Assessment of Right Ventricular Function Following Left Ventricular Assist Device Implantation – The Role of Speckle-Tracking Echocardiography: A Meta-Analysis.

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Abstract

Background: Right ventricular failure (RVF) following Left Ventricular Assist Device (LVAD) implantation is associated with worse outcomes. Prediction and early identification of RVF with speckle-tracking echocardiography (STE) has been proposed. Methods: We queried multiple databases for articles reporting on pre-operative/intraoperative global longitudinal strain (GLS) and free-wall strain (FWS) in LVAD recipients. We performed a systematic review and meta-analysis of published literature. The standard mean difference (SMD) in GLS and FWS in patients with and without RVF postoperatively was pooled using random effects model. Results: Fifteen studies, with a total of 967 LVAD recipients were included. There was statistically significant difference in GLS among patients who did and did not develop RVF; SMD= -3.09 (95% CI: -4.62 to -1.57; p-value <0.0001). There was significant difference in FWS between two groups; SMD: -2.75 (95% CI: -3.72 to -1.79; p-value <0.0001). Upon subgroup analysis of imaging modality, transthoracic echocardiography (TTE)-derived GLS and FWS remained predictive for RVF with SMD of -3.97 (95% CI: -5.40 to -2.54; p-value <0.001) and -3.05 (95% CI: -4.11 to -1.99; p-value <0.001), respectively. However, there was no significant difference between RVF and non-RVF groups upon using transesophageal echocardiography (TEE) to assess GLS and FWS. Conclusion: GLS and FWS assessment of the RV by STE is a useful tool to predict postoperative RVF in LVAD recipients. While the predictive role of TTE was robust, the TEE-derived measures seemed to be less predictive. Future studies need to specify the strain cut-off value that can predict the adverse outcome of RVF

ABSTRACT

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Conclusion: GLS and FWS assessment of the RV by STE is a useful tool to predict postoperative RVF in LVAD recipients. While the predictive role of TTE was robust, the TEE-derived measures seemed to be less predictive. Future studies need to specify the strain cut-off value that can predict the adverse outcome of RVF.

INTRODUCTION

In the year 2019, there was 9,000 LVAD implanted across the globe as an established therapy for patients with advanced heart failure (HF). With the comparable mortality outcomes to heart transplantation and the shortage of donor organs, the use of LVAD is projected to continue to increase.[1] Right ventricular failure (RVF) is a common complication following LVAD implantation that complicates 20–25% of cases and associated with increased morbidity and mortality postoperatively.[2] Proposed mechanisms for RVF suggest acute increase in right-sided preload due to improved left ventricular output, leading to stretching of the right ventricular wall with subsequent functional tricuspid regurgitation, and ultimately decreased right ventricular output.[2] Studies have demonstrated that early prediction of RVF and timely intervention often with biventricular mechanical support (BiVAD) confer favorable outcomes.[3] Hence, several predictive risk scores were modeled to assess the risk of RVF among LVAD recepients.[4–7] However, the performance of these predictive scores had not been consistent across studies[6,7] and their validity had not been well- established in continuous flow LVAD.[4,5]

The complexity of right ventricle (RV) anatomy and its location in the chest obscure the ability to obtain detailed anatomical and functional evaluation in every patient.[2] While the longitudinal shortening of the RV can be estimated by assessing the tricuspid annular plane systolic excursion (TAPSE), its discriminatory ability to predict RVF has been heterogeneous among studies.[5] Speckle tracking echocardiography (STE) is a novel imaging modality which demonstrates promising results in predicting RVF after LVAD implantation.[8] The Region of Interest (ROI) is delineated by speckles and followed through the cardiac cycle.[9,10] Correlation has been well-demonstrated with RV ejection fraction as measured by cardiac magnetic resonance (CMR).[11,12] RV assessment by STE can be either for the entire RV, including the interventricular septum, or limited to the RV free wall – which is considered a more focused and less biased assessment. Most published reports included small samples size, but with an overall common shared approach. To our knowledge, only one prior meta-analysis has evaluated the utility of RV strain in predicting RVF; the analysis only included three studies and was limited to TTE-derived FWS.[13] Thus, we performed a systematic review and meta-analysis of published studies that investigated the role of STE and longitudinal RV strain in predicting RVF following LVAD implantation.

2. METHODS

Search Strategy

Our study protocol followed the recommendation of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.[14] We conducted an electronic search of the literature to identify publications reporting on the predictive role of STE in post-operative RVF among LVAD recipients. Systematic search was conducted using the following databases: MEDLINE, EmCare, CINAHL, Cochrane

Database, and Google Scholar. The following keywords and search terms were used: ("echocardiography" AND "left ventricular assist device OR LVAD" AND "speckle-tracking echocardiography", AND "right ventricle"). Search results were limited to articles published in the English language.

Study Selection and Data Extraction

To be eligible for inclusion, studies should be (i) reporting on adult patients [?]18 years of age undergoing LVAD implantation, (ii) reporting on the occurrence of RVF, and (iii) reporting on preoperative and/or intraoperative two-dimensional echocardiography – with report on GLS and/or FWS. RVF was defined as the need for right ventricular assist device (RVAD), central venous pressure (CVP) >16 mmHg, cardiac index <2.3 L/min/m^2, or the need for post-operative ionotropic support.[36] We excluded case reports, review articles, editorials, and correspondences to the editor. Studies and those which did not include GLS and/or FWS or did not report post-operative right ventricular function were excluded. Data was extracted by two independent investigators K.B. and M.C. into a predefined collection sheet. All disagreements were resolved in consensus with a third reviewer (D.R.). Extracted data included baseline characteristics, definition of RVF, occurrence of RVF, GLS, and FWS.

Quality Assessment

The Newcastle-Ottawa Scale (NOS) was used to evaluate the quality of included studies.[15] The authors generated a checklist for representativeness of included cohort, ascertainment of exposure, comparability and adequacy of follow-up as per the NOS. A maximum of 9 stars were awarded to each study, as determined by 2 independent reviewers. Studies awarded [?]6 stars were considered moderate-to-high quality studies.[15]

2.4 Statistical Analysis

Continuous data (e.g., GLS and FWS) were pooled as a standard mean difference (SMD) between RVF and none RVF groups. Random effect model was adopted in all analyses. We assessed between-study heterogeneity using Q and I^2 statistics. AnI^2 statistic <25% indicates a low amount of heterogeneity and >50% indicates a high heterogeneity.[16] We explored sources of heterogeneity using subgroup analyses by subgrouping the studies based on: (i) echocardiography modality (transthoracic versus transesophageal echocardiography) and (ii) Software used for image acquisition (EchoPac software versus others). We assessed publication bias using Egger regression test and funnel plots. Analyses were conducted using STATA 16 (State Corp LLC, College Station, Texas). A P-value <0.05 was considered statistically significant.

3.RESULT

Preliminary search yielded 1,655 records and after duplicates removal, a total of 1,585 records were identified for 'title and abstract' screening. Upon 'title and abstract' screening, another 1,560 records were excluded. Twenty-five full-text articles were assessed for eligibility and of those fifteen studies were included in our analysis. The flow diagram of the study is depicted in **Figure 1** .

Study Characteristics

Fifteen studies, with a total number of 967 LVAD recipients, fulfilled our inclusion criteria.[8,13,25–29,17–24] Study characteristics and outcomes are summarized in Table 1 and 2. Eleven studies used transthoracic echocardiography (TTE) strain, while four studies utilized transesophageal echocardiography (TEE)[17,20,26,29]. The baseline characteristics and LVAD types of study participants are provided in Table 3. The population of the cohorts was male predominant, as the proportion of males was >70% in all studies. The type of LVAD device varied across the studies, including: HeartMate II, HeartMate III, and HeartWare (table 4). Five studies provided both the GLS and FWS.[8,22,23,28,30]

Global Longitudinal Strain (GLS)

GLS was reported in 9 studies (7 TTE and 2 TEE studies).[8,17,21–23,27–30] The GLS was predictive of post-operative RVF when analyzed for the whole cohort (TEE and TTE). The SMD between the No-RVF and the RVF groups was -3.09 (95% CI: -4.62 to -1.57; p-value <0.0001), I^2= 92.00%. When the TEE-derived GLS is sub-analyzed, there was no statistically significant difference in GLS between the two groups, with a SMD of -0.78 (95% CI: -1.13 to -0.43; p-value =0.54), I^2= 0.00%. Nonetheless, the TTE-derived GLS remained predictive of RVF when analyzed separately, SMD of -3.97 (95% CI: -5.40 to -2.54; p-value <0.0001), I^2= 76.19%. Forest plot for pooled SMD in GLS using TTE and TEE modalities is depicted in Figure 2.

Free Wall Strain (FWS)

FWS was reported in 12 studies (9 TTE and 3 TEE).[8,18,31,19,20,23,24,26,28–30] The FWS for the whole cohort (TEE and TTE) was found to be significantly worse (less negative) pre-operatively in patients who suffered RVF compared to non-RVF group; SMD: -2.75 (95% CI: -3.72 to -1.79; p-value <0.0001), I^2=88.08%. Upon subgroup analysis based on modality, there was no statistically significant difference in the TEE-derived FWS between RVF and non-RVF groups; SMD of –1.81 (95% CI: -4.00 to 0.38; p-value= 0.07), I^2=69.96%. However, the TTE-derived FWS was significantly different between both groups; SMD of -3.05 (95% CI: -4.11 to -1.99; p-value <0.0001), I^2= 84.13%. Forest plot for pooled SMD in FWS using TTE and TEE modalities is depicted in Figure 3.

Heterogeneity

We further explored between-study heterogeneity using subgroup analysis based on the software use for image acquisition (EchoPac software versus others). Subgroup analysis of studies that used EchoPac software was performed for both the TTE-derived GLS and FWS. Five studies used EchoPac to analyze the GLS strain,[8,22,23,27,31]whereas, four studies used EchoPac to analyze the strain values for the FWS.[8,22,23,31] In the studies using EchoPac, the pooled SMD in GLS between RVF and non-RVF groups (figure 4) was -3.71 (95% CI: -5.64 to -1.77; p-value= 0.04), I^2=61.69%. In EchoPac studies, the SMD in FWS between RVF and non-RVF groups (figure 5) was -4.48 (95% CI: -5.97 to -2.98; p-value <0.0001), I^2= 0.00%.

Quality Assessment

Quality assessment of included studies using the NOS tool demonstrated that all studies can be described to be “moderate-to-high” in quality. Of a maximum of 9 starts that can be awarded, all included studies were awarded either 7 or 8 stars. Detailed results of quality assessment are exhibited in Table 4.

4. DISCUSSION

Prognosis in patients with advanced HF is dismal, with a 1-year mortality rate exceeding 25% and 50% in patients with class III-IV and class IV HF, respectively.[32,33] Nonetheless, data from the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) have shown a promising 1-year survival rate of 80% among LVAD recipients.[34] With such favorable outcomes, LVAD implantation has become the standard of care among patients with advanced HF – especially in the face of shortage of donor organs required for heart transplant. Yet, survival post-LVAD implantation can be significantly impacted by RVF – the most common complication following LVAD implant, occurring in 20–25% of cases. Further, severe RVF necessitating additional mechanical support (e.g., RVAD) is reported to occur in about 15% of cases.[6]

Complex hemodynamics and a multitude of variables factor in the development of RVF following LVAD implantation.[35]First, a clinically and hemodynamically subtle RV dysfunction might have preexisted in many patients prior to LVAD implantation. This puts them at increased risk of apparent RVF post-operatively. In addition, RV stroke volume depends in part on the LV contraction through the interventricular septum, a phenomenon called “interventricular dependence”.[36] Improved LV output after LVAD implantation leads to LV decompression and leftward shift of the interventricular septum. This would disrupt the normal mechanics of the RV. Furthermore, fluids and blood products transfusion peri-operatively might lead to RV distention and exacerbation of RVF.[24,25] An intraoperative injury is also a potential contributor that may worsen RV function.[37]

In this meta-analysis of observational studies of 967 patients, we investigated the role of RV strain analysis in predicting RVF in LVAD recipients. The main findings of the study were: (1) TTE-derived FWS and RV-GLS were associated with RVF following LVAD implantation, (2) TEE-derived FWS and RV-GLS were not significantly different between LVAD recipients who developed RVF and those who did not. However, the second finding should be interpreted cautiously in light of the limited number of included studies assessing TEE utility.

The TTE-derived FWS was predictive of RVF postoperatively. Speckle tracking carries the advantage of angle-independent assessment of myocardial movement and is sensitive to subendocardial damage, which produces the strain.[17] However, it can affected by poor imaging,[19] previous cardiac surgery due to tethering of the RV to the sternum,[18] and load dependency.[17,38] Similarly, TTE-derived GLS showed discriminatory power to predict post-operative RVF. Muraru *et al* . showed that inclusion of interventricular septum in strain analysis yields significantly different strain values from the value from analyzing RV free-wall alone. Moreover, in their study RV-GLS, as compared to RV-FWS, correlated better with pulmonary artery systolic pressure.[39]

The European Association of Cardiovascular Imaging (EACVI)/the American Society of Echocardiography (ASE) task force recommends reporting the RV longitudinal strain as the RV free-wall deformation using the focused RV apical four-chamber view. They leave it "optional" to report the four-chamber global RV longitudinal strain, which would include the interventricular septum, as it contributes to a lesser extent to the RV function.[40] However, due to altered unloading conditions and septal mechanics in LVAD recipients, the role of the interventricular septum is more prominent and crucial to maintain RV function following implantation.[2] Therefore, it would be reasonable to include the interventricular septum in measuring the RV longitudinal strain. This meta-analysis supports this conclusion as GLS was predictive for RVF.

Studies have shown variable correlation between TTE- and TEE-derived strains.[41–43] Marucci *et al.* described "moderate" correlation for global strain, and "poor" correlation for regional stain for the left ventricle in anesthetized patients.[41] On the other hand, Kurt *et al.*demonstrated "good" correlation in healthy subjects not undergoing surgery.[43] Generally, speckle tracking quality is dependent on temporal and spatial resolution.[39] The higher frame rate provided by TEE results in a different temporal resolution than that of TTE. And upon adjustment of image sector to obtain a similar frame rate, the spatial resolution gets affected which in turn affects the accuracy of delineation of the endocardium.[31] Furthermore, mechanical ventilation increases the RV afterload due to increased intra-thoracic pressure,[44] hence decreasing the strain values. It is hard to draw accurate conclusion about TEE-derived strain given the small number in our analysis.

Five studies reported cut-offs for predicting post-operative RVF; -9.6, -10.5, -12.7, -14.4, and -15.5, respectively.[19,23,24,27,30] This variability might be attributed to the different methodologies used to evaluate the strain, and the definitions of RVF used in individual studies (table 2). The INTERMACS registry defined mild RVF as elevated CVP >16 mmHg and continued inotropes or pulmonary vasodilators at day 7, moderate if they are continued at day 14, severe if beyond day 14, and severe acute right heart failure if death occurs or RVAD is needed.[36] The studies included in this meta-analysis had different RVF definitions, and this may have affected the RVF reporting rate and contributed to between-study heterogeneity. Three studied have reported a milder spectrum of RVF.[19,21,30] However, other 3 studies reported a higher spectrum of RVF.[23,24,28]

In our study, between-study heterogeneity was high for both the pooled SMD estimate of GLS and FWS. In addition to the variations in RVF definitions, heterogeneity can be explained by the methodologies of obtaining the strain values. Sub-group analysis of TEE and TTE groups did reduce heterogeneity, however it remained moderate-to-high in the TTE group. Upon analyzing the studies that used ECHOPAC software separately, heterogeneity was completely eliminated ($I^2 = 0.00\%$) in the FWS group. However, the results were less robust in the GLS group.

This meta-analysis has certain limitations. First, it includes studies with retrospective design, that could have excluded potential participants due to poor image quality. This could have introduced a selection bias. Second, lack of a standardized RVF definition may have impacted the reported incidence and severity outcomes. Third, use of modalities (TTE and TEE) with different platforms for image acquisition, and being interpreted by different personnel could have introduced measurement and observer bias, respectively.

5. CONCLUSION

TTE-derived RV-FWS and RV-GLS are useful parameters to predict post-operative RVF in LVAD recipients. However, TEE-derived values seem to be less predictive. More studies are needed to specify a strain cut-off value that can reliably predict the adverse outcome of RVF after LVAD implantation.

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Figure 1: PRISMA flow-chart showing the search strategy and studies selection process.

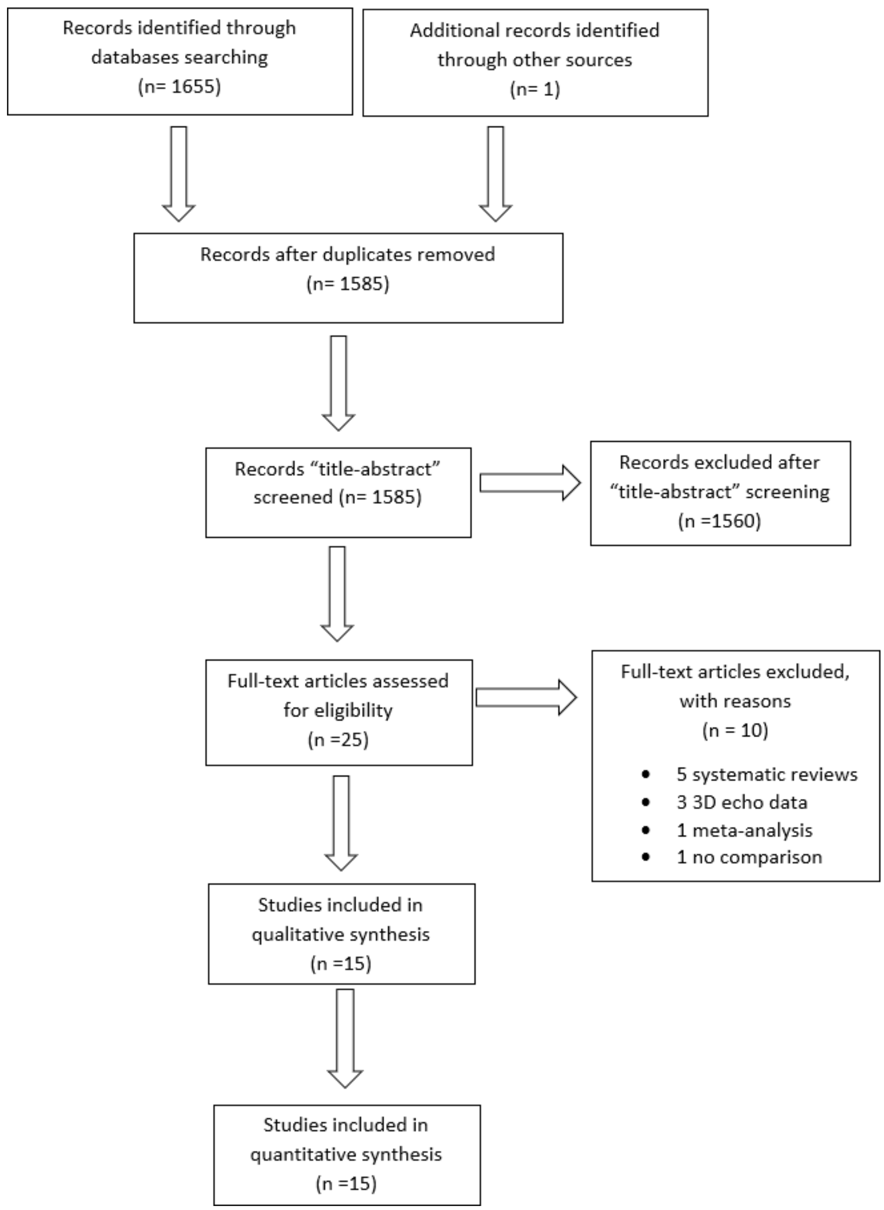

Figure 2: Forest plot depicting pooled SMD in GLS between RVF and non-RVF groups, stratified by imaging modality (TEE and TTE).

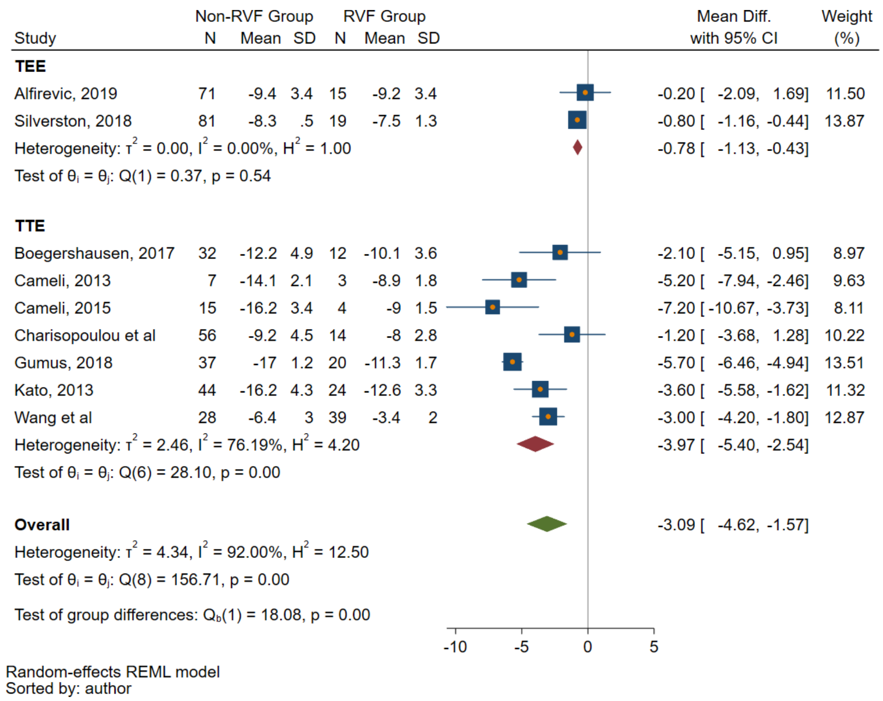

Figure 3: Forest plot showing pooled SMD in FWS between RVF and non-RVF groups, stratified by imaging modality (TEE and TTE).

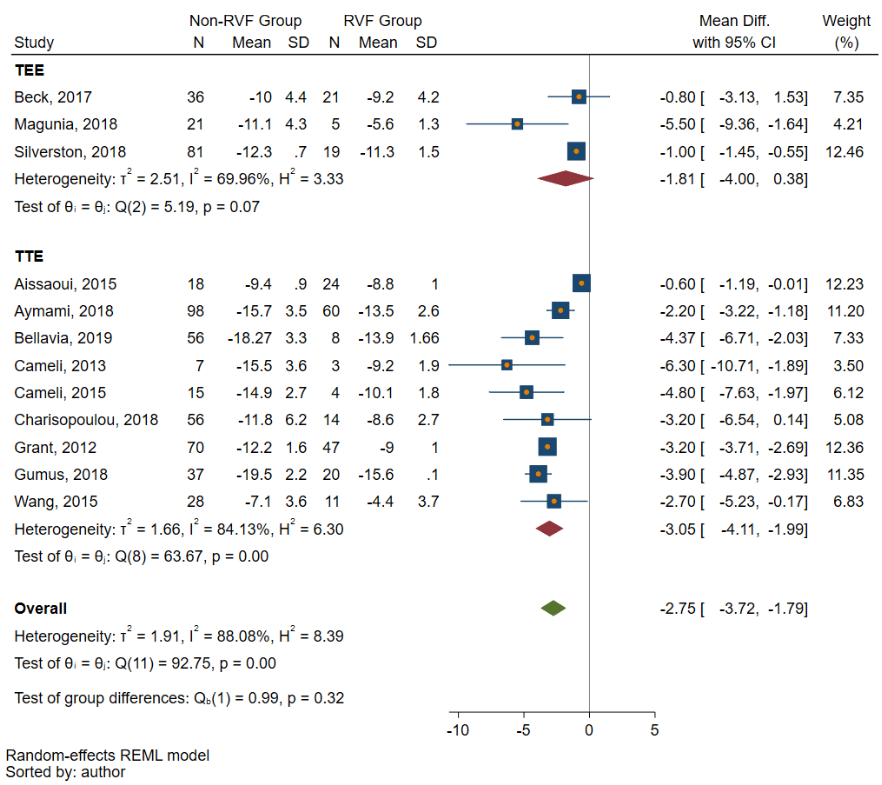

Figure 2: Forest plot showing pooled SMD in TTE-derived GLS between RVF and non-RVF groups in studies using ECHOPAC software.

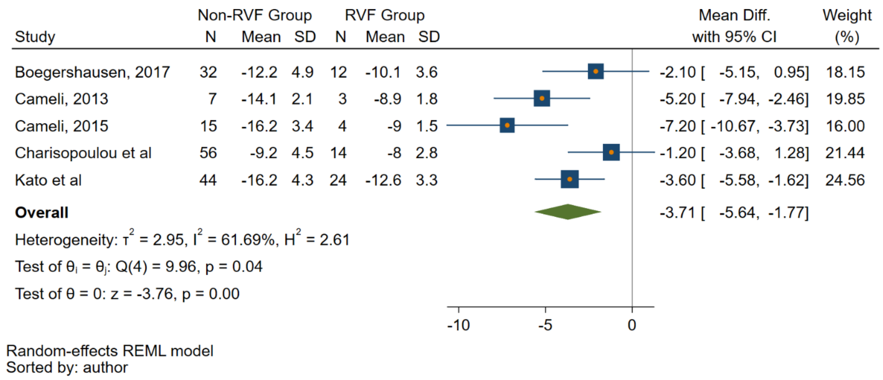

Figure 2: Forest plot showing pooled SMD in TTE-derived FWS between RVF and non-RVF groups in studies using ECHOPAC software., stratified by imaging modality (TEE and TTE).

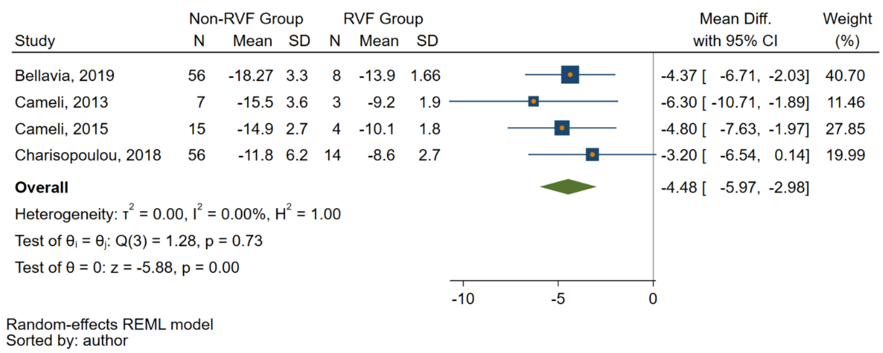

Table 1. Characteristics and Outcomes of Studies Included in the Analysis.

Study

Design

Modality

Software

Patients Number (N)

RVF,

n (%)

Inclusion criteria

Endpoints

Alfirevic, 2019

Retrospective

TEE

Ultrasound Philips platform

86

15 (17%)

LVAD patients with TAD, strain, and TAPSE measures available.

RVF occurring after LVAD implantation (before hospital discharge).

Assouie, 2015

Prospective

TTE

QLAB CMQ, Philips

42

24 (57%)

Patients undergoing LVAD therapy

RVF following LVAD implantation.

Aymami, 2017

Retrospective

TTE

Philips IE 33 US systems

158

60 (38%)

Patients who underwent implantation of CF- LVAD

Early ($<$ 30 days) postoperative RV failure

Beck, 2017

Retrospective

TEE

Syngo US Workplace

57

21(36.8%)

Patients with a non-pulsatile durable LVAD

A composite of 6-month death, $>$14 days inotropes, need for mechanical RV support, or device thrombosis requiring explant.

Bellavia, 2019

Retrospective

TTE

GE EchoPac

64

8 (11%)

Patients referred to HVAD implantation at ISMETT and Papa Giovanni XXIII.

RVF following LVAD implantation.

Boegershausen, 2017

Retrospective

TTE

GE EchoPac

54

13 (24%)

Patient with CF-LVAD implantation at the study site

RVF following CF-LVAD implantation.

Cameli, 2013

Prospective

TTE

GE EchoPac

10

3 (30%)

Patients referred for LVAD therapy.

RVF following LVAD implantation.

Cameli, 2015

Prospective

TTE

GE EchoPac

19

4 (16%)

Patients referred for LVAD therapy.

RVF following LVAD implantation.

Charisopoulou, 2018

Retrospective

TTE

Vivid 7 and EchoPac

70

14 (20%)

Patients who underwent CF- LVAD implantation

RV failure requiring RVAD implantation within 30 days.

Grant, 2012

Prospective

TTE

Syngo Velocity Vector Imaging, (Siemens)

117

47 (40%)

Patients undergoing LVAD implantation

RVF following LVAD implantation.

Gumus, 2018

Retrospective cohort study

TTE and TEE

Not Reported

57

20 (35%)

Patients with LVAD as a bridge to transplant.

RVF following LVAD implantation.

Kato, 2013

Prospective

TTE

GE EchoPac

68

24 (35.3%)

Patients undergoing LVAD

RVF following LVAD implantation.

Magunia, 2018

Retrospective study

TEE

TOMETEC Image-Arena

26

5 (19.2%)

Patients undergoing CF-LVAD implantation

RVF following CF-LVAD implantation.

Silverton, 2018

Retrospective

TEE

EchoInsight

100

19 (19%)

systolic heart failure patients with elective LVAD implantation.

RVF following LVAD implantation.

Wang, 2015

Prospective

TTE

Syngo Velocity Vector Imaging, (Siemens)

39

11 (39%)

Patients with second-generation CF- LVAD

Death or implantation of an RVAD due to acute RVF within 6 months of LVAD implant.

***Abbreviations** – TTE: transthoracic echocardiography; TEE: transesophageal echocardiography; LVAD: left ventricular assist device; CF-LVAD: continuous flow LVAD; RVF: right-ventricular failure; HVAD: HeartWare ventricular assist device.

Table 2. Definitions of Right Ventricular Failure (RVF) Across Included Studies.

Study	RVF definition
Alfirevic, 2019	The need for RVAD or prolonged (> 14 days) intravenous inotropic or inhaled vasodilator medications after LVAD implantation. Patients requiring RVAD owing to inability to separate from bypass during the LVAD procedure.
Assouie, 2015	The need for placement of a temporary RVAD or the use of inotropic agents for 14 days.
Aymami, 2017	Early (<30 days) RVF predefined according to the INTERMACS definition as sustained elevation of central venous pressure > 16 mmHg and the need for prolonged inotropes beyond 7 days, or the unplanned need for RVAD implantation.
Beck, 2017	Adverse events: A composite of one or more of the following: death within 6 months, >14 days on inotropes, need for mechanical RV support, or device thrombosis requiring explant.
Bellavia, 2019	The need for intravenous inotropes for >2 weeks; persistent RV stroke work index (RVSW) < 4.0 g/m2; or nitric oxide inhalation for > 48 h at any rotation speed or saline infusion; or presence of acute RVF when emergent/ urgent need for mechanical RV support was considered mandatory.

Study	RVF definition
Boegershausen, 2017	The need for an RVAD or the requirement of inhaled nitric oxide or inotropic therapy for >1 week any time after LVAD implantation in the presence of symptoms and signs of persistent RV dysfunction.
Cameli, 2013	The post-operative need of intravenous inotrope support for >14 days or of inhaled nitric oxide for >48 hours, or the need for right-sided circulatory support or RVAD, or for hospital discharge with an intravenous inotrope.
Cameli, 2015	The post-operative need of intravenous inotrope support for >14 days or of inhaled nitric oxide for >48 hours, or the need for right-sided circulatory support.
Charisopoulou, 2018	RVAD implantation within 30 days
Grant, 2012	The need for placement of an RVAD, or the use of inotropic agents for > 14 days.
Gumus, 2018	The need for RVAD, prolonged (> 14 days) intravenous inotropic or inhaled vasodilator medications after LVAD implantation, MAP < 55 mmHg, or CVP or right atrial pressure > 16 mmHg.
Kato, 2013	The need for salvage RVAD, or persistent need for inotrope and/ or pulmonary vasodilator therapy 14 days after surgery.
Magunia, 2018	Prolonged inotropic support for > 14 days after LVAD implantation or consecutive implantation of RVAD .
Silverton, 2018	14 consecutive days of inotrope therapy or subsequent RVAD implantation.
Wang, 2015	The need for continuous post-operative inotropic agents for >14 days, pulmonary vasodilator use (inhaled nitric oxide) > 48 hours, or right-sided mechanical support.

***Abbreviations** – LVAD: left ventricular assist device; RVAD: right ventricular assist device; RVF: right-ventricular failure; CVP: central venous pressure.

Table 3. Demographics (Age and Sex) and LVAD Type Across Included Studies.

Study	Age	Age	Sex (Male)	Sex (Male)	LVAD type	LVAD type
	No RVF	**RVF**	**No RVF**	**RVF**	**No RVF**	**RVF**
Alfirevic, 2019	58 ±12	56 ±14	57 (80%)	14 (93%)	HeartMate II: 36 (50.7) HeartMate III: 13 (18.3) HeartWare: 22 (31.0%)	HeartMate II: 7 (46.7%) HeartMate III: 4 (26.7%) HeartWare: 4 (26.7%)

Study	Age	Age	Sex (Male)	Sex (Male)	LVAD type	LVAD type
Assouie, 2015	60 (48-69)	52 (43-61)	18 (100%)	21 (88%)	—	—
Aymami, 2017	56.6 ±12.8	46.8 ±15.5	70 (71%)	45 (90%)	—	—
Beck, 2017	51.0 ±15.5	57.3 ± 10.5	32 (89%)	14 (67%)	HeartMate II: 31 (86) HeartWare: 5 (14)	HeartMate II :2 (10%) HeartWare :19 (90%)
Bellavia, 2019	59 ± 11	54 ± 13	51 (91%)	7 (88%)	—	—
Boegershausen, 2017	60.6 ±7.6	63.2±7.2	36 (88%)	10 (77%)	—	—
Cameli, 2013	66.4 (5.1)	65.8±4.8	6 (86%)	3 (100%)	—	—
Cameli, 2015	—	—	—	—	—	—
Charisopoulou, 2018	48 ± 12	45 ± 11	50 (89%)	9 (64%)	HeartMate III 4(10.8)	HeartMate III 4 (20)
Grant, 2012	58 (47–65)	—	92 (79%)	—	—	—
Gumus, 2018	40.0 ± 15.0	39.8 ± 22.6	34 (92%)	13 (65%)	HeartWare 21 (56.7)	HeartWare: 7 (35%)
Kato, 2013	62.5 ±12.4	62.8 ± 10.6	39 (89%)	22 (92%)	—	—
Magunia, 2018	64 ± 13	58 ± 30	19 (91%)	5 (100%)	Heartmate II: 14 (66.7%) Heartmate III: 4 (19%) HeartWare 3: (14.3%)	Heartmate II: 11 (20%) Heartmate III: 3 (60%) HeartWare: 1 (20%)
Silverton, 2018	60.6± 13.4	64± 11.2	71 (88%)	18 (95%)	HeartMate II: 39 (48.1) HeartMate III: 0 (0.0%) HeartWare: 37 (45.7%) Jarvik 2000: 4 (4.9%)	HeartMate II: 8 (42.1%) HeartMate III: 1 (5.3%) HeartWare 8: (42.1%) Jarvik 2000 2: (10.5%)
Wang, 2015	56±15	57±16	22 (78%)	9 (82%)	—	—

Table 4. Quality Assessment of Included Studies Using the Newcastle-Ottawa Scale (NOS).

	Selection (max of 4 stars)	Comparability (max of 2 stars)	Outcome (max of 3 stars)	Total Score (max of 9)	Overall Quality
Alfirevic, 2019	****	*	***	8	Moderate-to-high
Assouie, 2015	****	*	***	8	Moderate-to-high
Aymami, 2017	****	*	***	8	Moderate-to-high
Beck, 2017	***	*	***	7	Moderate-to-high

	Selection (max of 4 stars)	**Comparability (max of 2 stars)**	**Outcome (max of 3 stars)**	**Total Score (max of 9)**	**Overall Quality**
Bellavia, 2019	****	*	***	8	Moderate-to-high
Boegershausen, 2017	****	*	***	8	Moderate-to-high
Cameli, 2013	****	*	***	8	Moderate-to-high
Cameli, 2015	***	*	***	7	Moderate-to-high
Charisopoulou, 2018	***	*	***	7	Moderate-to-high
Grant, 2012	****	*	***	8	Moderate-to-high
Gumus, 2018	***	*	***	7	Moderate-to-high
Kato, 2013	****	*	***	8	Moderate-to-high
Magunia, 2018	****	*	***	8	Moderate-to-high
Silverton, 2018	****	*	***	8	Moderate-to-high
Wang, 2015	****	*	***	8	Moderate-to-high