REGIONAL RIGHT VENTRICULAR AND RIGHT ATRIAL STRAIN FOR PREDICTION OF EARLY AND LATE RVF FOLLOWING LEFT VAD IMPLANT: A MACHINE LEARNING APPROACH

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Abstract:	Background: Identifying candidates to left ventricular assist device (LVAD) surgery at risk of right ventricular failure (RVF) remains difficult. Our aim was to identify most accurate predictors of RVF among clinical, biological and imaging markers, assessed by agreement of different supervised machine learning algorithms Methods: Seventy-four patients, referred to Heartware LVAD since 2010 in 2 Italian centers were recruited. Biomarkers, RV standard and strain ECHO, as well as cath-lab measures were compared among patients who did not develop RV Failure (NO-RV, N = 56), those with Acute RVF (N =

8, 11%) or Chronic RVF (N=10, 14%). Logistic regression, Penalized Logistic Rgression, Linear Support Vector Machines and Naïve Bayes algorithms with Leave One Out validation were used to evaluate the efficiency of any combination of 3 collected variables in an "all-subsets" approach.
Results: Michigan Risk score combined with Central Venous Pression assessed invasively and Apical longitudinal systolic strain (sS) of the RV free wall were the most significant predictors of Acute RVF (Max ROC-AUC=0.95, 95% CI=0.91 – 1.00, by the Naïve Bayes), while the RV free wall sS of the middle segment Right atrial strain (QRS-synced), and TAPSE were the most significant predictors of Chronic RVF (ROC-AUC=0.97, 95% CI=0.91 – 1.00, according to Naïve Bayes)
Conclusions: Apical RV strain as well as RA strain provide complementary information, both critical to predict Acute and Chronic RVF, respectively.

USEFULNESS OF REGIONAL RIGHT VENTRICULAR AND RIGHT ATRIAL STRAIN FOR PREDICTION OF EARLY AND LATE RIGHT VENTRICULAR FAILURE FOLLOWING LEFT VENTRICULAR ASSIST DEVICES IMPLANT: A MACHINE LEARNING APPROACH

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Short Title: Deformation Analysis to Predict Right Ventricular Failure

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ABSTRACT

Background: Identifying candidates to left ventricular assist device (LVAD) surgery at risk of right ventricular failure (RVF) remains difficult. Our aim was to identify most accurate predictors of RVF among clinical, biological and imaging markers, assessed by agreement of different supervised machine learning algorithms.

Methods: Seventy-four patients, referred to Heartware LVAD since 2010 in two Italian centres were recruited. Biomarkers, RV standard and strain ECHO, as well as cath-lab measures were compared among patients who did not develop RV Failure (NO-RV, N = 56), those with Acute RVF (N = 8, 11%) or Chronic RVF (N=10, 14%). Logistic regression, Penalized Logistic Regression, Linear Support Vector Machines and Naïve Bayes algorithms with Leave One Out validation were used to evaluate the efficiency of any combination of three collected variables in an "all-subsets" approach.

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Conclusions: Apical RV strain as well as RA strain provide complementary information, both critical to predict Acute and Chronic RVF, respectively.

INTRODUCTION

Heart failure with reduced ejection fraction (HFrEF) is an emerging epidemic in adults aged 55 years or older in the European Union[1]. Heart transplantation (HTX), although effective, cannot be a generalizable treatment since there are not enough donors available for patients in need. Continuous Flow Left Ventricular Assist Devices (CF-LVADs) could be the alternative, but costs are still very high and this is partially due to related complications, such as Right Ventricular Failure (RVF)[2].

In facts, after LVAD implantation RV is exposed to the risk of failure: leftward shift of the interventricular septum (favored by the unloaded left ventricle) and the concomitant increase in RV preload, promoted by the device, disrupt the delicate RV geometry of an already impaired chamber, precipitating RVF in many cases. This usually happens within 2 weeks post-LVAD, but can rise up even later and portends a worse prognosis also in the long-term. Although several score systems have been defined to identify patients at risk[3-7], these are single centre experiences, retrospective analyses, and are most often focused on the out-dated pulsatile-flow LVADs. Finally, such score systems have high internal validity but usually low external validity (i.e. generalizability), since useful predictors have been defined and then validated using the same pool of patients/data.

Focusing on a homogeneous population of HFrEF patients referred specifically to the HeartWare HVAD/CF-LVAD (HeartWare, Oakville, California)[8] implantation, our aim in the present study was twofold: 1) to identify most accurate predictors of both early and late onset RVF among clinical, biological and imaging markers, including advanced RV as well as right atrial (RA) deformation analysis by echocardiography, and 2) to assure generalizability of our conclusions by employing machine learning algorithms applied to training and test (i.e. validation) sub-dataset.

METHODS

After Bioethical Committee approval, starting November 2010, all HFrEF patients referred to HVAD implantation at ISMETT and Papa Giovanni XXIII Hospital have been included in a centralized registry, built on clinical, biochemical, imaging and cath-lab data, collected as a result of the standard pre-operative work-up routinely performed on our study population. Patients with HFrEF judged unsuitable to LVAD (N = 22) by the Heart Team at each center, Patients undergoing replacement of an existing LVAD (N =1), or with a pre-operative plan for biventricular support with a total artificial heart or RVAD (N = 0), or who were supported with extracorporeal membrane oxygenation at the time of their echo (N = 0) were excluded.

Right Ventricular Failure and Primary Outcomes Definition

Acute RVF was defined as (1) need of a RV assist device (RVAD), or (2) 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, such as central venous pressure > 18 mm Hg with a cardiac index <2.3 L/min per square meter in the absence of elevated left atrial or pulmonary capillary wedge pressure (>18 mm Hg), cardiac tamponade, ventricular arrhythmias, or pneumothorax[9, 10].

Chronic RVF was defined as RV impairment, occurring after indexed hospital discharge and needing urgent re-admission to start IV diuretics and IV inotropes.

Detection of RVF was based on clinical findings, such as peripheral edema, weight gain, ascites and jugular venous distention. Heart failure related to device failure or suspected device failure, such as device thrombosis, inflow and outflow obstruction or drive-line fracture, was not considered as Chronic RVF. Each event was assessed prospectively by at least 2 reviewers (C.F. and S.S.), divergences were resolved by consensus.

Patients were subsequently divided into 3 groups based on the occurrence of post-operative RVF, as follows: Group I ("Acute-RVF"), Group II ("Chronic-RVF"), and Group III ("NO-RVF").

Primary end-points considered were: a) Development of Acute RVF (Acute-RVF), b) Development of Chronic RVF (Chronic-RVF), and c) Development of RVF anytime during follow-up (ANY-RVF),

Beyond these primary outcomes other clinical outcomes were collected as well and were considered as possible predictors of RVF, including major ventricular arrythmias, cardiac tamponade, transitory ischemic attack and stroke (either ischemic or hemorrhagic), LVAD thrombosis and major infective episodes. Finally, all-causes mortality was also collected (Median follow-up: 14 months, Range: 1-76 months).

Collected Variables

Demographic, clinical, biochemical and echocardiographic data were collected within 72 hrs preceding the LVAD implant, while invasive hemodynamic measurements by right heart catheterization (RHC) were obtained 5-7 days ahead of surgery.

Available risk scores for RVF were computed as well. In particular, the following scores were collected: HMRS HeartMate II Risk Score , Kormos Score, Michigan Score, MELD, MELD-NA, MELD XI[6, 7, 11-14]

Standard Echocardiography

Pre-operative transthoracic echocardiograms were analyzed by a reader blinded to clinical outcomes (D.B.). All echocardiographic examinations were performed with a commercially available instrument (Vivid E90 System; Vingmed, General Electric, Milwaukee, Wisconsin). Standard LV systolic and diastolic parameters from 2D and Doppler echocardiography, as well as pulsed-wave tissue

Doppler imaging of the mitral medial annulus were acquired and measured as previously described[15]. RV wall thickness and RV end-diastolic diameters at basal and midventricular levels were measured. RV end-diastolic and end-systolic 4-chamber areas were derived by manually tracing the endocardial. RV fractional area change (FAC) was calculated. To obtain tricuspid annulus plane systolic excursion (TAPSE), the apical 4-chamber view was used, and an M-mode cursor was placed through the lateral tricuspid annulus in real time. Pulsed wave tissue Doppler Imaging was performed, placing the sample volume on the lateral tricuspid annulus in the apical four chamber view, and S' velocity was collected. RV systolic pressure (RVSP) was calculated by inserting the tricuspid regurgitation velocity, obtained with continuous-wave Doppler, into the simplified Bernoulli equation. Diastolic Pulmonary Artery Pressure was computed from the pulmonary valve regurgitation (PR) flow according to the following equation: 4(PR-end velocity)2 + RA pressure[16].

2D Speckle Tracking Analysis

Both RV and RA Strain measurements were performed using standard commercial software (EchoPAC version BT13; GE Healthcare, Fairfield, Connecticut).

A narrow-sector view of the RV free wall was acquired using an RV-optimized apical 4-chamber view, in order to maintain frame rate > 80 frames per second.

Longitudinal systolic strain (sS) and strain rate (sSR), as well as early diastolic Strain Rate (dSR-E) of the RV free wall were collected. The endocardial border of the RV was traced, and strain curves were generated automatically for each of 3 segments (Figure 1A). The peak strain for the 3 segments corresponding to the RV free wall was averaged to produce a global longitudinal strain measurement.

To obtain RA strain, a narrow sector and zoomed view of the RA was obtained from an apical 4 chambers view. QRS complex served as the first reference frame. For current study the Right Peak Atrial Longitudinal strain (R-PALS) was measured as: εS + εA, and expressed as absolute number[17] (Figure 1B).

Data Analysis

Comparisons between groups and univariate as well as multivariable logistic regression were performed using STATA version 14.1 (Stata-Corp LP, College Station, TX). Continuous variables were compared using the unpaired t test for normally distributed variables or the Wilcoxon rank sum test according to normal/non normal distribution. The chi-square or Fisher exact test was used for categorical variables.

Serum levels of NT-proBNP, Blood Urea Nitrogen (BUN), creatinine, alanine transaminase (ALT), were log-transformed to meet the distributional assumptions.

Univariate logistic regression analysis was performed to calculate an odds ratio for different forms of RVF and for each baseline variable, using binary outcomes as follows: RVF (acute or chronic) / NO-RVF, Acute-RVF / No-Acute RVF and Chronic RVF / NO-Chronic RVF.

Receiver operating characteristic curves were generated and compared[18]. A series of exploratory models was created by multivariable logistic regression, using a mixed (i.e. backward and then forward) stepwise approach for model building, forcing the algorithm to identify the 3 most accurate predictors of the following 3 primary outcomes: Acute RVF only, Chronic RVF only, or any event of RVF respectively. "Best" models were selected according to the Bayesian Information Criterion (BIC). Candidate variables were selected on clinical grounds, including most used risk score systems (see above) within the categories of clinical features, standard biochemical markers, hemodynamics, echocardiographic assessment of LV, RV or RA function, and therapy. Data are presented as mean value ± SD, median value ± inter-quartile range or count (%), as appropriate. A difference was considered statistically significant when the p-value was less than 0.05. In the multivariable models, a variable was considered a significant predictor of primary end-points when the p-value was less than 0.1.

Machine Learning Algorithms

Machine Learning algorithms were applied using R Software, version 3.3.3 (R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/) and specifically the following packages were implemented: CARET, GLMNET, and E1071[19-21] .

As a preliminary step, in order to identify most performing machine learning algorithms for our dataset, we have tested several algorithms, both linear and non linear (including classification and regression trees) as well as ensemble methods. The 3 algorithms with the highest discrimination accuracy and Kappa statistics were selected and fine tuned to perform ultimate analysis.

Penalized Logistic regression

In brief, The *elastic-net* penalty is controlled by α, and bridges the gap between lasso (α=1, the default) and ridge (α=0). The tuning parameter λ controls the overall strength of the penalty. In order to identify "best" values of α and λ for our data, an α / λ grid was created and best values were identified using Repeated K-Fold cross validation method. Penalized Logistic regression was therefore implemented to train linear classifiers by using any three predictors available in our dataset. For each of the three considered outcomes (Acute RVF, Chronic RVF and ANY-RVF) compared with the NO-RVF outcome, we selected the most accurate GLMNET model. To test the predictive accuracy of the classifiers we calculated the area under the ROC curve (AUC) after performing a

repeated k-fold cross validation. We also computed the performance of the classifier trained with the entire dataset (SELF). K-Fold Cross Validated-AUC and SELF-AUC values were used to select the best classifier.

Support Vector Machines (SVM)

Briefly, in the three dimensional space of predictors, where each point is characterized by the patient's values of three selected predictors, SVM computes the best surface able to separate two classes of patients' outcome. The *cost* parameter defines the amount of penalty assigned to each mis-classification. Three values of *cost* were considered (0, 0.5, 1) and the classifier with the best performance was selected and associated to the used triplet of predictors.

For each of the three considered outcomes (RVF-All, Acute RVF and Chronic RVF) compared with the No RVF outcome, we selected the most accurate SVM model. To test the predictive accuracy of the classifiers we calculated the area under the ROC curve (AUC) after performing a Leave One Out validation (LOOV). We also computed the performance of the classifier trained with the entire dataset (SELF). LOOV-AUC and SELF-AUC values were used to select the best classifier.

Naïve Bayes

The naive Bayes classifier computes the conditional a-posterior probabilities of a categorical class variable, i.e. RVF/NO-RVF, given independent predictor variables, i.e. the clinical features. It uses the naïve Bayes rule to compute the probabilities and it assumes that each feature is conditionally independent of every other feature. We used the R function NaiveBayes[22] implemented in the klaR package.

RESULTS

Demographic, Clinical Characteristics and Biochemical Markers

Between January, 2010, and March 31, 2017, the HeartWare HVAD device was implanted in 74 patients at ISMETT center (N =45) and Papa Giovanni XXIII Hospital (N=29), who met the clinical criteria for study inclusion. Bridge to Transplant was the primary strategy in 43 (58%) patients, while 16 Patients (22%) were referred to LVAD as destination therapy, and the remaining 15 patients (20%) were implanted in a bridge to candidacy perspective.

Out of 74 patients, N=8 (11%) developed Acute RVF and N=10 (14%) Developed Chronic RVF. A comparison of the clinical characteristics of the 3 groups included in the study is shown in Table 1: there were no differences among the Acute-RVF, Chronic-RVF and No-RVF groups according to demographic, biometric and vital signs at baseline as well as INTERMACS and NYHA class pre-Implant. Optimal medical treatment, including furosemide dosage and way of administration was similar among RVF and NO-

RVF groups as well. Considering computed risk scores for RVF, only the Michigan score (Figure 1C) and MELD-XI were higher in patients that developed Acute- as well as Chronic-RVF, as compared to No-RVF group.

Finally, number of patients needing mechanical ventilation, intra-aortic balloon pump (IABP), or ExtraCorporeal Membrane Oxygenation (ECMO) were minimal and comparable among the 3 groups.

Total bilirubin pre-implant was elevated in Acute-RVF patients as compared to Chronic-RVF or NO-RVF groups (Table 2). Blood Urea Nitrogen (BUN) was higher and platelets were lower in patients that developed Chronic-RVF as compared to NO-RVF group.

Standard and Strain Echocardiography

LV-EF was marginally lower in Acute-RVF group as compared to NO-RVF, while LA volume as well as LV dimensions (either systolic or diastolic) were comparable among the groups (Table 3A).

Regarding the RA or the RV, geometry was similar among groups: RA volume, RV end diastolic dimensions, as well as RV end-diastolic or end-systolic area were all comparable among patients with RVF and those with NO-RVF. ECHO parameters of RV performance, including TAPSE, tricuspid annular S' velocity, and RV fractional area change were similar as well. Finally, also prevalence of moderate to severe tricuspid regurgitation, estimated systolic or diastolic pulmonary artery pressure (PAP), as well as estimated RA pressure by inferior vena cava dimensions and collapsibility were comparable among RVF and NO-RVF patients.

Right Ventricular Free Wall Deformation Analysis

Although RV systolic strain (sS) was < -20%, and therefore impaired, in all recruited patients, RV dysfunction as assessed by either longitudinal sS or sSR was greater in patients who developed Acute- or Chronic-RVF as compared to NO-RVF (Table 3B). On the other hand, dSR-E was comparable among RVF and NO-RVF groups. According to segmental analysis, the RV longitudinal sS of the Apex was significantly lower in either Acute- or Chronic-RVF groups as compared to NO-RVF patients (Figure 1D). RV Longitudinal sSR of the basal and middle segment was lower in Acute-RVF as compared to NO-RVF but was similar at all segments between patients with Chronic-RVF and NO-RVF.

RA total strain was comparable between patients in the Acute-RVF and NO-RVF, while it was significantly reduced in the Chronic-RVF as compared to NO-RVF group (Figure 1E).

Right Heart Catheterization

Patients with either Acute- or Chronic-RVF had higher central venous pressure (CVP, i.e. RA pressure) as compared to NO-RVF (Table 4). The difference between diastolic PAP and pulmonary capillary wedge pressure was higher in Chronic-RVF group as compared to NO-RVF. No other hemodynamic measurements collected invasively were different between RVF and NO-RVF groups.

All-causes Mortality and Other HVAD complications

Distribution of several LVAD-related complications was similar across RVF groups, and no complication was a significant predictor of any form of RVF (Table 5). Overall, 23 LVAD patients died at follow-up. Although patients with RVF (both acute and chronic) had higher all-causes mortality compared to the NO-RVF group, such difference was not significant.

Predictors of Acute RVF

According to univariate, simple logistic regression, MELD-XI and Michigan Scores were the only significant predictors of Acute-RVF among demographic, clinical and biochemical markers (serum total bilirubin was marginally significant, Tables 1-2) and a Michigan Score ≥ 6.0 discriminated between Acute-RVF and NO-RVF groups with a sensitivity of 50% and a specificity of 89%. Among standard echocardiographic measurements, no predictors were significantly associated to acute-RVF, although RV end-diastolic area was marginally significant. RV free wall Longitudinal sS average was a significant predictor as well and a low sS of the RV apex was specifically associated to higher risk of developing Acute-RVF already at the univariate logistic regression (Tables 3A-B) (apical sS less negative than -12.7 % had a sensitivity of 83.2% and a specificity of 81.4% in discriminating between Acute-RVF and NO-RVF).

Higher CVP at RHC was the only invasive parameter to predict greater risk of Acute-RVF (Table 4, a CVP ≥ 13 mmHg discriminated between Acute-RVF and NO-RVF groups with a sensitivity of 38% and a specificity of 91%).

According to multivariable logistic regression and Machine learning algorithms both set to identify the most accurate 3 predictors of Acute-RVF, there was fair agreement among the different analytic methods implemented: as depicted in Table 6A (showing ROC-AUC and AUC 95% CIs obtained on the training dataset), Table 6B (showing ROC-AUC and AUC 95% Cis obtained on the testing dataset) and Figure 2A-B, the combination of the Michigan score, longitudinal sS of the Apical segment of the RV free wall, and the CVP reached the highest accuracy in discriminating between Acute-RVF and NO-RVF patients. Comparable accuracy was obtained considering RA area by ECHO instead of CVP, while the combination of RV apical sS, CVP and RV stroke work index was the third most accurate triad, although its accuracy was slightly lower than the first 2 options.

Predictors of Chronic RVF

According to univariate analysis, history of cardiac surgery (i.e. previous sternotomy) was the only predictor of Chronic-RVF, while low circulating platelets was marginally associated to Chronic-RVF (Tables 1-2). Among standard echocardiography higher LA area/volume, lower RV-FAC, TAPSE and tricuspid annulus S' velocity were all predictive of Chronic-RVF. Longitudinal sS of the RV free wall was also associated to Chronic-RVF and sS of the RV middle segment less negative than – 13% had the highest accuracy

in predicting Chronic-RVF, with a sensitivity of 67% and a specificity of 91%. Likewise, RA PALS and RA total strain were both predictive of higher risk (Table 3A-B). In particular, a total RA strain ≤ 11.13 had a sensitivity = 92% and specificity = 63%. Finally, among invasive hemodynamic parameters, higher difference between diastolic PAP and pulmonary capillary wedge pressure was the only significant predictor of Chronic-RVF at the univariate analysis (Table 4).

According to the multivariable logistic regression and different machine learning algorithms, longitudinal sS of the RV free wall at the middle segment, RA total strain and LA volume (index) were the 3 best predictors of Chronic-RVF, combination of RV sS with TAPSE or the need for milrinone drip pre-implant were also highly predictive of Chronic-RVF (Table 6A-B).

Predictors of Either Acute or Chronic (ANY) RVF

According to simple logistic regression, the following parameters were significant predictors of ANY-RVF Acute or chronic): Michigan score index (OR 1.43, p = 0.04) , LA Volume Index (OR 1.03, p = 0.01), RV End systolic Area (OR = 1.15 p = 0.03), longitudinal RV sS average (OR 1.49 p < 0.001) as well as sS of the RV Apical and Middle segment (OR 1.41 and 1.55 respectively, p-values < 0.001 for both) , longitudinal RV free wall sSR (OR 2.5 p 0.04) RA PALS as well as RA Total Strain (OR 0.86 and 0.82,p-values 0.04 and 0.01, respectively). Finally CVP (OR 1.19, p 0.01) was the only invasive hemodynamic measure to be associated to ANY-RVF.

The combination of global longitudinal sS of the RV free wall, CVP, and either TAPSE, RA Total Strain, or the velocity time integral of the tricuspid regurgitation flow at the CW-Doppler spectral analysis, were the most accurate predictors of any form of RVF, according to the different algorithms deployed.

DISCUSSION

To our knowledge, this is the first study to have identified independent predictors of both acute and chronic RVF in patients undergoing specifically HVAD implantation, employing innovative imaging parameters (regional RV free wall as well as RA strain) as well as alternative approaches of data analysis (machine learning algorithms).

The current investigation had several main findings. First, Longitudinal sS of the RV free wall pre-implant, and in particular sS of the Apical segment, had the highest accuracy in identifying patients who will develop any form of RVF (either acute or chronic) or early-RVF, respectively. Second, RA strain is specifically impaired in patients referred to HVAD who have the greatest risk of developing late onset RVF. Finally, the integration of the Michigan Score Index with deformation analysis of the right chambers by ECHO and

CVP by Right Heart Catheterization reached the highest accuracy in discriminating patients at risk of developing either acute o chronic RVF.

CF-LVADs could realistically be the only alternative to transplantation, although high costs and major complications are major limiting factors to wide use of such devices. Among major complications, early- as well as late-onset RVF still occurs in roughly 29% of patients[2] and results upon a 6-fold increase risk of death. So, the depiction of reliable, independent and generalizable predictors of such complication is of paramount importance in this context.

Predicting Early Onset RVF post HVAD

First of all, results of our prospective registry has confirmed that no demographic or biometric characteristic is able to identify patients at risk of RVF, as initially believed. This has also been suggested by a recent meta-analysis completed by our group[2].

On the other hand, biomarkers of liver function, and total bilirubin in particular, were elevated in patients who developed acute RVF, as a proxy of liver congestion due to increased RV end-diastolic pressure in a dysfunctional chamber. It is therefore not surprising that the Michigan RVF risk score in our study population was an independent predictor of acute RVF, consistently in all mutivariable combination of models we have tested.

In agreement with most recent publications [2, 3] CVP was the only hemodynamic measurement, collected at RHC, that was higher in Acute-RVF as compared to NO-RVF group. In facts CVP was also an independent predictor of either Acute-RVF or ANY-RVF. The equation “higher CVP = higher RA pressure and higher RV End diastolic pressure” is straightforward, but CVP is also one of those parameters effectively modifiable in the pre-implant phase to decrease risk of early post-operative RVF. It is indeed common ICU practice in our institution to assess CVP 48 hrs pre-implant in order to start an RV unloading strategy by aggressive IV diuretics and/or inotropes or even prophilactic intra-aortic balloon pump placement if needed. Several studies have reported RV-SWI to be abnormally low in patients with early onset RVF and most recent international guidelines highlight predictive role of such parameter in identifying patients at risk of Acute-RVF[23]. We have recently shown that role of RV-SWI as predictor of Acute-RVF relies primarily on oldest studies based on pulsatile flow (PF) LVADs, and its usefulness in CF-LVADs is lower [2]. Furthermore, In the present prospective study RV-SWI was highly variable and therefore not different among groups. However, 2 out of 3 machine learning algorithms identified it as an independent predictor of Acute-RVF, when it is combined with RV free wall strain and RA area. In summary, although our observations confirm RV-SWI as a significant predictor of Acute RVF, it should be considered as a complementary parameter to RV free wall Strain by ECHO, and assessment of other hemodynamic measures (i.e. CVP) should be a priority in patients referred to HVAD (CF-LVAD) implant.

Standard echocardiographic measurements were not different between patients with early onset RVF and those who did not develop RVF, so it is somewhat expected that no standard ECHO measure but RA area was useful in predicting Acute-RVF (see after). On the opposite RV free wall systolic deformation analysis was helpful: both global longitudinal RV free wall sS and sSR were increased (i.e. less negative) in Acute-RVF as compared to NO-RVF. On the other hand, longitudinal diastolic strain rate, was similar between the 2 groups and was uninfluent in Acute RVF prediction. To date, 3 studies have reported that RV longitudinal sS is an independent predictor of Acute RVF[24-26] one the which enrolled the biggest sample number [24]. We have confirmed the importance of global RV free wall sS in predicting Acute-RVF, but we have gone a step further, focusing our analysis on the segmental evaluation of the RV free wall, as well as the RA strain. In our population, the sS of the RV free wall at the apex was substantially increased (i.e. it was less negative) at baseline in patients who developed Acute-RVF and was identified as one of the 3 most accurate predictors of early onset RVF by standard or alternative classification algorithms. Why the apex of the RV is the most impaired segment in this population is uncertain, but segmental regionality by strain is quite common in cardiomyopathies [27] and previous research may help in understanding this phenomenon: Kulkusky and coworkers[28] were the first to report an RV Apex to Base strain gradient already in healthy elderly subjects, showing that apical Doppler sS was lower as compared to the basal RV free wall sS. The observation was subsequently confirmed in the pulmonary hypertension arena: 2 groups have independently shown that either adult[29] or pediatric[30] patients with pulmonary hypertension had a more severe impairment of the Apical (or middle) sS as compared to the Basal RV free wall sS, and that this phenomenon was absent in controls. Finally, similar findings have been recently reported in the same population employing 3D Speckle tracking[31]. It could be argued that orientation of RV apical myo-fibers is oblique at the subendocardium as compared to the basal region that preserve a more longitudinal orientation[32]. An appealing hypothesis is that apical RV deformation is mostly influenced by the LV dimensions, so that in patients with higher LV volume (i.e. greater apex) the RV apex is compressed affecting strain specifically at that level. However, independently on the reason, our results highlight one of the main benefits offered by strain analysis, that is the opportunity to perform an exaustive regional analysis of the myocardial deformation. It is therefore important to avoid combining/averaging values, and report segmental strain separately.

Interestingly, RA strain was comparable between Acute-RVF and NO-RVF patients, and was not associated to early onset RVF in our population. The importance of RA area in this context is reasonable and is consistent with the higher CVP(RA pressure) documented in this group of patients.

Predicting Late Onset RVF post HVAD

Counting on a longer follow-up we have also looked for independent predictors of Chronic-RVF: first of all incidence of Chronic-RVF in our sample was consistent with available reports[33, 34]. Likewise, patients developing late onset RVF had comparable survival as compared to NO-RVF patients, although, due to relatively small number of events, we had no chance to perform stratified analysis or check subgroups. Moreover, it is noteworthy that in our population, there is no overlapping between Acute- and Chronic-RVF: in other words, patients developing post-operative RVF were different from those readmitted for late onset RVF. This suggests that Acute- and Chronic-RVF should not be considered as a unique disease with wide spectrum and timing of clinical presentation, rather distinct issues affecting RV, with different patho-physiology and risk factors.

Although BMI was not associated to late onset RVF in our population [33], consistently with Takeda and collaborators , patients at higher chronic-RVF risk had greater BUN levels and lower platelets. The explanation of pre-implant milrinone drip as an independent predictor of late onset RVF is not immediately evident: according to our common protocol (implemented either at ISMETT and at Papa Giovanni Hospital), milrinone is begun 24-48 hr ahead of LVAD implant, in those patients with extremely low LV-EF and high trans-pulmonary gradient at the RHC, to provide inotropic support at both ventricles at the same time reducing pulmonary resistances. In other words, milrinone is used in patients at higher risk of developing early onset RVF to reduce such risk. Milrinone could therefore be really helpful in preventing acute RVF, but it cannot influence RV performance in the long term, so that patients that need the drip are also those at higher risk of RVF after hospital discharge.

Surprisingly, ECHO measurements collected pre-implant are reasonably useful in predicting RVF occurring several months after implantation: Left Atrial volume is a well known indicator of LV filling pressures[35]. Since higher LV filling pressure is necessarily related to higher RV afterload, is perhaps not surprising that patients with higher LA dimensions have higher risk of late onset RVF. Regional longitudinal sS of the RV free wall is useful in predicting chronic RVF too, and deformation analysis of the middle segment seems more accurate than apical strain to assess long-term risk of RVF. Furthermore, we for the first time report the importance of assessing RA performance by total strain, to stratify the risk of patients with LVAD in the long-term. It is in facts reasonable that RA function more than the mere chamber dimensions, is helpful in identifying patients with chronically high CVP, specifically due to advanced RV impairment. Finally, it is worth to remark the role of a simple and immediate measurement such as TAPSE in this context: consistently with previous reports [36], we confirm that TAPSE at pre-implant is not useful in predicting early, post-operative RVF. Nonetheless, TAPSE has been identified by several algorithms as an independent predictor of late onset RVF in this population. Putting all together, we can legitimately speculate that loading conditions and volemic status are more important than

intrinsic myocardial performance in determining early RVF, while RV muscle function is the predominant factor in predicting late onset RVF.

Predicting any form of RVF in patients undergoing HVAD implantation

Combining acute and chronic RVF events improved statistical power and offered the best way to define "overall" risk of RVF in this population: it is indeed not surprising that global average of longitudinal RV free wall sS was the main predictor of any form of RVF, being a combined parameter of apical strain (useful for acute-RVF prediction) and middle segment strain (helpful for late onset RVF prediction). CVP, as an indirect measure of RV impairment, is extremely useful for defining risk of acute-RVF, but it is evidently involved in late onset events as well, so to be among the parameters with the highest predictive accuracy of any form of RVF. This supplementary analysis confirmed the role of RA total strain and TAPSE in risk stratification, while the tricuspid regurgitation velocity time integral (an indicator of mPAP[37] seems useful only when it is combined with RV strain and CVP.

Limitations

The primary limitation of our study is the relatively low number of events, either in the acute- or in the chronic- context. Some level of uncertainty due to low statistical power is also shown by the wide ROC-AUC 95% confidence intervals, in particular those obtained in the testing dataset. However, this limitation is partially mitigated by the highly homogeneous study population (all patients were referred to HVAD) and by the specific analysis employed: although as expected ROC-AUCs of the multivariable models were all reduced when applied to a new ("test") subset of patients, machine learning algorithms have substantially confirmed results obtained by standard logistic regression. This assures generalizability and comfort our conclusions. Finally, our analysis is consistent with previous reports and extend available knowledge highlighting the importance of regional strain assessment of the RV as well as the RA deformation.

Another weakness of our analysis is the definition of either Acute- as well as Chronic-RVF: although we have relied on the most recent guidelines[10] such rigid definition has been questioned and a more flexible classification based on clinical severity of Acute-RVF has been proposed[38]. Finally, although no formal consensus has been published we have defined late onset RVF according to research groups that have worked in the field, using a reasonable definition based on clinical assessment[34, 39].

CONCLUSIONS

In conclusion, predicting RVF following LVAD implantation cannot rely on just one parameter, and several factors, including clinical assessment, as well as hemodynamic, biochemical and imaging markers need to be considered together. Among available score

systems, the Michigan risk score has the highest accuracy in identifying patients at risk of early onset RVF among those referred specifically to HVAD implant. Such risk is further improved by the integration with the apical systolic strain of the RV free wall and CVP pre-implant. Strain of the middle segment of the RV free wall as well as RA strain and TAPSE are helpful in predicting late onset RVF, so we recommend to complete a regional as well as global strain assessment of both RV free wall and RA when standard measures of RV performance by ECHO (i.e. TAPSE) have been collected, to assess the overall risk of developing RVF post-HVAD either in the short- as well as in the long-term. Further studies enrolling bigger sample of patients and different LVADs models are certainly warranted to confirm our results.

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REFERENCES

1. Bleumink GS, Knetsch AM, Sturkenboom MC, et al. Quantifying the heart failure epidemic: prevalence, incidence rate, lifetime risk and prognosis of heart failure The Rotterdam Study. *Eur Heart J* 2004; **25**(18): 1614-9.
2. Bellavia D, Iacovoni A, Scardulla C, et al. Prediction of right ventricular failure after ventricular assist device implant: systematic review and meta-analysis of observational studies. *Eur J Heart Fail* 2017; **19**(7): 926-46.
3. Atluri P, Goldstone AB, Fairman AS, et al. Predicting right ventricular failure in the modern, continuous flow left ventricular assist device era. *The Annals of thoracic surgery* 2013; **96**(3): 857-63; discussion 63-4.
4. Dang NC, Topkara VK, Mercando M, et al. Right heart failure after left ventricular assist device implantation in patients with chronic congestive heart failure. *The Journal of heart and lung transplantation : the official publication of the International Society for Heart Transplantation* 2006; **25**(1): 1-6.
5. Fitzpatrick JR, 3rd, Frederick JR, Hsu VM, et al. Risk score derived from pre-operative data analysis predicts the need for biventricular mechanical circulatory support. *The Journal of heart and lung transplantation : the official publication of the International Society for Heart Transplantation* 2008; **27**(12): 1286-92.
6. Kormos RL, Teuteberg JJ, Pagani FD, et al. Right ventricular failure in patients with the HeartMate II continuous-flow left ventricular assist device: incidence, risk factors, and effect on outcomes. *The Journal of thoracic and cardiovascular surgery* 2010; **139**(5): 1316-24.
7. Matthews JC, Koelling TM, Pagani FD, Aaronson KD. The right ventricular failure risk score a pre-operative tool for assessing the risk of right ventricular failure in left ventricular assist device candidates. *J Am Coll Cardiol* 2008; **51**(22): 2163-72.
8. https://www.heartware.com/. https://www.heartware.com/.
9. Kirklin JK, Naftel DC, Pagani FD, et al. Sixth INTERMACS annual report: a 10,000-patient database. *The Journal of heart and lung transplantation : the official publication of the International Society for Heart Transplantation* 2014; **33**(6): 555-64.
10. Feldman D, Pamboukian SV, Teuteberg JJ, et al. The 2013 International Society for Heart and Lung Transplantation Guidelines for mechanical circulatory support: executive summary. *The Journal of Heart and Lung Transplantation* 2013; **32**(2): 157-87.
11. Griffith BP, Kormos RL, Borovetz HS, et al. HeartMate II left ventricular assist system: from concept to first clinical use. *The Annals of thoracic surgery* 2001; **71**(3 Suppl): S116-20; discussion S4-6.
12. Kamath PS, Wiesner RH, Malinchoc M, et al. A model to predict survival in patients with end-stage liver disease. *Hepatology* 2001; **33**(2): 464-70.
13. Ruf AE, Kremers WK, Chavez LL, Descalzi VI, Podesta LG, Villamil FG. Addition of serum sodium into the MELD score predicts waiting list mortality better than MELD alone. *Liver transplantation : official publication of the American Association for the Study of Liver Diseases and the International Liver Transplantation Society* 2005; **11**(3): 336-43.
14. Heuman DM, Mihas AA, Habib A, et al. MELD-XI: a rational approach to "sickest first" liver transplantation in cirrhotic patients requiring anticoagulant therapy. *Liver transplantation : official publication of the American Association for the Study of Liver Diseases and the International Liver Transplantation Society* 2007; **13**(1): 30-7.
15. Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *Journal of the American Society of Echocardiography* 2015; **28**(1): 1-39. e14.
16. Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the american society of echocardiography and the European association of cardiovascular imaging. *Journal of the American Society of Echocardiography : official publication of the American Society of Echocardiography* 2015; **28**: 1-39.e14.
17. Vieira MJ, Teixeira R, Goncalves L, Gersh BJ. Left atrial mechanics: echocardiographic assessment and clinical implications. *Journal of the American Society of Echocardiography : official publication of the American Society of Echocardiography* 2014; **27**(5): 463-78.
18. Hanley JA, McNeil BJ. The meaning and use of the area under a receiver operating characteristic (ROC) curve. *Radiology* 1982; **143**(1): 29-36.
19. Max Kuhn. Contributions from Jed Wing SW, Andre Williams, Chris Keefer, Allan Engelhardt, Tony Cooper, Zachary Mayer,, Brenton Kenkel tRCT, Michael Benesty, Reynald Lescarbeau, Andrew Ziem, Luca Scrucca, Yuan Tang, Can Candan and Tyler, Hunt. caret: Classification and Regression Training. R package version 6.0-77. 2017. https://CRAN.R-project.org/package=caret.

20. Friedman J, Hastie T, Tibshirani R. Regularization Paths for Generalized Linear Models via Coordinate Descent. *Journal of statistical software* 2010; **33**(1): 1-22.
21. Cortes CV, V. . Support-vector network. Machine Learning. 1995; **20**: 1-25.
22. K.M. Al-Aidaroos AABaZO. Medical Data Classification with Naive Bayes Approach. *Information Technology Journal* 2012; **11**: 1166-74.
23. Feldman D, Pamboukian SV, Teuteberg JJ, et al. The 2013 International Society for Heart and Lung Transplantation Guidelines for mechanical circulatory support: executive summary. *The Journal of heart and lung transplantation : the official publication of the International Society for Heart Transplantation* 2013; **32**(2): 157-87.
24. Grant AD, Smedira NG, Starling RC, Marwick TH. Independent and incremental role of quantitative right ventricular evaluation for the prediction of right ventricular failure after left ventricular assist device implantation. *J Am Coll Cardiol* 2012; **60**(6): 521-8.
25. Kato TS, Jiang J, Schulze PC, et al. Serial echocardiography using tissue Doppler and speckle tracking imaging to monitor right ventricular failure before and after left ventricular assist device surgery. *JACC: Heart Failure* 2013; **1**(3): 216-22.
26. Cameli M, Lisi M, Righini FM, et al. Speckle tracking echocardiography as a new technique to evaluate right ventricular function in patients with left ventricular assist device therapy. *The Journal of heart and lung transplantation : the official publication of the International Society for Heart Transplantation* 2013; **32**(4): 424-30.
27. Bellavia D, Pellikka PA, Abraham TP, et al. Evidence of impaired left ventricular systolic function by Doppler myocardial imaging in patients with systemic amyloidosis and no evidence of cardiac involvement by standard two-dimensional and Doppler echocardiography. *Am J Cardiol* 2008; **101**(7): 1039-45.
28. Kukulski T, Hubbert L, Arnold M, Wranne B, Hatle L, Sutherland GR. Normal regional right ventricular function and its change with age: a Doppler myocardial imaging study. *Journal of the American Society of Echocardiography : official publication of the American Society of Echocardiography* 2000; **13**(3): 194-204.
29. Lopez-Candales A, Rajagopalan N, Gulyasy B, Edelman K, Bazaz R. Differential strain and velocity generation along the right ventricular free wall in pulmonary hypertension. *The Canadian journal of cardiology* 2009; **25**(3): e73-7.
30. Muntean I, Benedek T, Melinte M, Suteu C, Toganel R. Deformation pattern and predictive value of right ventricular longitudinal strain in children with pulmonary arterial hypertension. *Cardiovascular ultrasound* 2016; **14**(1): 27.
31. Vitarelli A, Mangieri E, Terzano C, et al. Three-dimensional echocardiography and 2D-3D speckle-tracking imaging in chronic pulmonary hypertension: diagnostic accuracy in detecting hemodynamic signs of right ventricular (RV) failure. *Journal of the American Heart Association* 2015; **4**(3): e001584.
32. Ho SY, Nihoyannopoulos P. Anatomy, echocardiography, and normal right ventricular dimensions. *Heart* 2006; **92 Suppl 1**: i2-13.
33. Takeda K, Naka Y, Yang JA, et al. Timing of temporary right ventricular assist device insertion for severe right heart failure after left ventricular assist device implantation. *ASAIO Journal* 2013; **59**(6): 564-9.
34. M.S. Kiernan IG, K. Sundareswaran, J. Abraham, B. Bethea, J. Cowger, P. Eckman, S. Joseph, J.N. Katz, A. Kilic, S. Lee, B. Lima, C. Patel, J. Rich, D. Farrar, N. Uriel. Late Right Heart Failure Is Associated With Reduced Quality of Life and Functional Capacity in Continuous-Flow Left Ventricular Assist Device Recipients. *The Journal of Heart and Lung Transplantation* 2015; **34**(4): S65.
35. Abhayaratna WP, Seward JB, Appleton CP, et al. Left atrial size: physiologic determinants and clinical applications. *J Am Coll Cardiol* 2006; **47**(12): 2357-63.
36. Kato TS, Farr M, Schulze PC, et al. Usefulness of two-dimensional echocardiographic parameters of the left side of the heart to predict right ventricular failure after left ventricular assist device implantation. *Am J Cardiol* 2012; **109**(2): 246-51.
37. Aduen JF, Castello R, Lozano MM, et al. An alternative echocardiographic method to estimate mean pulmonary artery pressure: diagnostic and clinical implications. *Journal of the American Society of Echocardiography : official publication of the American Society of Echocardiography* 2009; **22**(7): 814-9.
38. LaRue SJ, Raymer DS, Pierce BR, Nassif ME, Sparrow CT, Vader JM. Clinical outcomes associated with INTERMACS-defined right heart failure after left ventricular assist device implantation. *The Journal of heart and lung transplantation : the official publication of the International Society for Heart Transplantation* 2017; **36**(4): 475-7.
39. Takeda K, Takayama H, Colombo PC, et al. Incidence and clinical significance of late right heart failure during continuous-flow left ventricular assist device support. *The Journal of heart and lung transplantation : the official publication of the International Society for Heart Transplantation* 2015; **34**(8): 1024-32.

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Table 1: Demographics and Clinical Characteristics Pre-Implant

Variable (Mean ± SD o Median (25th-75th perc))	Acute RVF (N=8)	Chronic RVF (N=10)	No RVF (N=56)	p- value (Acute RVF vs No-RVF)	p- value (Chronic RVF vs NO-RVF)	Odds-ratio (p-value) Outcome: Acute-RVF	Odds-ratio (p-value) Outcome: Chronic-RVF
Age (years)	54 ±13	63 ± 6	59 ± 11	0,253	0,189	0.96 (0.16)	1.07 (0.14)
Females (N(%))	1 (12)	1 (10)	5 (9)	0,75	0,94	0.7 (0.76)	0.93 (0.95)
BMI (Kg/m^2)	28 ± 6	25 ± 4	26 ± 4	0,261	0,472	1.12 (0.15)	0.92 (0.38)
BSA (m^2)	1.97 ± 0.21	1.94 ± 0.14	1.91 ± 0.16	0,308	0,698	6.77 (0.39)	2.4 (0.67)
Systolic Blood Pressure (mmHg)	99 ± 15	94 ± 10	95 ± 12	0,155	0,818	1.03 (0.34)	0.99 (0.65)
Diastolic Blood Pressure (mmHg)	56 ± 5	56 ± 15	59 ± 11	0,614	0,767	0.98 (0.63)	0.98 (0.62)
Heart Rate (bpm)	76 ± 13	74 ± 9	76 ± 14	0,827	0,776	1 (0.93)	0.99 (0.62)
NYHA III/IV (N(%))	4 (80)	8 (80)	41 (85)	0,67	0,5	0.84 (0.85)	NA
INTERMACS 1 (N(%))	1(12)	2 (20)	5 (9)	0,35	0,29	0.67 (0.37)	
INTERMACS 2 (N(%))	4 (50)	2 (20)	26 (46)	0,35	0,29	0.67 (0.37)	
INTERMACS 3 (N(%))	3 (37)	5 (50)	23 (41)	0,35	0,29	0.67 (0.37)	
INTERMACS 4 (N(%))	0 (0)	1 (10)	2 (3.5)	0,35	0,29	0.67 (0.37)	1.29 (0.57)
ICU Lenght of Stay (days)	25 ± 26	19 ± 15	11 ± 8	0,008	0,075	1.05 (0.03)	1.03 (0.16)
Hospital Lenght of Stay (days)	65 ± 33	43 ± 24	41 ± 27	0,036	0,851	1.02 (0.05)	1 (0.89)
Previous Cardiac Surgery (N(%))	1 (12)	4 (40)	9 (16)	0,62	0,67	0.58 (0.63)	3.6 (0.008)
ACE-Inhibitors (N(%))	4 (50)	7 (70)	30 (53)	0,74	0,31	0.78 (0.75)	2.06 (0.33)
ARB (N(%))	0 (0)	1 (10)	7 (12)	0,29	0,91	NA	0.89 (0.92)
Beta-Blockers (N(%))	6 (75)	9 (90)	44 (78)	0,72	0,38	0.74 (0.73)	2.52 (0.40)
Aldosterone Antagonists (N(%))	6 (75)	6 (60)	41 (73)	0,82	0,38	1.21 (0.82)	0.54 (0.39)
Furosemide PO (mg/die)	292 ± 176	330 ± 177	272 ± 174	0.96	0.28	1 (0.87)	1 (0.35)
Furosemide IV (N(%))	6 (75)	5 (50)	23 (42)	0,87	0,81	3.96 (0.11)	1.17 (0.82)
IV Inotropes (pre-LVAD) (N(%))	8 (100)	9 (90)	41 (73)	0,11	0,33	NA	2.76 (0.35)
Milrinone Drip (pre-LVAD) (N(%))	3 (37)	5 (50)	12 (21)	0,48	0,07	1.73 (0.48)	3.27 (0.09)
IV Vasodilators (pre-LVAD) (N(%))	3 (37)	1 (10)	8 (14)	0,83	0,56	3.8 (0.1)	0.54 (0.57)
Mechanical Ventilation (pre-LVAD) (N(%))	0 (0)	1 (10)	1(2)	0,63	0,13	NA	6.67 (0.19)
ECMO (pre-LVAD)	0(0)	1 (10)	2 (3)	0,56	0,31	NA	3.39 (0.34)
IABP (pre-LVAD)	3 (37)	3 (30)	19 (34)	0,81	0,78	1.2 (0.81)	0.82 (0.79)
Heart Mate risk score	1.44 ± 0.45	1.43 ± 1.02	1.2 ± 0.66	0,158	0,831	1.47 (0.44)	1.47 (0.40)
Kormos Risk Score	0.43 ± 0.24	0.38 ± 0.13	0.31 ± 0.17	0,233	0,168	28.96 (0.1)	6.13 (0.33)
MELD Risk Score	14.55 ± 6.21	13.27 ± 4.13	11.48 ± 4.02	0,088	0,22	1.13 (0.1)	1.07 (0.35)
MELD-Na Risk Score	16.16 ± 6.13	15.83 ± 5.66	14.48 ± 4.14	0,682	0,443	1.07 (0.39)	1.06 (0.46)
MELD-XI Risk Score	16.03 ± 4.12	14.07 ± 2.02	13.11 ± 3.33	0,027	0,354	1.25 (0.04)	1.05 (0.6)
Michigan score	5.19 ± 1.28	4.05 ± 1.71	3.38 ± 2.08	0,015	0,549	1.88 (0.03)	1.13 (0.51)

Table 2: Biochemical Markers Pre-Implant

Variable Median (25th-75th perc))	Acute RVF (N=8)	Chronic RVF (N=10)	No RVF (N=56)	p- value (Acute RVF vs No-RVF)	p- value (Chronic RVF vs NO-RVF)	Odds-ratio (p-value) Outcome: Acute-RVF	Odds-ratio (p-value) Outcome: Chronic-RVF
Serum Albumin (gr/dL)	3.37 (2.6 , 3.8)	3.6 (3.4 , 3.8)	3.55 (3.1 , 3.9)	0,342	0,476	0.47 (0.22)	1.39 (0.56)
Serum ALT (U/L)	35 (25 , 60.5)	44 (31 , 49)	30 (22 , 49)	0,702	0,135	1.29 (0.59)	1.53 (0.31)
Serum AST (U/L)	23 (17.5 , 46.5)	25 (22 , 33)	24.5 (18 , 31)	0,841	0,641	0.94 (1.0)	0.00 (0.5)
NT-proBNP (pg/mL)	1184 (515 , 10725)	2445 (1467 , 3632)	1488 (580 , 3248)	0,881	0,199	1.08 (0.83)	1.31 (0.38)
BUN (mg/dL)	60 (41.5 , 82)	79 (59 , 89)	50.5 (39 , 66)	0,536	0,028	1.68 (0.55)	5.93 (0.04)
Total Cholesterol (mg/dL)	100 (94 , 160)	136 (115 , 160)	150 (119 , 171)	0,064	0,73	0.98 (0.09)	1.0 (0.58)
Serum Creatinine (mg/dL)	1.53 (1.1 , 1.65)	1.4 (1.15 , 1.6)	1.2 (1 , 1.5)	0,257	0,292	4.54 (0.30)	3.52 (0.34)
eGFR (mL/min)	45 (42.04 , 71.86)	50.39 (44.94 , 56.5)	61 (47.84 , 69.86)	0,334	0,206	0.98 (0.43)	0.97 (0.17)
Hemoglobin (gr/dL)	11.7 (9.45 , 13.6)	12.3 (10.7 , 13.6)	12.15 (9.85 , 12.9)	0,715	0,402	0.95 (0.75)	1.18 (0.32)
Hematocrit (%)	37.15 (30.65 , 40.1)	37.25 (34.1 , 39.1)	36.6 (31.55 , 39.6)	0,917	0,482	0.99 (0.84)	1.05 (0.41)
INR	1.19 (1.09 , 1.36)	1.18 (1.08 , 1.35)	1.08 (1.03 , 1.19)	0,108	0,116	0.25 (0.29)	0.36 (0.39)
Lymphocytes (10^3/uL)	16.65 (15.25 , 25.5)	16.1 (12.9 , 24.9)	19 (12.75 , 24.1)	0,676	0,71	1.57 0.60)	0.76 (0.71)
Serum Na (mmol/L)	137.5 (136 , 140)	135.5 (133 , 136)	136 (133 , 138)	0,195	0,473	1.1 (0.27)	0.99 (0.88)
Platelets (10^3/uL)	196 (158.5 , 271.5)	181 (131 , 218)	218 (181.5 , 269)	0,728	0,042	1 (0.78)	0.99 (0.05)
Serum Total Bilirubin (mg/dL)	1.85 (0.95 , 2.36)	0.84 (0.7 , 1.35)	0.8 (0.58 , 1.11)	0,023	0,641	3.14 (0.05)	1.31 (0.59)
Uric Acid (10^3/uL)	7.35 (5.85 , 8.95)	7.4 (5.9 , 9.5)	7.4 (5.9 , 9.2)	0,813	0,798	0.96 (0.80)	1.02 (0.90)

Table 3A: Standard Echocardiography

Variable Mean ± SD	Acute RVF (N=8)	Chronic RVF (N=10)	No RVF (N=56)	p- value (Acute RVF vs No-RVF)	p- value (Chronic RVF vs NO-RVF)	Odds-ratio (p-value) Outcome: Acute-RVF	Odds-ratio (p-value) Outcome: Chronic-RVF
LV Ejection Fraction (%)	19.25 ± 3.41	21.7 ± 6.06	23.55 ± 6.15	0,061	0,404	0.88 (0.08)	0.96 (0.53)
Left Atrial Area (cm^2)	37 ± 9.49	38.3 ± 8.29	31.56 ± 5.51	0,13	0,025	1.08 (0.11)	1.12 (0.02)
Left Atrial Volume (mL)	143.5 ± 55.73	164.2 ± 52.41	120.65 ± 31.69	0,409	0,021	1.01 (0.3)	1.02 (0.01)
Left Atrial Volume Index (mL/m^2)	73.62 ± 30.4	84.28 ± 26.08	63.55 ± 17.14	0,579	0,021	1.01 (0.39)	1.04 (0.01)
LV End Diastolic Diameter (mm)	74.88 ± 7.04	72.8 ± 7.3	70.09 ± 8.64	0,108	0,361	1.06 (0.17)	1.03 (0.46)
LV End Diastolic Diameter Index (mm/m^2)	38.28 ± 4.22	37.63 ± 4.26	36.89 ± 4.93	0,324	0,531	1.06 (0.47)	1.02 (0.73)
LV End Diastolic Volume (mL)	318.75 ± 106.27	267.2 ± 65.1	266.98 ± 96.97	0,324	0,794	1.01 (0.15)	1.0 (0.84)
LV End Diastolic Volume Index (mL/m^2)	162.23 ± 51.31	138.1 ± 36.4	141.32 ± 54.23	0,197	0,948	1.01 (0.27)	1.0 (0.74)
LV End Systolic Diameter (mm)	68.25 ± 6.5	67.5 ± 6.8	64.95 ± 8.78	0,187	0,325	1.04 (0.37)	1.03 (0.48)
LV End Systolic Diameter Index (mm/m^2)	34.83 ± 3.25	34.9 ± 4.02	33.82 ± 5.22	0,46	0,481	1.04 (0.66)	1.04 (0.58)
LV End Systolic Volume (mL)	256.75 ± 91.58	208.4 ± 56.21	212.94 ± 84.51	0,112	0,801	1.01 (0.16)	1 (0.71)
LV End Systolic Volume Index (mL/m^2)	130.89 ± 45.13	107.81 ± 31.49	112.49 ± 47.29	0,172	1.00	1.01 (0.26)	1.0 (0.64)
Mitral Regurgitation 1+/2+ (N(%))	0 (0)	6 (60)	10 (18)				
Mitral Regurgitation 3+/4+ (N(%))	4 (50)	4 (40)	8 (14)	0,57	0,99	1.52 (0.29)	1.03 (0.94)
Right Atrial Area (cm^2)	20.75 ± 4.43	26.7 ± 7.56	21.7 ± 5.81	0,524	0,013	0.95 (0.45)	1.14 (0.02)
Estimated Right Atrial Pressure (mmHg)	10.63 ± 6.23	8 ± 3.5	8.18 ± 3.59	0,355	0,77	1.15 (0.11)	0.97 (0.71)
Right Atrial Volume (mL)	67.38 ± 21.67	93 ± 42.2	72.72 ± 32.04	0,73	0,073	0.99 (0.49)	1.02 (0.08)
RV End Diastolic Diameter (Base, mm)	43 ± 6.09	43 ± 6.77	40.69 ± 6.18	0,239	0,443	1.05 (0.4)	1.05 (0.34)
RV End Diastolic Lenght (mm)	76.86 ± 30.23	87.3 ± 8.39	74.31 ± 24.81	0,364	0,108	1 (0.96)	1.06 (0.15)
RV End Diastolic Area (cm^2)	27.14 ± 6.09	24.58 ± 5.73	23.06 ± 4.41	0,047	0,602	1.18 (0.06)	1.05 (0.53)
RV End Systolic Area (cm^2)	18.31 ± 5.8	17.39 ± 6.01	14.65 ± 4.31	0,17	0,358	1.14 (0.1)	1.1 (0.17)
RV Fractional Area Change (%)	0.34 ± 0.07	0.31 ± 0.08	0.38 ± 0.1	0,412	0,056	0.02 (0.42)	0.99 (0.04)
RV Basal End Diast. Diam / RV Lenght	1.04 ± 1.44	0.5 ± 0.09	0.9 ± 1.17	0,787	0,667	0.88 (0.55)	1.17 (0.38)
Systolic Pulm. Artery Pressure (mmHg)	49.06 ± 9.13	47.9 ± 9.01	46.57 ± 18.09	0,585	0,823	1.01 (0.71)	1.0 (0.86)
Diastolic Pulm. Artery Pressure (mmHg)	10.63 ± 6.23	8 ± 3.5	8.39 ± 3.56	0,403	0,651	1.15 (0.13)	0.95 (0.61)
Right Atrio-Ventricular Gradient (mmHg)	39.08 ± 7.07	40.69 ± 8.69	40.17 ± 16.06	0,971	0,603	0.99 (0.83)	1 (0.89)
S' Velocity, Tricuspid Annulus (mt/sec)	0.1 ± 0.01	0.08 ± 0.03	0.1 ± 0.02	0,589	0,021	8.58 (0.44)	0.96 (0.02)
Tricuspid Annular Plane Systolic Excursion (mm)	17.29 ± 3.4	15.22 ± 3.63	18.22 ± 3.76	1	0,032	0.96 (0.74)	0.74 (0.04)
Tricuspid Regurgitation 1+/2+	5 (62)	7 (70)	12 (21)				
Tricuspid Regurgitation 3+/4+	2 (25)	3(30)	5 (28)	0,32	0,81	1.31 (0.52)	1.37 (0.41)
Tricuspid Regurgitation Duration (msec)	456 ± 51	451 ± 61	419 ± 87	0,186	0,35	1 (0.32)	1 (0.35)
TR Velocity-Time Integral (cm)	101 ± 18	107 ± 17	105 ± 17	0,567	0,365	1.09 (0.7)	1.16 (0.42)
TR Max Velocity (mt/sec)	3.09 ± 0.26	3.14 ± 0.38	3.08 ± 0.63	0,993	0,62	1.0 (1.0)	1.18 (0.78)
RV EDD / LV EDD	0.58 ± 0.1	0.59 ± 0.09	0.58 ± 0.14	0,964	0,916	0.82 (0.95)	2.22 (0.77)
Dilated Inferior Vena Cava (N(%))	4 (50)	4 (40)	23 (42)	0,67	0,83	1.37 (0.67)	0.86 (0.83)
Plethoric Inferior Vena Cava (N(%))	3 (43)	5 (50)	18 (46)	0,83	0,8	0.85 (0.84)	1.19 (0.8)

LV = Left Ventricle, RV = Right Ventricle,

Table 3B: Strain Echocardiography

Variable Mean ± SD	Acute RVF (N=8)	Chronic RVF (N=10)	No RVF (N=56)	p- value (Acute RVF vs No-RVF)	p- value (Chronic RVF vs NO-RVF)	Odds-ratio (p-value) Outcome: Acute-RVF	Odds-ratio (p-value) Outcome: Chronic-RVF
Longitudinal sS, RV Free Wall, Base (%)	-14.81 ± 2.56	-15.43 ± 7.61	-18.36 ± 4.79	0.03	0.22	1.15 (0.16)	1.11 (0.27)
Longitudinal sS, RV Free Wall, Middle (%)	-14.4 ± 2.92	-13.39 ±4.33	-18.11 ± 3.5	0.05	0.01	1.23 (0.08)	1.36 (0.02)
Longitudinal sS, RV Free Wall, Apex (%)	-12.61 ±1.21	-12.95 ±3.25	-18.34 ± 4.5	0,01	0.02	1.47 (0.04)	1.38 (0.05)
Longitudinal sS, RV Free wall Average (%)	-13.94 ±1.66	-13.92 ±4.84	-18.27 ±3.33	0,007	0,022	1.33 (0.03)	1.34 (0.03)
Longitudinal sSR, RV Free Wall, Base (s^{-1})	-1.13 ± 0.15	-1.13 ± 0.43	-1.51±0.55	0,044	0,259	1.27 (0.1)	1.25 (0.1)
Longitudinal sSR, RV Free Wall, Middle (s^{-1})	-0.95 ± 0.2	-1.02 ± 0.29	-1.33 ± 0.4	0,03	0,113	4.81 (0.05)	1.22 (0.13)
Longitudinal sSR, RV Free Wall, Apex (s^{-1})	-1.17 ± 0.16	-1.13 ± 0.32	-1.35 ± 0.5	0,473	0,201	2.17 (0.45)	2.86 (0.32)
Longitudinal sSR, RV Free Wall, Average (s^{-1})	-1.08 ± 0.1	-1.09 ± 0.3	-1.42 ± 0.47	0,061	0,165	1.59 (0.11)	1.34 (0.12)
Longitudinal dSR-E, RV Free Wall, Base (s^{-1})	1.62 ± 0.39	1.28 ± 0.78	1.71 ± 0.77	0,915	0,123	0.93 (0.91)	0.34 (0.18)
Longitudinal dSR-E, RV Free Wall, Middle (s^{-1})	1.1 ± 0.29	0.87 ± 0.32	1.41 ± 0.56	0,464	0,019	0.39 (0.32)	0.07 (0.04)
Longitudinal dSR-E, RV Free Wall, Apex (s^{-1})	1.15 ± 0.28	0.99 ± 0.5	1.39 ± 0.56	0,417	0,138	0.5 (0.45)	0.19 (0.13)
Longitudinal dSR-E, RV Free Wall, Average (s^{-1})	1.29 ± 0.18	1.04 ± 0.52	1.52 ± 0.59	0,542	0,047	0.54 (0.5)	0.11 (0.07)
Right Atrial Kick (%)	-3.35 ± 3.93	-6.66 ± 3.07	-7.13 ± 5.9	0,179	0,705	1.21 (0.20)	1.01 (0.99)
Right Atrial PALS (%)	10.95 ±5.66	4.98 ± 5.28	13.95 ±7.71	0.04	0,017	0.97 (0.67)	0.77 (0.04)
Total Systolic Strain Right Atrium (%)	18.7 ± 10	11.08 ± 3.2	19.88 ± 6.8	0.93	0,001	1.01 (0.94)	0.72 (0.01)

Table 4: Invasive Hemodynamics

Variable Mean ± SD	Acute RVF (N=8)	Chronic RVF (N=10)	No RVF (N=56)	p- value (Acute RVF vs No-RVF)	p- value (Chronic RVF vs NO-RVF)	Odds-ratio (p-value) Outcome: Acute-RVF	Odds-ratio (p-value) Outcome: Chronic-RVF
Cardiac Output (Lit./min)	4.17 ±0.9	4.05 ± 1.18	3.73 ± 0.96	0,299	0,406	1.53 (0.29)	1.33 (0.42)
Cardiac Index (Lit./min/m^2)	2.19 ± 0.5	2.15 ± 0.62	1.99 ± 0.49	0,441	0,388	2.09 (0.34)	1.72 (0.43)
Stroke Volume Index (mL/m^2)	29.74 ± 9.55	28.52 ± 8.17	27.15 ± 9.27	0,417	0,563	1.03 (0.48)	1.01 (0.75)
Central Venous Pressure (mmHg)	10.5 ±5.83	9.2 ± 3.58	6.52 ± 3.97	0,028	0,05	1.19 (0.04)	1.11 (0.15)
Systolic Pulm Art Pressure (mmHg)	53.43 ± 15.85	45.9 ± 8.96	48.28 ± 17.12	0,294	0,541	1.02 (0.38)	0.99 (0.57)
Diastolic Pulm Art Pressure (mmHg)	26.86 ±7.31	26.8 ± 5.16	24.33 ± 10.2	0,424	0,314	1.02 (0.57)	1.03 (0.50)
Mean Pulm Art Pressure (mmHg)	37.13 ±9.26	36.6 ± 6.52	32.57 ± 10.94	0,244	0,316	1.04 (0.31)	1.03 (0.33)
Pulmonary Capillary Wedge Press (mmHg)	24.13 ±5.36	23.8 ± 4.96	21.87 ± 7.81	0,518	0,63	1.04 (0.47)	1.03 (0.5)
dPAP-PWCP	3 ± 2.83	5.9 ± 4.65	2.71 ± 4.3	0,798	0,031	0.98 (0.82)	1.17 (0.05)
Trans-Pulmonary Gradient (mmHg)	11.71 ± 4.54	12.8 ± 4.44	10.7 ± 5.96	0,505	0,182	1.02 (0.76)	1.06 (0.31)
RV-Stroke Work Index (gr/m^2/beat)	800.52 ±420.44	662.2 ± 201.98	585.19 ± 321.51	0,162	0,251	1.01 (0.11)	1 (0.65)
Systemic Vascular Resistances (dyn·s/cm^5)	525.79 ± 158.06	608.91 ± 312.71	611.36 ± 359.63	0,734	0,922	1.01 (0.5)	1.01 (0.94)
Pulmonary Vascular Resistances (Wood Units)	3.32 ± 1.63	3.44 ± 1.69	3.31 ± 2.15	0,796	0,681	1.01 (0.98)	1.03 (0.85)

Table 5: Clinical Outcomes, post-LVAD Implant

Variable N (%)	Acute RVF (N=8)	Chronic RVF (N=10)	No RVF (N=56)	p- value (Acute RVF vs No-RVF)	p- value (Chronic RVF vs NO-RVF)	Odds-ratio (p-value) Outcome: Acute-RVF	Odds-ratio (p-value) Outcome: Chronic-RVF
GI Bleeding (N(%))	0 (0)	2 (22)	8 (19)	0,22	0,7	NA	1.39 (0.71)
Ischemic Stroke (N(%))	0 (0)	1 (10)	7 (16)	0,26	0,71	NA	0.67 (0.72)
Hemorrhagic Stroke (N(%))	0 (0)	2 (20)	6 (15)	0,24	0,56	NA	1.67 (0.57)
Transitory Ischemic Attack (N(%))	0 (0)	3 (30)	6 (14)	0,23	0,15	NA	3.07 (0.17)
Cardiac Tamponade (N(%))	2 (28)	3 (30)	8 (20)	0,71	0,57	1.38 (0.72)	1.54 (0.58)
Ventricular Tachic. / Fibrillation (N(%))	1 (14)	4 (40)	14 (33)	0,28	0,56	0.31 (0.3)	1.51 (0.56)
LVAD Thrombosis (N(%))	0 (0)	1 (10)	8 (19)	0,22	0,59	NA	0.56 (0.6)
Driveline Infection (N(%))	0 (0)	2 (20)	10 (24)	0,14	0,95	NA	0.95 (0.95)
LVAD infection (N(%))	0 (0)	0 (0)	1 (2)	0,7	0,63	NA	NA
Other Complicances (N(%))	5 (71)	6 (60)	27 (60)	0,55	0,92	1.67 (0.56)	0.94 (0.93)
Heart Transplantation (N(%))	1 (14)	3 (30)	13 (27)	0,45	0,76	0.44 (0.46)	1.26 (0.76)
Death (All-Causes) (N(%))	5 (38)	4 (40)	16 (29)	0.55	0.70	1.38 (0.68)	1.58 (0.52)

Table 6A: Most Accurate Predictors of RVF according to Different Machine Learning Algorithms, UNTRAINED results

Predictors (AUC-ROC (AUC Conf. Interval)	Logistic Regression	Penalized Logistic Regr.	Support Vector Machines	Naive Bayes
Acute RVF				
Michigan, sS RV Apex, CVP	0.88 (0.78 - 0.97)	0.87 (0.76 - 0.98)	0.84 (0.74 - 0.94)	0.95 (0.90 - 1.00)
Michigan, sS RV Apex, RA Area	0.80 (0.72 - 0.89)	0.84 (0.76 - 0.88)	0.86 (0.78 - 1.00)	0.90 (0.82 - 0.99)
sS RV Apex, RA Area, RV-SWI	0.71 (0.58 - 0.87)	0.81 (0.65 - 0.97)	0.74 (0.52 -0.84)	0.86 (0.73 - 0.98)
Chronic RVF				
sS RV Middle, RA Total Strain, TAPSE	0.84 (0.68 - 1.00)	0.83 (0.67 - 0.99)	0.83 (0.70 - 0.96)	0.97 (0.92 - 1.00)
sS RV Middle, RA sS Total, LA Vol Index	0.85 (0.72 - 0.98)	0.86 (0.74 - 0.98)	0.85 (0.71 -0.99)	0.93 (0.87 - 1.00)
sS RV Middle, Milrinone Drip, TAPSE	0.87 (0.77 - 0.97)	0.87 (0.76 - 0.98)	0.88 (0.77 - 0.98)	0.86 (0.81 - 0.90)
Acute and Chronic RVF				
RV sS Average, CVP, TAPSE	0.83 (0.71 - 0.94)	0.83 (0.71 - 0.95)	0.83 (0.71 - 0.95)	0.92 (0.86 - 0.98)
RV sS Average, CVP, RA Total Strain	0.81 (0.68 - 0.94)	0.81 (0.68 - 0.94)	0.81 (0.67 - 0.96)	0.89 (0.80 - 0.98)
RV sS Average, CVP, TR-VTI	0.81 (0.68 - 0.94)	0.81 (0.68 - 0.94)	0.79 (0.66 - 0.91)	0.90 (0.83 - 0.98)

AUC = Area Under the Curve; ROC = Receiver-Operator Curve; sS = Longitudinal systolic strain;

RV = Right Ventricular: CVP: Central Venous Pressure; RA: Right Atrial, TR: Tricupsid Regurgitation, VTI: Velocity Time Integral

Table 6B: Most Accurate Predictors of RVF according to Different Machine Learning Algorithms, TRAINED Results

Predictors (AUC-ROC (AUC Conf. Interval)	Logistic Regression	Penalized Logistic Regr.	Support Vector Machines	Naive Bayes
Acute RVF				
Michigan, sS RV Apex, CVP	0.82 (0.70 - 0.94)	0.69 (0.49 - 0.88)	0.51 (0.17 - 0.85)	0.79 (0.68 - 0.91)
Michigan, sS RV Apex, RA Area	0.83 (0.70 - 0.96)	0.74 (0.62 - 0.86)	0.57 (0.25 - 0.89)	0.78 (0.60 - 0.96)
sS RV Apex, RA Area, RV-SWI	0.73 (0.54 - 0.91)	0.48 (0.26 - 0.69)	0.51 (0.30 - 0.71)	0.61 (0.40 - 0.81)
Chronic RVF				
sS RV Middle, RA Total Strain, TAPSE	0.77 (0.58 - 0.96)	0.68 (0.49 - 0.87)	0.72 (0.58 - 0.86)	0.73 (0.54 - 0.92)
sS RV Middle, RA sS Total, LA Vol Index	0.76 (0.59 - 0.94)	0.69 (0.51 - 0.87)	0.79 (0.53 - 1.00)	0.86 (0.76 - 0.95)
sS RV Middle, Milrinone Drip, TAPSE	0.73 (0.51 - 0.95)	0.68 (0.46 - 0.89)	0.80 (0.54 - 1.00)	0.79 (0.61 - 0.96)
Acute and Chronic RVF				
RV sS Average, CVP, TAPSE	0.83 (0.71 - 0.94)	0.83 (0.71 - 0.95)	0.83 (0.71 - 0.95)	0.92 (0.86 - 0.98)
RV sS Average, CVP, RA Total Strain	0.74 (0.58 - 0.91)	0.74 (0.60 - 0.88)	0.77 (0.62 - 0.92)	0.75 (0.61 - 0.89)
RV sS Average, CVP, TR-VTI	0.75 (0.61 - 0.90)	0.76 (0.62 - 0.90)	0.75 (0.61 - 0.88)	0.79 (0.65 - 0.92)

AUC = Area Under the Curve; ROC = Receiver-Operator Curve; sS = Longitudinal systolic strain;

RV = Right Ventricular: CVP: Central Venous Pressure; RA: Right Atrial, TR: Tricupsid Regurgitation, VTI: Velocity Time Integral

Figure 1

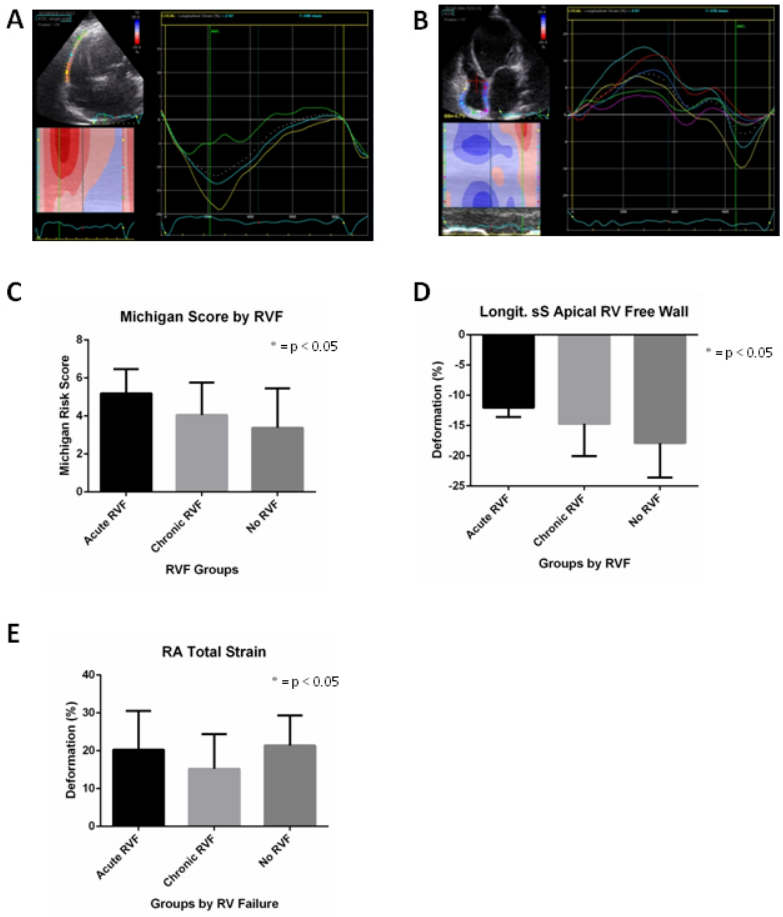

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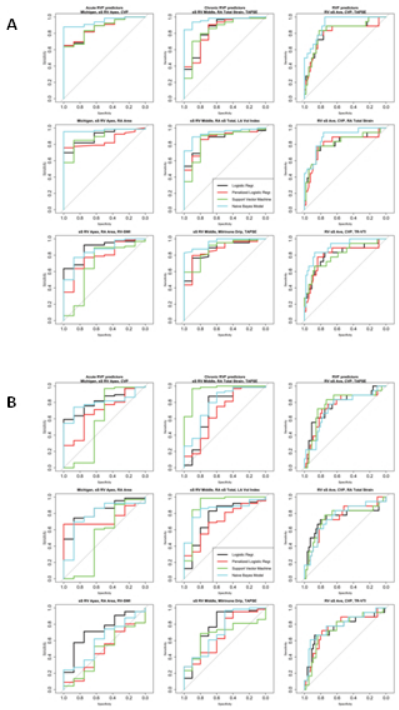
Figure 2



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