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Journal
ASAIO Journal, 69(1)

ISSN
1058-2916

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Publication Date
2023

DOI
10.1097/mat.0000000000001710

Peer reviewed

Prepared for Submission to: Journal of Cardiac Failure

Preoperative CT Assessment of Risk of RV Failure After Left Ventricular Assist Device Placement

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Word Count: 3283/3500 maximum

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Highlights

- ECG-gated CT imaging can be used to evaluate RV morphology and function in patients with heart failure being evaluated for LVAD
- Patients with enlarged RV volumes (EDVI and ESVI) were found to be at higher risk of post-LVAD RV failure.
- The performance of CT-derived RV volumes in predicting post-LVAD RV failure was better than demographic, clinical catheterization, blood, and echocardiographic measures.

Abstract (183 out max 200 words)

Background: Identification of patients who are at a high risk for right ventricular failure (RVF) after left ventricular assist device (LVAD) implantation using conventional 2-dimensional echocardiography, hemodynamic, and clinical parameters is limited. We retrospectively examined the ability of CT ventricular volume measures to identify patients who experienced RVF after LVAD implantation.

Methods and Results: Between 9/17 and 9/20, 77 patients underwent LVAD surgery at our institution. Preoperative CT-derived ventricular volumes were obtained in 18 patients. Patients who underwent CT evaluation had a similar demographics and rate of RVF after LVAD as patients who did not undergo cardiac CT imaging. In the study cohort, 7/18 (38.9%) patients experienced RVF (2 unplanned BiVAD, 5 prolonged inotropic support). Demographics, blood biomarkers, echocardiographic measures, and hemodynamic values were not predictive of RVF. However, CT-derived RV end-diastolic (RVEDVI) and end-systolic volume indices (RVESVI) was predictive with area under the receiver operating curve of 0.779 and 0.753 respectively.

Conclusions: CT volumetric assessment of RV size can be performed in patients evaluated for LVAD treatment. RV measures of size provide a promising means of pre-LVAD assessment for postoperative RV failure.

Keywords: LVAD, Right Ventricle Failure, Computed Tomography, Right Ventricular Volumes

Introduction

Left ventricular assist devices (LVADs) have become a standard option for patients with late-stage heart failure (1). LVADs can serve as both a destination therapy for patients ineligible for transplant and a bridge-to-transplant (2). However, right ventricular failure (RVF) after LVAD implantation is a major cause of morbidity and mortality (3). As such, prior research has tried to identify preoperative parameters that indicate a patient may be at high risk for RVF after LVAD implantation (4–6).

Meta-analysis has identified poor right ventricular (RV) performance metrics as predictive of postoperative RVF, though the effect size is only mild to moderate (7). Currently, the strongest predictor of post-LVAD RV failure is preoperative, qualitative assessment of RV size and function with 2D echocardiography (7,8). However, 2D evaluation and qualitative scoring is thought to limit accuracy (9). Quantitative, 3D evaluation with echocardiography has identified RV dilation and depressed RV ejection fraction (RVEF) as predictors of RVF (10–12). However, 3D echocardiography can require specialized data acquisition and processing (which limits clinical availability) and can be less accurate when evaluating large RV volumes (13).

Alternatively, ECG-gated CT angiography can obtain volumetric RV assessments that have been validated against CMR (14). In addition, patients being evaluated for LVAD implantation routinely undergo non-contrast, chest CT evaluations as part of their work-up. To-date, the utility of ECG-gated 3D cine CT assessment of RV size and function in patients undergoing LVAD has not been reported. In this study, we tested the hypothesis that CT-derived preoperative measures of RV enlargement and decreased systolic function predict RVF after LVAD implantation. As a secondary aim, we compared performance of cine CT-derived metrics of RV function to clinical parameters previously found to be predictors of RVF – namely older age, female gender, elevated INR, low RV stroke work index (RVSWI), elevated right atrial pressure (RAP), and moderate-to-severe right ventricular dysfunction and enlargement on qualitative echocardiographic assessment.(15).

Materials and Methods

Study Population

In September 2017, a cine CT evaluation protocol for RV function was implemented at our institution for patients undergoing LVAD workup with GFRs > 40 mL/min. Under IRB approved waiver of informed consent, 77 consecutive patients who underwent LVAD implantation between September 2017 and December 2020 were reviewed as part of our retrospective study. The inclusion criteria for enrollment was LVAD implantation at our institution, the availability of clinically-acquired preoperative hemodynamic and echocardiographic assessments, and the lack of congenital heart disease. 63 of the 77 LVAD patients met the inclusion criteria.

Of the 63 patients, 21 had cine CT imaging prior to subsequent LVAD implantation. 3 patients were excluded due to clinically-documented worsening of ventricular function and ventricular enlargement between the time of cine CT imaging and LVAD implantation surgery. This resulted in a study cohort of n=18 and comparison cohort of n=43. Demographic, blood biomarkers, hemodynamics, and echocardiographic parameters for both groups are shown in Table 1.

Blood Biomarkers and Hemodynamic Assessments

Blood biomarkers and hemodynamic measurements before LVAD surgery were obtained as part of standard preoperative care. Pulmonary vascular resistance (Woods units) was calculated as mean arterial pressure - pulmonary capillary wedge pressure over cardiac output. RV stroke work index (RVSWI, g m^{-3} $beat^{-1}$) was calculated as (mean pulmonary arterial pressure - right atrial pressure) x stroke volume index.

Echocardiography

2-dimensional echocardiography was performed before LVAD implantation as part of standard preoperative care. The right ventricle was evaluated qualitatively as having either normal or reduced function. Right ventricular size was qualitatively evaluated as either normal or mild, moderately, or severely enlarged. Tricuspid valve regurgitation was evaluated on a scale of none, mild, moderate, or severe regurgitation.

Tricuspid annular plane systolic excursion (TAPSE) was measured on a four chamber view and reported in millimeters.

Computed Tomography

Cine CT imaging was performed on a 256-slice Revolution CT scanner (GE Healthcare, Chicago, IL). All patients were examined in the supine position. After a scout image was taken, a single axial slice was selected to monitor contrast arrival. 80 to 120 ml of contrast agent (Omnipaque; GE Healthcare, Chicago, IL) was injected, followed by a saline flush, all at 4 mL/s. The scans were performed during a single breath-hold, using retrospective ECG gating. The kVp (80 to 120 kV) and x-ray tube current (400 to 600 mA) were determined based on a clinical imaging protocol. Images were acquired with a median noise index of 28 (range: 10.4 to 36). Axial images were reconstructed at 10% intervals across the cardiac cycle (0 to 90% of the R-R). Volumetric evaluation was performed by cardiothoracic-trained radiologists and end-diastolic volumes, end-systolic volumes, stroke volumes, and ejection fractions were reported for the right and left ventricles.

Right Ventricular Failure after LVAD Implantation

INTERMACS criteria were used to define postoperative RVF after LVAD implantation: prolonged (>13 days) need for inotropes in the setting of elevated filling pressures (RAP > 15 mmHg) or the unplanned placement of a right ventricular assist device (RVAD) following LVAD surgery.

Associations with RV Failure

Prediction of post-LVAD RVF from pre-implantation CT-derived volumetric parameters was evaluated using area under the receiver-operating-characteristic curves (AUROC). Confidence intervals were calculated using the approach outlined by Hanley and McNeil (16) for continuous variables. Previously reported predictors of RVF (older age, female gender, elevated INR, low RVSWI, elevated CVP, and moderate-to-severe right ventricular dysfunction on echocardiography) were compared to CT-derived measures of RV size and function. Significant predictors of RVF were subsequently analyzed using ROC curves to identify an optimal cutoff point and we report sensitivity and specificity.

Statistical Analysis

Continuous variables are represented as mean ± standard deviation (SD) and were compared with the use of Student unpaired t-test. Variables that were not normally distributed are represented as median with interquartile range values (Q1 to Q3), and differences were analyzed with the Wilcoxon rank sum test. Normality was evaluated using the Shapiro-Wilk test. Categorical variables are presented as percentages and were compared using the Fisher exact test. Univariate logistic regression was used to identify parameters that were predictive of a binary outcome.

Results

Study Population

Table 1 describes the demographics, blood biomarkers, hemodynamic, and echocardiography measures of our cohort. There were no statistically significant differences between patients who underwent cine CT and those who did not in terms of demographics (gender, age, body mass index, or prevalence of ischemic cardiomyopathy). Further, there was no difference in rate of right ventricular failure after LVAD implantation (38.9 vs 30.2%, p=0.519).

Patients who underwent cine CT had lower median BUN (22 vs 35 mg/dL, p = 0.016), lower creatinine (1.10 vs 1.60 mg/dL, p = 0.023), higher GFR (72 vs 46, p < 0.001), lower bilirubin (0.55 vs 1.05 mg/dL, p = 0.013), and higher hematocrit (36% vs 33 %, p = 0.016) than patients who underwent non-contrast imaging. There was no significant difference in AST, Albumin, INR, and white blood cell count between populations.

RAP/PCWP ratio was lower (median: 0.39 vs 0.50, p=0.035) in patient who underwent cine CT. Otherwise, there were no significant differences in catheterization-derived hemodynamics including heart rate (HR), right atrial pressure (RAP), pulmonary capillary wedge pressure (PCWP), systolic (PAs), diastolic (PAd), or mean pulmonary pressure (MPAP), pulmonary vascular resistance (PVR), cardiac index (CI) or right ventricular stroke work (RVSWI).

There were no significant differences in qualitative evaluation of RV size, dysfunction, tricuspid regurgitation (TR), or TAPSE on echocardiography.

Cine CT-derived measures of RV size and function were successfully obtained in all cases that underwent scanning.

LVAD Implantation and Development of RV Failure

In our study cohort, the median time from cine CT scan to LVAD implantation was 32 days (IQR 14 - 64). Of the LVADs implanted, 16 patients received Heartmate III (Thoratec, Pleasanton, CA) devices while 2 received Heartware HVAD (Heartware, Framingham, Massachusetts) devices.

7/18 (38.9%) patients with pre-LVAD cine CT imaging developed postoperative right ventricular failure. 2 of these patients required spontaneous RVAD implantation and 5 required long term (≥14 days) of inotropic support.

Association of pre-LVAD Clinical Parameters with RV Failure

In our study cohort, there were no significant differences ($p > 0.05$) in previously-reported predictors of RVF including age, gender, INR, qualitative scoring of RV enlargement or dysfunction on echocardiography, RAP,

RAP/PCWP, or RVSWI between patients that experienced postoperative RVF and those that did not (**Table 2**). In the overall cohort (n=61), only RAP was significantly different in patients who experience RV failure after LVAD implantation (RVF: 14 ± 8 mmHg vs No RVF: 10 ± 6 mmHg, p = 0.02).

Association of pre-LVAD Volumes with RV Failure

Patients with RVF had significantly increased indexed right ventricular volumes measured with CT (RVEDVI: 162 ± 43 mL vs 113 ± 39 mL, p = 0.011; RVESVI: 120 ± 38 mL/m^2 vs 79 ± 40 mL/m^2, p = 0.025). Indexed RV stroke volume was not significantly different (p = 0.211) between patients with and without RVF. The resulting difference in RV ejection fraction (with RVF: 24 ± 11% vs without: 32 ± 11%, p = 0.075) did not reach statistical significance. These findings, along with association of pre-LVAD clinical parameters with RVF, are summarized in **Table 2**.

Univariate logistic regression confirmed RV EDVI (χ^2= 5.531, p = 0.019) and RV ESVI (χ^2= 4.060, p = 0.044) as predictors of RVF.

ROC analysis for CT-derived predictors yielded a higher area-under-the-curve (AUC) for RV EDVI (0.779 ± 0.12) than RV ESV (0.753 ± 0.13) (**Figure 2**). CT-derived predictors yielded a higher AUC than RAP (0.72 ± 0.13), RVSWI (0.57 ± 0.15), INR (0.66 ± 0.14), and Age (0.53 ± 0.15).

RVEDVI >150mL/m^2 and RVESVI >110 mL/m^2 identified patients who went on to have RVF with 85.7% sensitivity and 81.8% specificity. The optimal cutoff value for RAP was > 12 mmHg (sensitivity: 57.1%, specificity:100%), RVSWI was > 382 g m^{-3} $beat^{-1}$ (sensitivity: 28.6%, specificity: 100%), INR was < 1.4 (sensitivity: 72.7, specificity: 57.1), and Age was > 80 years (sensitivity: 90.9%, specificity: 28.6%).

Discussion

In a cohort of patients being evaluated for LVAD implantation, we obtained ECG-gated 3D cine CT estimates of RV size and function prior to LVAD implantation. In our cohort, we found preoperative CT-derived right ventricular volumes significantly larger in patients who had postoperative RVF than those who did not. Additionally, cine CT-derived RV EDVI and ESVI were better predictors than conventional hemodynamic, blood biomarker, or demographic measures. To our knowledge, this is the first use of cine CT to assess RV function prior to LVAD implantation. Our findings add to the body of research that examines preoperative RV volumes and affirms that preoperative CT-derived ventricular volumetric enlargement predicts postoperative RVF.

Our results largely agree with findings from prior studies using 3D echocardiographic assessment of RV volumes and function for patients undergoing LVAD implantation. Specifically, Kiernan et al (10) measured preoperative RV volumes in a similarly sized (n=26) cohort using 3D echocardiography and found RV EDVI and RV ESVI to be significantly larger in patients who went on to have RVF and that 2D echocardiography measures were not different. They also found RVF patients had reduced

RVEF, though this relationship did not hold after accounting for RVSWI in multivariate analysis.

Additionally, Otten et al (12) examined preoperative RV volumes using 3D echocardiography and found RV enlargement, similar to those in Kiernan et al, led to higher 60-day mortality. However, patients with severe enlargement RV EDVI (>82 ml/m^2) appeared to be protected effect from 90-day mortality. Magunia et al (11) examined 3D echocardiography metrics in 26 patients and, unlike other studies, did not find a significant difference in volumes for patients with and without RVF. However, they did observe significant differences in function (reduced RVF and reduced RV free wall strain).

The RV volumetric sizes we report in our cohort are larger than those reported by Kiernan et al and by Magunia et al. This could be due to echocardiography limitations in measuring severe RV enlargement or differences in patient population. Only one patient (5%) in our cohort presented as INTERMACS Profile 1, while Kiernan et al had 50% INTERMACS Profile 1 patients and Magunia et al. had 12% INTERMACS Profile 1 patients.

In addition to echocardiography and CT, CMR can be used to obtain RV volume metrics. However, use of CMR in this population is limited by the severity of their heart failure and high prevalence of devices such as balloon pumps and ICDs. For example, 83% (n=15) of our cohort who underwent CT imaging had implanted ICDs and 16% (n=3) had implanted balloon pumps.

RVF is believed to arise from a host of factors, which motivates multifactorial evaluation. For example, most risk scores combine hemodynamics, demographics, and direct echocardiographic assessment of RV function(4–6). Our findings suggest that cine CT could be used to augment this type of multifactorial assessment by providing robust quantitative evaluation of RV function. Given that patients typically undergo non-contrast CT as part of the surgical evaluation, cine CT is well position to robustly and routinely assess RV size and function.

This study has several limitations. First, this is a retrospective, single-center cohort analysis. As a result, we did not prospectively evaluate the prognostic ability of the proposed RV EDVI or ESVI cutoff values. Additionally, the small sample size limits the use of multivariate analysis. Further, timing between CT scanning and LVAD implantation was variable within the cohort (IQR 14 - 64 days); however, patients with significant changes in cardiovascular status between imaging and implantation were excluded via record review. Lastly, cine CT requires the use of iodinated contrast. As a result, contrast-enhanced scanning targeted patients with >40 GFR. As expected, this led our study cohort to have better renal function than patients who did not undergo contrast-enhanced cine CT, as shown in **Table 1**. Future work aims to extend our 3D CT imaging to the broader population of patients undergoing LVAD evaluation.

Conclusion:

ECG-gated contrast-enhanced CT imaging can be used to obtain volumetric, quantitative measures of RV size and function in heart failure patients being evaluated for LVAD implantation. CT-derived RV enlargement was associated with a higher risk of RVF. Given that patients typically undergo non-contrast CT as part of the surgical evaluation, use of cine CT could augment clinical evaluations and further establish routine assessment of RV size and function.

	ECG-gated cine CT (n=18)	Non-contrast chest CT (n=43)	*p*-value
Demographics			
Gender Female (%)	0	14	0.231
Age (years)	63 (45-71)	63 (53-70)	0.857
BMI (kg/m^2)	27.0 (23.7-30.8)	27.2 (22.7-32.8)	0.865
Ischemic HF (%)	44	47	0.895
Blood Biomarkers			
BUN (mg/dL)	22 (16-27)	35 (22.3-49)	**0.016**
Creatinine (mg/dL)	1.10 (0.95-1.41)	1.60 (1.19-2.19)	**0.023**
GFR	72 (56-86)	46 (32-65)	**0.001**
Bilirubin (mg/dL)	0.55 (0.48-0.99)	1.05 (0.60-1.76)	**0.013**
AST (units/L)	23 (18-33)	28 (20-40)	0.126
Albumin (g/dL)	3.9 (3.6-4.2)	3.8 (3.4-4.2)	0.136
INR	1.4 (1.3-2.0)	1.4 (1.2-1.8)	0.575
WBC (10^9 cells/L)	7.2 (5.0-9.4)	8.4 (5.9-10.9)	0.091
Hematocrit (%)	36 (5)	33 (6)	**0.016**
Catheterization			
HR (bpm)	89 (15)	90 (19)	0.730
RAP (mmHg)	8 (5 - 11)	10 (7-15)	0.200
PCWP (mmHg)	23 (10)	23 (9)	0.992
RAP/PCWP	0.39 (0.28-0.50)	0.5 (0.36-0.59)	**0.035**
PAs (mmHg)	46 (16)	50 (14)	0.350
PAd (mmHg)	24 (11)	26 (9)	0.640
MPAP (mmHg)	33 (13)	35 (11)	0.526
PVR (Woods)	2.1 (1.7-3.3)	2.6 (2.0-4.8)	0.135
CI (L/m^2)	1.88 (1.68-2.18)	1.86 (1.55-2.17)	0.794
RVSWI (g beat^{-1} m^{-3})	0.51 (0.38-0.64)	0.43 (0.36-0.55)	0.482
Echocardiography			
RV dysfunction (%)	67	86	0.167
RV enlargement (%)	11	19	0.733
Mod-Sev TR (%)	28	44	0.166
TAPSE (mm)	1.3 (1.2-1.9)	1.4 (1.1 - 1.7)	0.427
Outcome			
RVF (%)	38.9	30.2	0.519

Table 1: Comparison of patients with and without CT scan. Patients scanned with ECG-gated cine CT were had expectedly better BUN, creatinine, GFR, bilibrubin, and hematocrit values given enrollment criteria. Except for a lower RAP/PCWP ratio, demographic, catheterization, echocardiography, and outcome values were comparable. Bold indicates significant different ($p < 0.05$).

BMI: Body Mass Index, BUN: Blood Urine Nitrogen, GFR: Glomerular Filtration Rate, AST: Aspartate Transaminase, INR: Internal Normalized Ration, WBC: White Blood Cell Count, HR: Heart Rate, RAP: Right Atrial Pressure, PCWP: Pulmonary Capillary Wedge Pressure, PAs: Systolic Pulmonary Artierial Pressure, PAd: Diastolic Pulmonary Arterial Pressure, MPAP: Mean Pulmonary Arterial Pressure, PVR: Pulmonary Vascular Resistance, CI: Cardiac Index, RVSWI: RV Stroke Work Index, TAPSE: Tricuspid Annular Plane Systolic Excursion, RVF: Right Ventricular Failure.

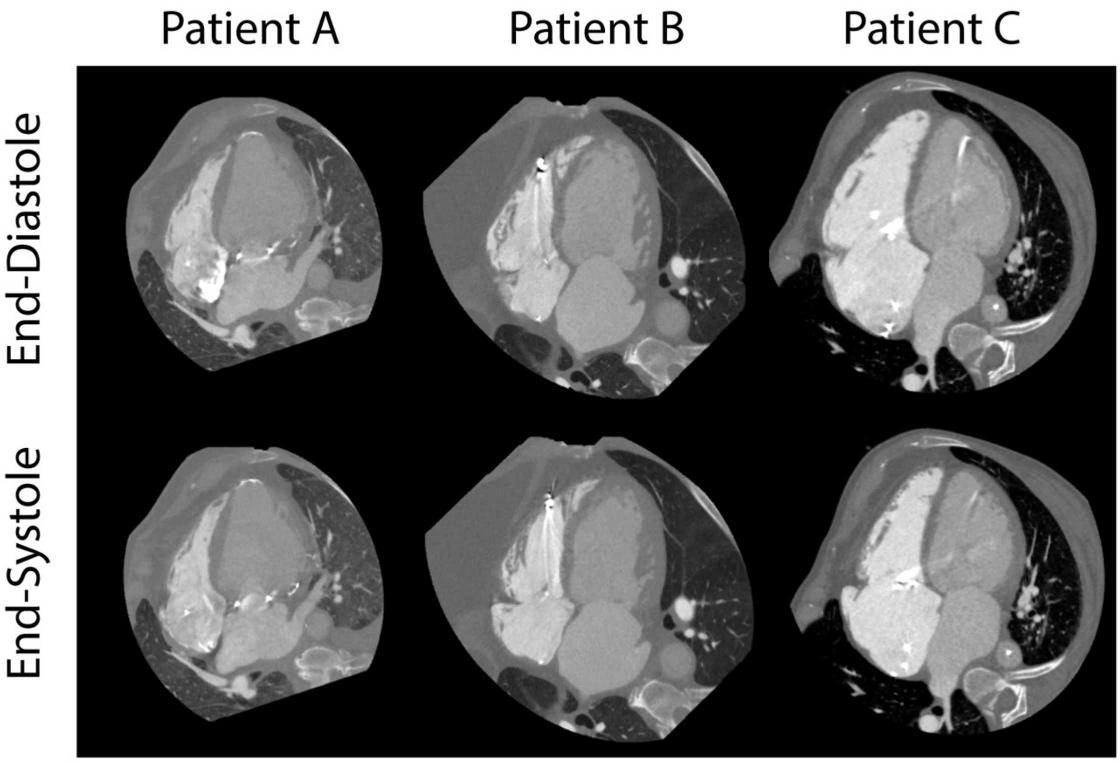
	No RVF (n=11)	RVF (n=7)	*p*-value	AUC
Demographics				
Age (years)	60 (14)	57 (18)	0.694	0.53
Female Gender (%)	0	0	1	0.50
Blood Biomarker				
INR	1.5 (1.2-2.7)	1.3 (1.3-1.4)	0.269	0.66
2D Echocardiography				
RV Enlargement (Mod-Sev) (%)	43	83	0.239	0.58
RV Dysfunction (%)	64	100	0.260	0.63
Hemodynamics				
RAP (mm Hg)	8 (5-9)	12 (6-22)	0.129	0.72
RAP/PCWP ratio	0.39 (0.30-0.43)	0.40 (0.31-0.64)	0.465	0.61
RVSWI (g beat^{-1} m^{-3})	6.1 (2.8)	8.1 (2.8)	0.169	0.67
RV CT Assessment				
RV EDVI (mL/m^2)	113 (39)	162 (43)	**0.010**	0.78
RV ESVI (mL/m^2)	79 (40)	120 (38)	**0.025**	0.75
RV SVI (mL/m^2)	33 (30-38)	39 (32-44)	0.211	0.69
RV EF (%)	32 (11)	24 (11)	0.075	0.68

Table 2: Association of pre-LVAD parameters with RV Failure after LVAD in patients who underwent pre-LVAD CT. RV EDVI and ESVI were significantly increased in patients with RVF with AUC of 0.78 and 0.75 respectively. Bold indicates significant different ($p < 0.05$).

INR: International Normalized Ratio, RAP: Right Atrial Pressure, PCWP: Pulmonary Capillary Wedge Pressure, RVSWI: Right Ventricular Stroke Work Index, EDVI: End Diastolic Volume Index, ESVI: End Systolic Volume Index, SVI: Stroke Volume Index, EF: Ejection Fraction.

	Optimal Cutoff	Sensitivity	Specificity	AUC
RV EDVI	150 mL/m^2	85.7	81.8	0.78 ± 0.12
RV ESVI	110 mL/m^2	85.7	81.8	0.75 ± 0.13
Age	80 years	90.9	28.6	0.53 ± 0.15
INR	1.4	72.7	57.1	0.66 ± 0.14
RAP	12 mmHg	57.1	100	0.72 ± 0.13
RVSWI	382 g m^{-3} $beat^{-1}$	28.6	100	0.57 ± 0.15
Echo Size	>Moderate Enlarg.	72.7	71.4	N/A
Echo Function	Depressed	36.4	71.4	N/A

Table 3: Sensitivity, Specificity and Cutoff value for RVEDVI and RVESVI in terms of predicting RVF. Of the continuous parameters available for AUC analysis, RV EDVI and ESVI had the highest discriminatory power (AUC of 0.78 and 0.75 respectively). RV EDVI: RV End Diastolic Volume Index, RV ESVI: RV End Systolic Volume Index, RAP: Right Atrial Pressure, RVSWI: RV Stroke Work Index, INR: International Normalized Ratio.



	Patient A	Patient B	Patient C
RV EDVI:	103 mL/m^2	156 mL/m^2	218 mL/m^2
RV ESVI:	78 mL/m^2	139 mL/m^2	179 mL/m^2
RV SVI:	25 mL/m^2	17 mL/m^2	39 mL/m^2
RV EF:	24%	11%	18%

Figure 1: Four-chamber images of three patients who underwent CT-based evaluation of RV size and function prior to LVAD implantation. All three patients were found to have mild RV enlargement and reduced RV function on echocardiographic assessment. However, there are notable differences in RV EDVI and ESVI are notable. Patient A did not experience post-operative RVF while patients B and C required prolonged inotropic support.

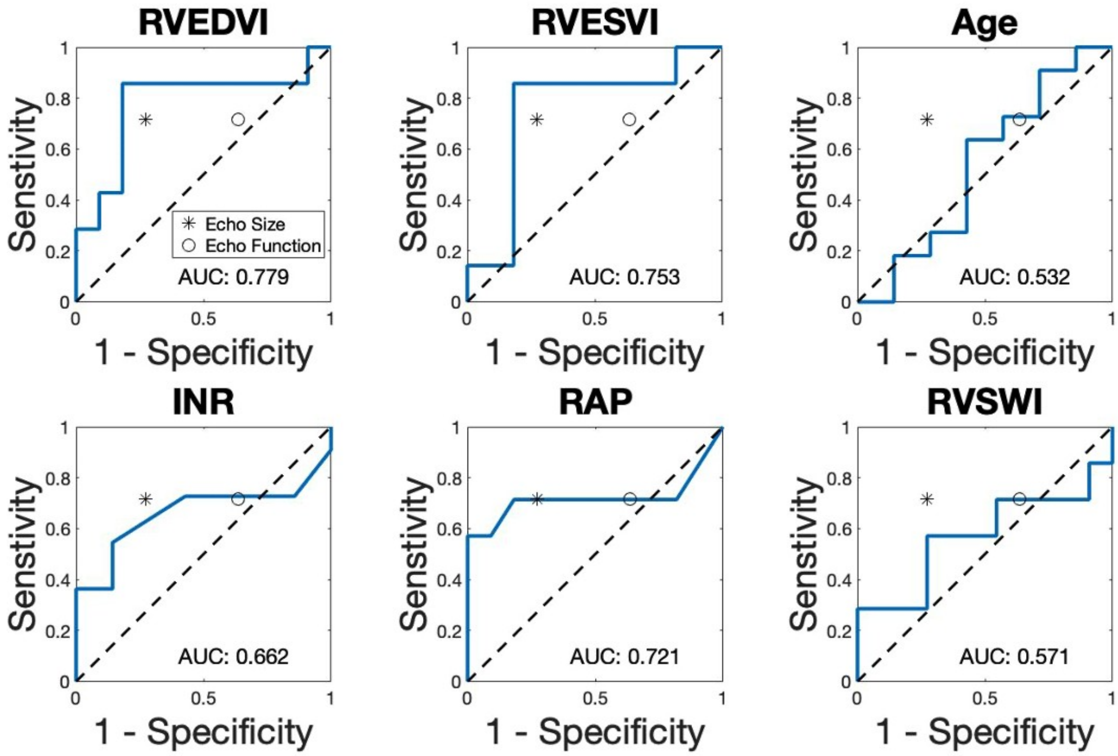


Figure 2: ROC curves of RVEDVI, RVESVI, RAP, RVSWI, INR, and Age. RV EDVI and RV ESVI each had higher AUC values than the other clinical parameters. Sensitivity and specify of moderate or severe enlargement and reduced function on echocardiography are indicated as an asterisk and open circle.

RAP: Right Atrial Pressure, RVSWI: RV Stroke Work Index, INR: International Normalized Ratio

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