejia, Egbe
Data analysis: Yogeswaran, Kanade, Mejia, Egbe
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Critical revision: Yogeswaran, Kanade, Mejia, Egbe, Fatola, Kothapalli, Ananthaneni, Sandhyavenu, Abdelsamid, Hagler
Final review/approval: Yogeswaran, Kanade, Mejia, Egbe, Fatola, Kothapalli, Ananthaneni, Sandhyavenu, Abdelsamid, Hagler

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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