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Performance of Prognostic Heart Failure Models in Patients With Nonischemic Cardiomyopathy Undergoing Ventricular Tachycardia Ablation

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ABSTRACT

OBJECTIVES This study sought to assess the performance of established risk models in predicting outcomes after catheter ablation (CA) in patients with nonischemic dilated cardiomyopathy (NIDCM) and ventricular tachycardia (VT).

BACKGROUND A correct pre-procedural risk stratification of patients with NIDCM and VT undergoing CA is crucial. The performance of different pre-procedural risk stratification approaches to predict outcomes of CA of VT in patients with NIDCM is unknown.

METHODS The study compared the performance of 8 prognostic scores (SHFM [Seattle Heart Failure Model], MAGGIC [Meta-analysis Global Group in Chronic Heart Failure], ADHERE [Acute Decompensated Heart Failure National Registry], EFFECT [Enhanced Feedback for Effective Cardiac Treatment-Heart Failure], OPTIMIZE-HF [Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure], CHARM [Candesartan in Heart Failure-Assessment of Reduction in Mortality], EuroSCORE [European System for Cardiac Operative Risk Evaluation], and PAINESD [Chronic Obstructive Pulmonary Disease, Age $>$ 60 Years, Ischemic Cardiomyopathy, New York Heart Association Functional Class III or IV, Ejection Fraction $<$25%, Presentation With VT Storm, Diabetes Mellitus]) for the endpoints of death/cardiac transplantation and VT recurrence in 282 consecutive patients (age 59 $\pm$ 15 years, left ventricular ejection fraction: 36 $\pm$ 13%) with NIDCM undergoing CA of VT. Discrimination and calibration of each model were evaluated through area under the curve (AUC) of receiver-operating characteristic curve and goodness-of-fit test.

RESULTS After a median follow-up of 48 (interquartile range: 19–67) months, 43 patients (15%) died, 24 (9%) underwent heart transplantation, and 58 (21%) experienced VT recurrence. The prognostic accuracy of SHFM (AUC = 0.89; goodness-of-fit p = 0.68 for death/transplant and AUC = 0.77; goodness-of-fit p = 0.16 for VT recurrence) and PAINESD (AUC = 0.83; goodness-of-fit p = 0.24 for death/transplant and AUC = 0.68; goodness-of-fit p = 0.58 for VT recurrence) were significantly superior to that of other scores.

CONCLUSIONS In patients with NIDCM and VT undergoing CA, the SHFM and PAINESD risk scores are powerful predictors of recurrent VT and death/transplant during follow-up, with similar performance and significantly superior to other scores. A pre-procedural calculation of the SHFM and PAINESD can be useful to predict outcomes.
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All authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the *JACC: Clinical Electrophysiology* author instructions page.

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ABBREVIATIONS AND ACRONYMS

AAD = antiarrhythmic drugs

AIC = Akaike information criterion

AUC = area under the curve

CA = catheter ablation

CL = cycle length

HF = heart failure

ICD = implantable cardioverter-defibrillator

IQR = interquartile range

LV = left ventricular

LVEF = left ventricular ejection fraction

NIDCM = nonischemic dilated cardiomyopathy

NYHA = New York Heart Association

RV = right ventricular

VT = ventricular tachycardia

In patients with nonischemic dilated cardiomyopathy (NIDCM) presentation with recurrent ventricular tachycardia (VT) poses major management challenges due to the complexity of the arrhythmic substrates together with the competing risks associated with the underlying heart failure (HF) status and associated comorbidities (1). In some cases, recurrent VT may simply represent a marker of worsening HF status, with limited possibility for achieving clinically impactful arrhythmia control, despite attempts with antiarrhythmic drug (AAD) therapy and/or catheter ablation (CA) procedures (2,3). From a procedural perspective, the abnormal substrate and ablation targets in NIDCM, unlike ischemic cardiomyopathy, may be difficult to identify when mapping only in sinus rhythm, and repeated VT induction may be necessary to determine the optimal ablation sites, further increasing the risk of adverse procedural and post-procedural outcomes (4).

As such, a proper upfront identification of NIDCM patients at high risk of adverse outcomes has important clinical implications with regard to patient selection for complex CA procedures versus more advanced HF treatment or even palliative care. Several multiparameter scores have been developed to predict prognosis in patients with HF, with the SHFM (Seattle Heart Failure Model) being the most popular and the most widely validated (5). There is substantial lack of evidence on the potential application and performance of different HF risk stratification models in patients with NIDCM and VT referred to CA. In the present study, we compared the performance of established prognostic risk scores in predicting outcomes after CA of VT in patients with NIDCM.

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METHODS

PATIENT POPULATION. The study population consisted of 282 consecutive patients with NIDCM and recurrent VT referred to the Hospital of the University of Pennsylvania for radiofrequency CA between January 1, 1999 and December 31, 2014. All patients had evidence of left ventricular (LV) dilation (echocardiographic LV end-diastolic volume indexed for body surface area ≥75 ml/m^2 in men and ≥62 ml/m^2 in women) and systolic impairment (left ventricular ejection fraction [LVEF] <50%) persistent for at least 90 days despite optimal medical treatment after the initial diagnosis. Patients with significant coronary artery disease (>50% stenosis, assessed by coronary angiography or coronary artery computed tomography), congenital heart disease, hypertrophic cardiomyopathy, arrhythmogenic right ventricular (RV) cardiomyopathy, LV noncompaction, restrictive cardiomyopathy, previous myocarditis, cardiac sarcoidosis, toxic cardiomyopathy, tachycardia-induced cardiomyopathy, or primary valvular abnormalities were excluded. All patients signed a written informed consent according to the institutional guidelines of the University of Pennsylvania Health System, and data were entered in registry approved by the university's investigational review board.

PROGNOSTIC RISK SCORES SELECTION AND CALCULATION. We included 6 models designed to predict mortality in patients with HF in different settings (i.e., ambulatory patients with chronic HF or patients hospitalized for acute decompensated HF). These included the SHFM score (5), the ADHERE (Acute Decompensated Heart Failure National Registry) score (6), the MAGGIC (Meta-analysis Global Group in Chronic Heart Failure) score (7), the CHARM (Candesartan in Heart Failure-Assessment of Reduction in Mortality) score (8), the EFFECT (Enhanced Feedback for Effective Cardiac Treatment-Heart Failure) score (9), and the OPTIMIZE-HF (Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure) score (10). We also included a model specifically designed to estimate in-hospital mortality after cardiac surgery, namely the EuroSCORE (European System for Cardiac Operative Risk Evaluation) (11) and a score previously developed by our group to estimate the risk of acute hemodynamic decompensation during CA of VT, namely the PAINESD (Chronic Obstructive Pulmonary Disease, Age >60 Years, Ischemic Cardiomyopathy, New York Heart Association Functional Class III or IV, Ejection Fraction <25%, Presentation With VT Storm, Diabetes Mellitus) score (12). Each patient underwent a clinical examination, 12-lead electrocardiography, transthoracic echocardiography, and a panel of laboratory tests, including those required for the calculation of prognostic risk scores at the time of hospital admission before the procedure.

CATHETER ABLATION. AAD were routinely discontinued ≥5 half-lives before the procedure with the exception of amiodarone, which was discontinued at least 3 days beforehand whenever possible. All patients underwent electroanatomic mapping using CARTO system (Biosense Webster, Inc., Diamond Bar, California). The primary ablation endpoint was elimination of the clinical VT and all

mappable nonclinical VT. All induced VT with a cycle length (CL) ≥250 ms were considered potentially relevant and routinely targeted for ablation. A deflectable 3.5-mm open irrigated tip catheter (NaviStar ThermoCool, Biosense Webster) or a closed irrigated ablation catheter (Chilli, Boston Scientific, Natick, Massachusetts) were used for mapping and ablation. The mapping/ablation catheter was advanced to the RV (transvenous approach), LV (retrograde aortic or transseptal approach), or epicardial space according to the presumed site of origin of the VT or the underlying substrate. Programmed ventricular stimulation was delivered, with triple extrastimuli from at least 2 RV or LV sites with at least 2 drive CL. Induced VT were identified as clinical if they matched the CL and morphology of stored implantable cardioverter-defibrillator (ICD) electrograms (near-field and far-field) and the 12-lead electrocardiography when available.

For hemodynamically tolerated VT, entrainment mapping was performed at sites showing diastolic activity to identify critical sites of the VT re-entrant circuit (13). For hemodynamically unstable VT, substrate modification was performed targeting sites identified by pace mapping as well as abnormal electrograms, as previously reported (14). Established criteria were used to identify epicardial VT and to guide the need for an epicardial approach for ablation. Radiofrequency energy was delivered using powers up to 50 W with a goal 10- to 15-Ω impedance drop.

ACUTE AND LONG-TERM OUTCOMES. The acute procedural outcomes consisted of noninducibility of any VT (excluding very fast [<250 ms] nonclinical VT/ventricular flutter). The acute efficacy was assessed based on inducibility of VT at the end of the ablation procedure with a consistent stimulation protocol (up to triple extrastimuli from up to 2 ventricular sites with at least 2 drive CL) and at the time of repeat programmed stimulation before hospital discharge noninvasively from a single RV site via the ICD system (noninvasive programmed stimulation). Long-term outcomes included: survival free of any VT (defined as any sustained VT on ICD interrogation or 12-lead electrocardiography including episodes of sustained VT appropriately treated by adenosine triphosphate) after single or multiple procedures, and survival free from death/cardiac transplantation.

CLINICAL FOLLOW-UP. Patients were evaluated at 4 to 8 weeks after ablation and then at 3- to 6-month intervals. For patients not followed at our institution, the referring cardiologists were contacted and ICD interrogations were reviewed to determine VT recurrence. Telephone interviews were performed at 6- and 12-month intervals with patients or family members to confirm the absence of arrhythmia symptoms. The Social Security Death Index database was queried for vital status. No patient was lost at follow-up.

STATISTICAL ANALYSIS. Continuous variables are expressed as mean ± SD if normally distributed or median (interquartile range [IQR]: 25th–75th percentiles) if not normally distributed. All continuous variables were tested for normal distribution using the 1-sample Kolmogorov-Smirnov test. Categorical data are expressed as counts and proportions. Continuous variables were compared using independent-sample parametric (unpaired Student's *t*-) or nonparametric (Mann-Whitney *U*) tests. Categorical variables were compared using chi-square test or Fisher exact test when appropriate. Each risk score was calculated by using the beta coefficients reported in the derivation cohort of the original studies (Online Table 1). The discriminatory power of each model in predicting the main endpoints of death/transplant and VT recurrence at the median follow-up time, was assessed with the receiver-operating characteristic curve and the calculation of the area under the curve (AUC). Each AUC was then compared with the best AUC using De Long method to highlight significant differences. Given the ratio of events to the predictor variables included in each model, the Akaike information criterion (AIC), accounting for the small number of events relative to the number of covariates, was also analyzed to select parsimonious models (15). Calibration of the models was evaluated using the goodness-of-fit test described by Grønnesby and Borgan (16). Finally the more accurate prognostic scores were identified as those having the lowest AIC and the highest AUC (15). Observed versus predicted outcomes at 30 days and 12 months were compared for quintiles of these final models to evaluate their performance at different levels of risk. Calibration of these models was also graphically checked as follows: we subdivided the population in 3 prognostic groups (low, moderate, and high risk) using recognized cut-points of the score or determining them by the Cox method in the absence of widely recognized ones (17). Then, we estimated the baseline survival function of our validation cohort and combined it with the original prognostic index by fitting a Cox model to the validation data with no covariates other than the prognostic index to predict survival probabilities, and finally we superimposed in a graph the predicted (by the Cox model) and observed (estimated by the Kaplan-Meier method) survival curves for each risk group as described elsewhere (18,19). The

TABLE 1 Baseline Characteristics of the Study Population

	Total (N = 282)	SHFM	MAGGIC	ADHERE	EFFECT	OPTIMIZE-HF	CHARM	EuroSCORE	PAINESD
Age, yrs	59 ± 15	✓	✓		✓	✓	✓	✓	✓
Male	227 (80)	✓	✓				✓	✓	
Weight, kg	80 ± 24	✓							
BMI, kg/m^2	28 ± 5		✓				✓		
Heart rate, beats/min	71 ± 12					✓	✓		
Respiratory rate, breaths/min	26 ± 6				✓				
Systolic blood pressure, mm Hg	119 ± 17	✓	✓	✓	✓	✓			
Diastolic blood pressure, mm Hg	74 ± 12					✓	✓		
Smoking status			✓			✓	✓		
Current	8 (3)								
Former	99 (35)								
Never	175 (62)								
Clinical characteristics									
Heart failure history >12 months	225 (80)		✓			✓	✓		
NYHA functional class III/IV	84 (30)	✓	✓				✓		✓
Arterial hypertension	95 (34)								
Diabetes mellitus	36 (13)		✓				✓		✓
Hyperlipidemia	65 (23)					✓			
History of atrial fibrillation/flutter	66 (23)						✓		
Current smoker	6 (2)								
Chronic kidney disease	57 (20)								
Chronic obstructive pulmonary disease	26 (9)		✓		✓	✓		✓	✓
Cerebrovascular disease	15 (5)				✓	✓		✓	
Peripheral vascular disease	4 (1)					✓		✓	
Clinical presentation with VT storm	71 (25)								✓
LBBB or QRS duration >120 ms	176 (62)	✓					✓		
Transthoracic echocardiography									
LVEF, %	36 ± 13	✓	✓				✓	✓	✓
LVEF ≤35%	137 (49)								
Lab results									
Hemoglobin, g/dl	13 ± 2	✓			✓				
Serum creatinine, mg/dl	1.4 ± 0.6		✓	✓		✓		✓	
Blood urea nitrogen, mg/dl	21 ± 10			✓	✓				
Sodium, mEq/l	137 ± 5	✓			✓	✓			
Total cholesterol, mg/dl	170 ± 40	✓							
Uric acid, mg/dl	6 ± 2	✓							
Lymphocytes, %	23 ± 11	✓							
Medical therapy									
Furosemide daily dose, mg/kg	0.2 ± 0.3	✓							
Beta-blockers	217 (77)	✓	✓			✓			
Angiotensin-converting enzyme inhibitors/ angiotensin receptor blockers	125 (44)	✓	✓			✓			
Mineralocorticoid receptor antagonists	57 (20)	✓							
Allopurinol	4 (1)	✓							
Statin	60 (21)	✓							
Failed antiarrhythmic drugs	2 (1–2)								
Amiodarone before procedure	166 (59)								
Device		✓							
ICD	240 (85)								
CRT-D	66 (23)								

Values are mean ± SD, n (%), or mean (25th-75th percentile).

ADHERE = Acute Decompensated Heart Failure National Registry; BMI = body mass index; CHARM = Candesartan in Heart Failure-Assessment of Reduction in Mortality; CRT-D = cardiac resynchronization therapy device; EFFECT = Enhanced Feedback for Effective Cardiac Treatment-Heart Failure; EuroSCORE = European System for Cardiac Operative Risk Evaluation; ICD = implantable cardioverter-defibrillator; LBBB = left bundle branch block; LVEF = left ventricular ejection fraction; MAGGIC = Meta-analysis Global Group in Chronic Heart Failure; NYHA = New York Heart Association; OPTIMIZE-HF = Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure; PAINESD = Chronic Obstructive Pulmonary Disease, Age > 60 Years, Ischemic Cardiomyopathy, New York Heart Association Functional Class III or IV, Ejection Fraction <25%, Presentation With VT Storm, Diabetes Mellitus; SHFM = Seattle Heart Failure Model; VT = ventricular tachycardia.

proportional hazards assumption was assessed using Schoenfeld residuals test. Two-tailed tests were considered statistically significant at the 0.05 level. The p values were adjusted for multiple comparisons using the Benjamini and Hochberg method. Analyses were performed using SPSS software version 24.0 (IBM, Armonk, New York).

RESULTS

BASELINE CHARACTERISTICS OF THE STUDY POPULATION AND OUTCOMES. The baseline clinical characteristics of the study population are summarized in Table 1. A total of 282 consecutive patients with NIDCM (age 59 ± 15 years, 80% male) underwent CA after failure of 2 (range 1 to 2) AAD. One-hundred and thirty-seven patients (49%) had LVEF ≤35%, 71 (25%) presented with VT storm (at least 3 appropriate ICD interventions within the last 24 h or incessant VT), and 84 patients (30%) had New York Heart Association (NYHA) functional class III/IV. Overall 166 patients (59%) were on amiodarone therapy before the procedure. An ICD was present in 240 patients (85%) of whom 66 (28%) had also a cardiac resynchronization therapy.

A total of 442 procedures were performed among the 282 patients (median: 1; range 1 to 8 procedures per patient). A second procedure was performed in 66 patients (23%), and 3 or more procedures were performed in 36 (13%). A median number of 2 (range 1 to 4) different VT were induced with a mean CL of 386 ± 98 ms. All patients underwent endocardial mapping and ablation. Epicardial mapping was performed in 122 patients (43%) and epicardial ablation in 90 (32%). At the end of the last procedure, a total of 262 patients (92%) underwent programmed ventricular stimulation. The clinical VT was still inducible in 32 patients (12%), and 46 patients (18%) had at least 1 nonclinical VT still inducible. A total of 101 patients (36%) underwent noninvasive programmed stimulation from the ICD a median of 3 (IQR: 2–4) days after the last procedure: the clinical VT was not inducible in 84 of 101 patients (83%) while noninducibility of any VT was achieved in 63 of 101 patients (62%). A total of 19 complications (4%) occurred during the 442 procedures. Two patients had pericardial tamponade and required open chest surgery to control the bleeding. In 10 patients, a pericardial effusion occurred during mapping/ablation and was successfully drained percutaneously without consequence. Two patients had an occlusion of a small coronary artery branch during epicardial ablation; 1 patient had phrenic nerve injury during epicardial ablation with transient hemidiaphragm paralysis; and 4 patients had complications related to the vascular access site. Following the procedure, 62 patients (22%) were maintained on amiodarone.

TABLE 2 Performance of the Scores in Predicting Death/Transplant and Arrhythmia Recurrence After VT Ablation

	Goodness-of-Fit*			Discriminatory Power			Akaike Information Criterion	
Scoring System	Chi-Square	DF	p Value	AUC	95% CI	p Value	AIC_c	Relative Likelihood
Death/transplant								
SHFM	5.69	8	0.68	0.89	0.84–0.94	<0.01	619	1.00
MAGGIC	14.94	8	0.06	0.78	0.72–0.85	<0.01	656	<0.01
ADHERE	23.96	8	<0.01	0.70	0.62–0.78	<0.01	660	<0.01
EFFECT	14.22	8	0.08	0.75	0.69–0.82	<0.01	650	<0.01
OPTIMIZE-HF	12.76	8	0.12	0.75	0.68–0.82	<0.01	655	<0.01
CHARM	16.76	8	0.03	0.73	0.65–0.80	<0.01	664	<0.01
EuroSCORE	17.08	8	0.03	0.77	0.70–0.84	<0.01	659	<0.01
PAINESD	6.74	5	0.24	0.83	0.77–0.88	<0.01	644	<0.01
VT recurrence								
SHFM	11.84	8	0.16	0.77	0.70–0.84	<0.01	569	0.02
MAGGIC	10.94	8	0.21	0.62	0.54–0.71	<0.01	577	<0.01
ADHERE	7.15	8	0.52	0.54	0.46–0.62	0.33	571	<0.01
EFFECT	12.67	8	0.12	0.62	0.54–0.70	<0.01	564	0.22
OPTIMIZE-HF	24.70	8	<0.01	0.60	0.52–0.68	0.02	590	<0.01
CHARM	5.91	8	0.66	0.61	0.52–0.69	0.01	600	<0.01
EuroSCORE	10.66	8	0.22	0.66	0.58–0.75	<0.01	569	0.02
PAINESD	3.79	5	0.58	0.70	0.60–0.76	<0.01	561	1.00

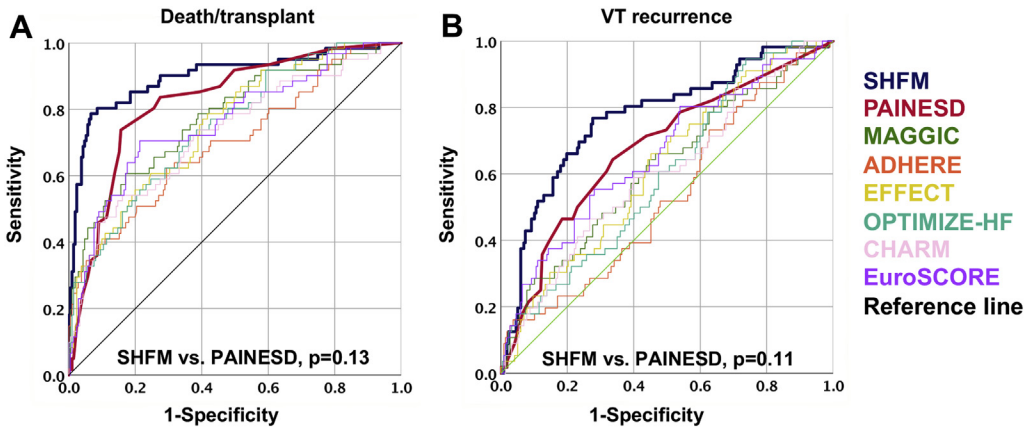
*Grønnesby and Borgan (16) test.

AIC_c = corrected Akaike information criterion; AUC = area under the curve; CI = confidence interval; DF = degrees of freedom; other abbreviations as in Table 1.

After a median follow-up of 48 (IQR: 19–67) months after the last procedure, 58 patients (21%) experienced at least 1 VT recurrence episode, 43 (15%) died, and 24 (9%) underwent heart transplantation. Cumulative VT-recurrence-free survival was 95% and 85% at 30-day and 12-month follow-ups, respectively, whereas cumulative death/transplant-free survival was 96% and 87% at 30-day and 12-month follow-ups, respectively. Cumulative VT-recurrence rates after the first CA procedure were 18% at 30-day and 30% at 12-month follow-ups (Online Figure 1, Online Table 2). Survival at 12 months was significantly lower in the NYHA functional class III/IV group than in the NYHA functional class I/II group (69% vs. 94%; log-rank $p < 0.01$). Similarly, the 12-month VT-free survival was lower in patients with NYHA functional class III/IV than in those with NYHA functional class I/II (71% vs. 91%; log-rank $p < 0.01$) (Online Figure 2).

RISK SCORE COMPARISON. The performance of each risk score is shown in Table 2. Discrimination was good overall for death/transplant (AUC >0.70 for all the models) with the SHFM (AUC = 0.89) and the PAINESD (AUC = 0.83) scores appearing to have the

FIGURE 1 ROC Curves Comparing AUC of Risk Scores



Receiver-operating characteristic (ROC) curves comparing the areas under the curve (AUC) of risk scores for death/transplant **(A)** and ventricular tachycardia (VT) recurrence **(B).** ADHERE = Acute Decompensated Heart Failure National Registry; CHARM = Candesartan in Heart Failure-Assessment of Reduction in Mortality; EFFECT = Enhanced Feedback for Effective Cardiac Treatment-Heart Failure; EuroSCORE = European System for Cardiac Operative Risk Evaluation; MAGGIC = Meta-analysis Global Group in Chronic Heart Failure; OPTIMIZE-HF = Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure; PAINESD = Chronic Obstructive Pulmonary Disease, Age > 60 Years, Ischemic Cardiomyopathy, New York Heart Association Functional Class III or IV, Ejection Fraction <25%, Presentation With VT Storm, Diabetes Mellitus; SHFM = Seattle Heart Failure Model.

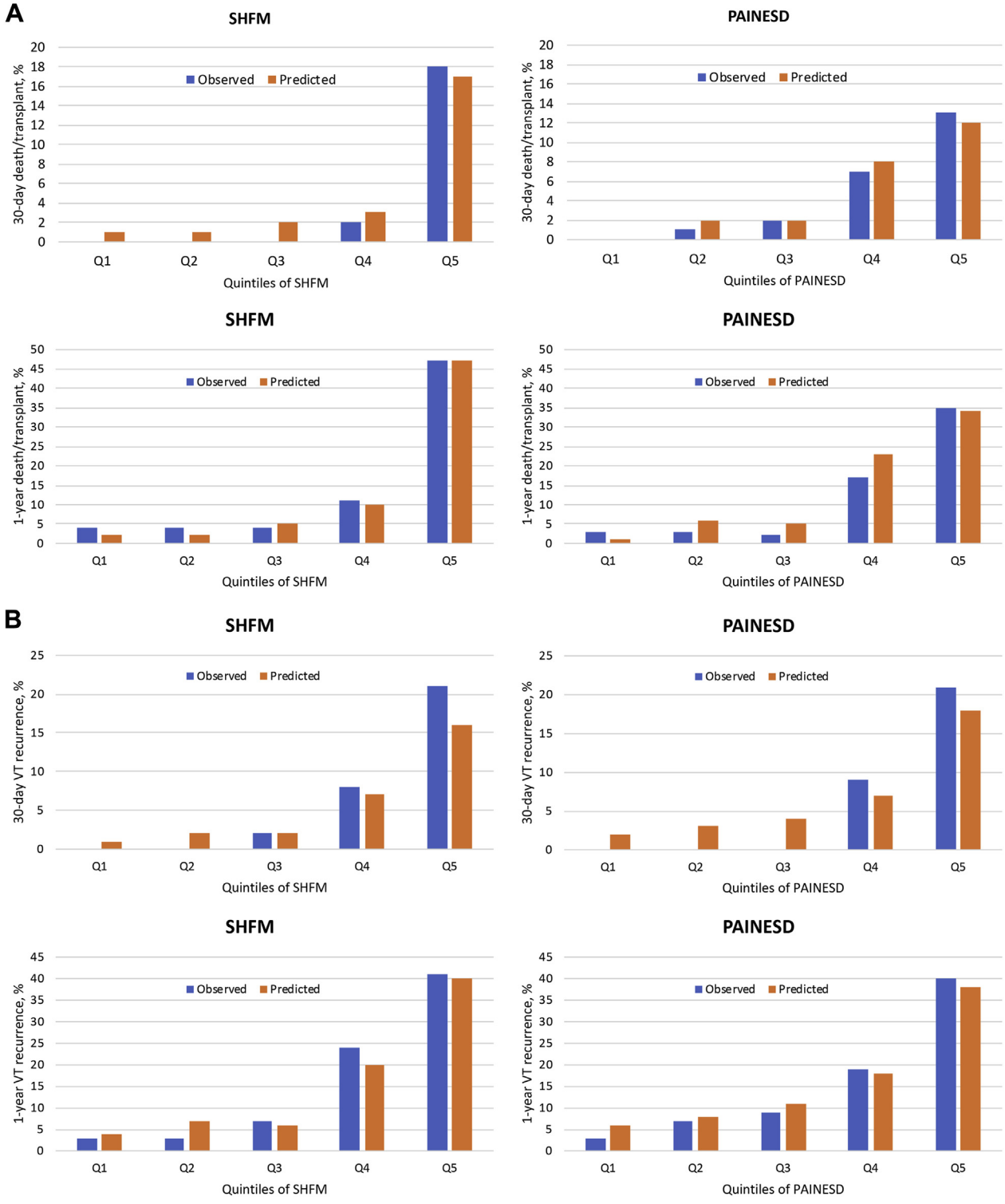
best accuracy without a significant difference between them ($p = 0.13$). The ADHERE score had the lowest accuracy (AUC = 0.70), with a significant difference when compared with the SHFM ($p < 0.01$) and PAINESD ($p = 0.02$) scores (Figure 1A). According to the AIC, each predictive model analyzed appeared to be <0.01× as probable as the SHFM score (AIC = 619) to minimize the information loss. The goodness-of-fit test demonstrated a substantial lack of fit for all the models except for SHFM ($p = 0.68$), OPTIMIZE-HF ($p = 0.12$), and PAINESD ($p = 0.24$).

The prognostic accuracy for VT recurrence was poor for all the scores except the SHFM (AUC = 0.77) and PAINESD (AUC = 0.70), without a significant difference between the 2 ($p = 0.11$) (Figure 1B). According to the AIC, each predictive model analyzed with the exception of EFFECT (AIC = 564; relative likelihood = 0.22) had a very low probability of minimizing the information loss compared with that of the PAINESD score (AIC = 561). The goodness-of-fit test demonstrated that all the models had an overall good calibration with the exception of OPTIMIZE-HF ($p < 0.01$).

Overall, the SHFM and PAINESD risk scores showed the best performance (highest AUC, lowest AIC, and no significant lack of fit) in predicting both death/transplant and VT recurrence. The histograms represented in Figure 2 show the observed versus model-predicted 30-day and 12-month event rates according to quintiles of the SHFM and PAINESD scores. There was a slight overprediction of mortality/transplant for all risk groups except the highest using the PAINESD score, whereas the SHFM score underpredicted mortality/transplant in all risk groups except the highest. The 2 scores had a substantially similar accuracy in predicting death/transplant as demonstrated also by the nearly identical curves of observed versus predicted death/transplant-free stratified according to the 3 risk groups (Figure 3A). A modest overestimation of VT recurrence in the low-to-mid risk range was seen using either SHFM or PAINESD scores, whereas both of them slightly underpredicted VT recurrence among patients at higher risk. The observed versus predicted VT-free survival curves in 3 risk groups appeared nearly superimposable supporting a good calibration of both models (Figure 3B).

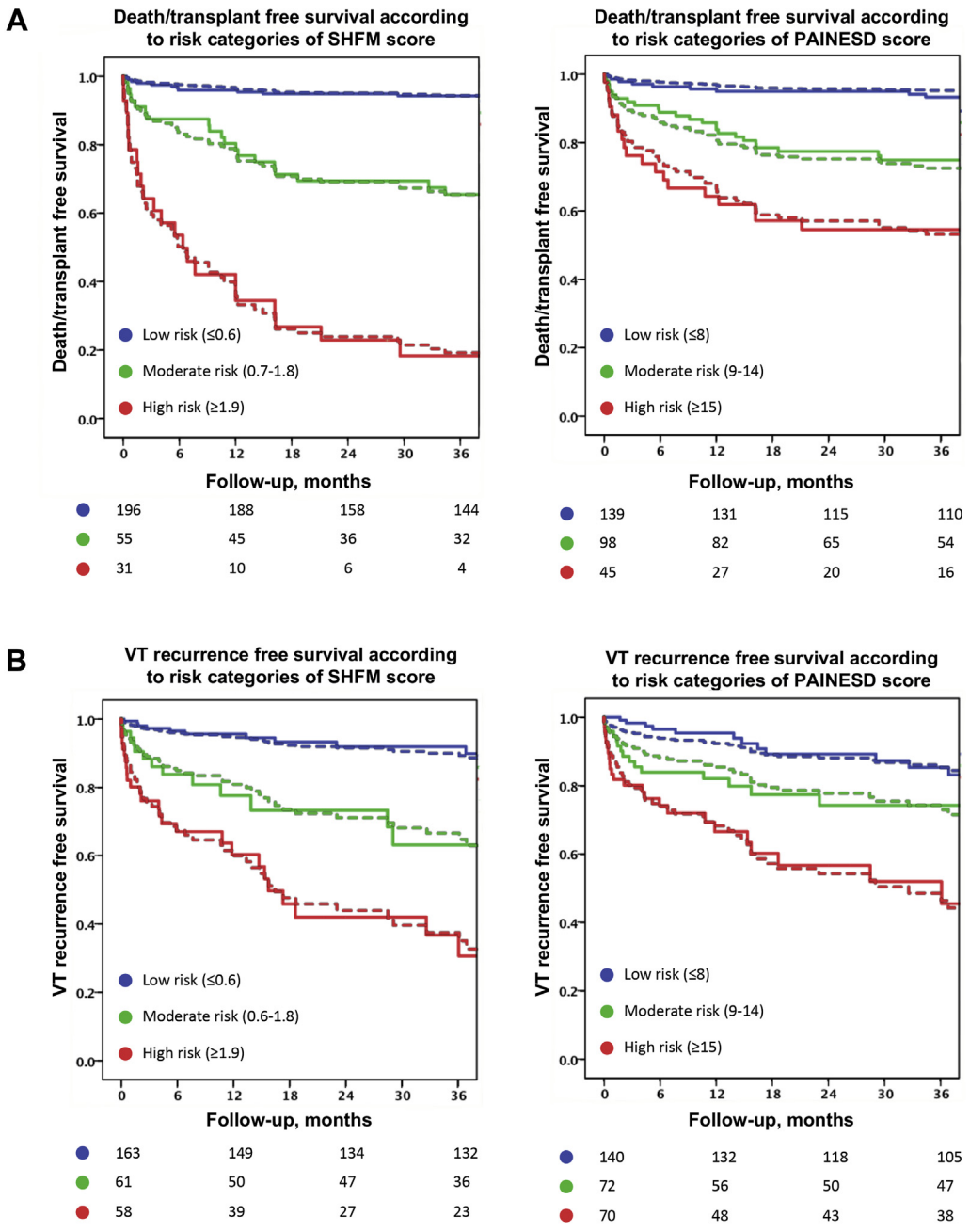
IDENTIFICATION OF HIGH-RISK PATIENTS USING THE SHFM AND PAINESD SCORES. Baseline characteristics and procedural and long-term outcomes according to SHFM and PAINESD risk groups are presented in Table 3. High-risk patients were identified as those having a pre-procedural SHFM score of ≥1.9 and a PAINESD score of ≥15 (Central Illustration). Patients at high risk according to both SHFM and PAINESD scores were older, had a lower LVEF, higher NYHA functional class, and were more frequently affected by comorbidities such as diabetes

FIGURE 2 **Observed vs. Predicted 30-Day and 12-Month Mortality/Transplant and VT Recurrence**



Observed versus predicted 30-day and 12-month mortality/transplant **(A)** and ventricular tachycardia recurrence **(B)** according to quintiles (Q) of SHFM and PAINESD. Abbreviations as in Figure 1.

FIGURE 3 Observed vs. Predicted Death/Transplant-Free and VT-Free Survival



Observed **(solid lines)** versus predicted **(dotted lines)** death/transplant-free survival **(A)** and VT-free survival **(B)** according to risk groups of SHFM and PAINESD. Abbreviations as in Figure 1.

mellitus, chronic obstructive pulmonary disease, and chronic kidney disease. High-risk features based on pre-procedural SHFM and PAINESD scores predicted both acute and long-term procedural efficacy. In particular, noninducibility of any VT with CL ≤250 ms at post-procedural programmed ventricular stimulation was achieved in 15 of 24 high-risk patients (63%) and 23 of 37 (62%) according to SHFM and PAINESD scores, respectively, versus 159 of 186 lower risk patients (85%) and 120 of 136 (88%)

TABLE 3 Baseline Characteristics and Procedural and Long-Term Outcomes According to SHFM and PAINESD Risk Groups

	Low-Risk SHFM (≤0.6)	Moderate-Risk SHFM (0.7-1.8)	High-Risk SHFM (≥1.9)	p Value
Patients	198	56	28	
Age, yrs	57 ± 14	60 ± 16	67 ± 14	<0.01
Male	153 (77)	48 (86)	25 (89)	0.17
Diabetes mellitus	19 (10)	9 (16)	8 (29)	0.01
Chronic obstructive pulmonary disease	12 (6)	10 (18)	5 (18)	<0.01
Chronic kidney disease	25 (13)	18 (32)	14 (50)	<0.01
History of atrial fibrillation/flutter	37 (19)	18 (30)	12 (43)	<0.01
NYHA functional class III/IV	29 (15)	29 (52)	26 (93)	<0.01
LVEF, %	39 ± 13	31 ± 12	27 ± 12	<0.01
LVEF ≤35%	79 (40)	34 (61)	24 (86)	<0.01
Clinical presentation with VT storm	37 (19)	20 (36)	14 (50)	<0.01
Programmed stimulation at the end of the procedure	186 (94)	52 (93)	24 (86)	0.28
Noninducibility of any VT with CL ≥250 ms at the end of the procedure	159 (85)	42 (81)	15 (63)	0.02
Death/transplant	14 (7)	26 (46)	25 (89)	<0.01
30-day mortality/transplant, %	1	7	21	<0.01*
6-month mortality/transplant, %	4	12	46	<0.01*
12-month mortality/transplant, %	5	20	66	<0.01*
VT recurrence	15 (8)	14 (26)	29 (51)	<0.01
30-day VT recurrence, %	1	5	20	<0.01*
6-month VT recurrence, %	3	16	33	<0.01*
12-month VT recurrence, %	3	22	40	<0.01*
	Low-Risk PAINESD (≤8)	**Moderate-Risk PAINESD (9–14)**	**High-Risk PAINESD (≥15)**	**p Value**
Patients	141	99	42	
Age, yrs	55 ± 15	63 ± 12	66 ± 13	<0.01
Male	107 (76)	82 (83)	37 (88)	0.16
Diabetes mellitus	9 (6)	15 (15)	12 (29)	<0.01
Chronic obstructive pulmonary disease	1 (1)	14 (14)	12 (29)	<0.01
Chronic kidney disease	17 (12)	22 (22)	18 (43)	<0.01
History of atrial fibrillation/flutter	21 (15)	29 (30)	16 (38)	<0.01
NYHA functional class III/IV	3 (2)	42 (42)	39 (93)	<0.01
LVEF, %	40 ± 12	36 ± 13	24 ± 10	<0.01
LVEF ≤35%	54 (38)	48 (49)	35 (83)	<0.01
Clinical presentation with VT storm	12 (9)	29 (29)	30 (71)	<0.01
Programmed stimulation at the end of the procedure	136 (96)	89 (90)	37 (88)	0.06
Noninducibility of any VT with CL ≥250 ms at the end of the procedure	120 (88)	73 (82)	23 (62)	<0.01
Death/transplant	9 (6)	33 (33)	23 (55)	<0.01
30-day mortality/transplant, %	1	6	12	<0.01*
6-month mortality/transplant, %	4	11	29	<0.01*
12-month mortality/transplant, %	5	16	36	<0.01*
VT recurrence	16 (11)	15 (21)	27 (40)	<0.01
30-day VT recurrence, %	0	5	18	<0.01*
6-month VT recurrence, %	3	16	26	<0.01*
12-month VT recurrence, %	5	18	33	<0.01*

Values are n, mean ± SD, or n (%), unless otherwise indicated. *Log-rank test.
CL = cycle length; other abbreviations as in Table 1.

($p = 0.02$ and $p < 0.01$ for comparison). VT noninducibility at the end of the procedure was not an independent predictor of mortality and VT recurrence when the SHFM or PAINESD scores were included in the multivariable model (Online Tables 3 and 4). The 30-day and 12-month mortality/transplant rates for patients with high-risk SHFM score were 21% and 66% and were 12% and 36% for patients with high-risk PAINESD score. These rates were significantly higher than what was observed for lower risk patients (**Table 3**). Similarly, the 30-day and 12-month VT recurrence rates were 20% and 40% for high-risk

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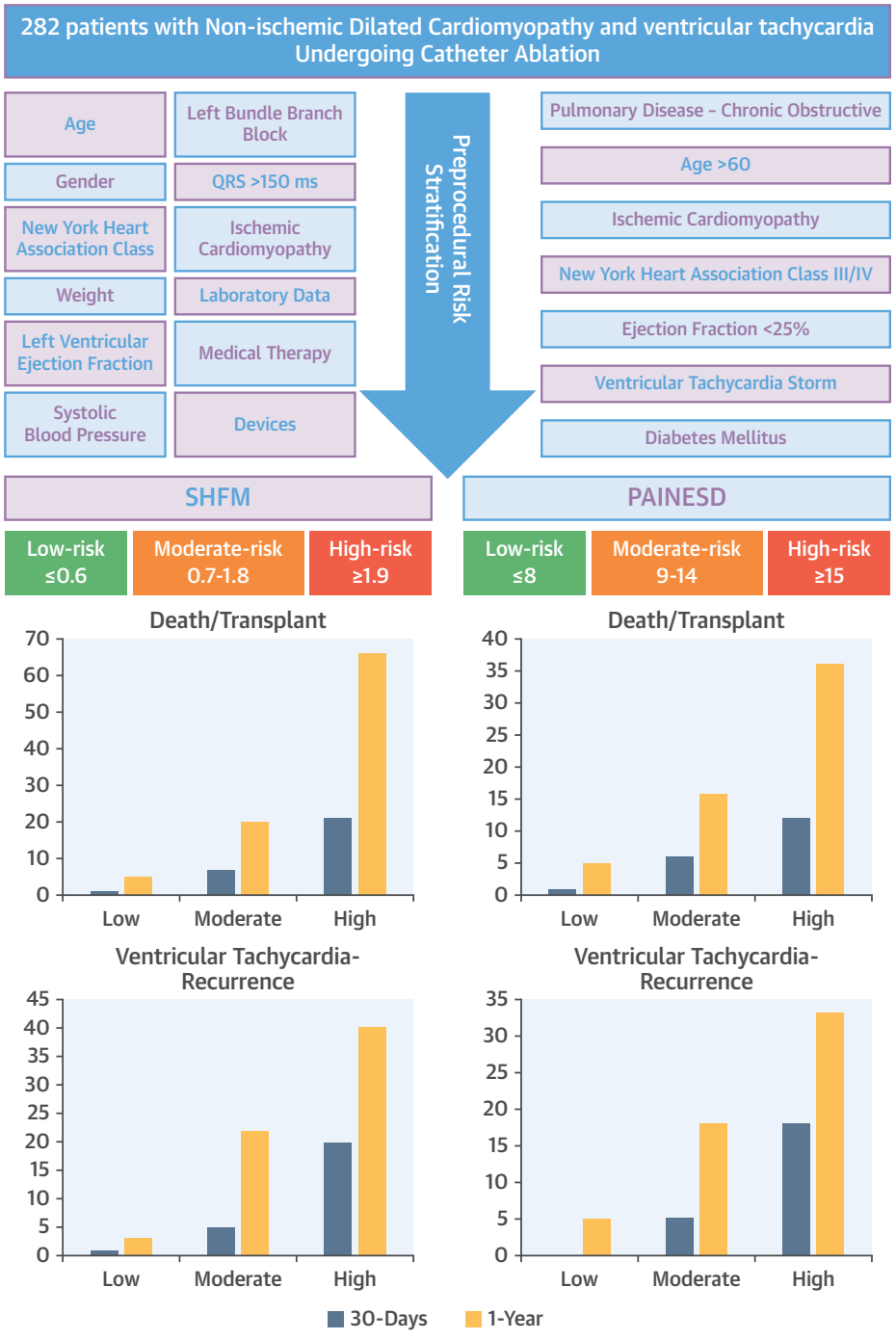
CENTRAL ILLUSTRATION **Risk-Stratification of Patients With NIDCM and VT Undergoing CA**



Muser, D. et al. J Am Coll Cardiol EP. 2019;5(7):801–13.

Risk-stratification of patients with nonischemic dilated cardiomyopathy (NICDM) undergoing ventricular tachycardia (VT) catheter ablation (CA) by the use of SHFM (Seattle Heart Failure Model) and PAINESD (Chronic Obstructive Pulmonary Disease, Age >60 Years, Ischemic Cardiomyopathy, New York Heart Association Functional Class III or IV, Ejection Fraction <25%, Presentation With VT Storm, Diabetes Mellitus) score. BP = blood pressure; LBBB = left bundle branch block; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association.

SHFM patients, and 18% and 33% for high-risk PAINESD score were also significantly higher than those observed in lower risk patients.

DISCUSSION

The present study is the first to investigate pre-procedural risk stratification of patients with NIDCM undergoing CA of VT by systematically evaluating the predictive role of existing HF prognostic risk scores. The main findings are as follows: 1) in patients with NICDM, pre-procedural risk stratification utilizing established HF risk scores is feasible, and it can provide important prognostic information on both the acute procedural efficacy and post-procedural outcomes including death/transplant and recurrent VT; 2) there was a significant difference in the accuracy of different risk scores, with the SHFM and PAINESD scores significantly outperforming others; 3) a SHFM score ≥1.9 and a PAINESD score ≥15 identified a subgroup of patients at particularly high risk, with a 30-day and 12-month mortality rates of up to 31% and 66%, respectively. Of note, this was associated with a lower acute procedural efficacy and worse long-term VT-free survival.

Compared with subjects with ischemic cardiomyopathy, the efficacy of VT ablation in patients with NIDCM is suboptimal, with post-procedural recurrence rates varying from 29% to 60% (1,20). These figures are mostly related to the complexity of the underlying arrhythmogenic substrates, with a high prevalence of endo-epicardial and intramural components, and an overall paucity of abnormal electrograms that are potential targets for substrate-based ablation procedures (4). In this context, repeated VT inductions may be necessary to detect critical substrate components to target for ablation, and this may result in adverse hemodynamic consequences with increased risk of periprocedural acute hemodynamic decompensation (12,21). In select NIDCM cases, presentation with VT may also merely represent a marker of worsening HF status with limited possibility of achieving clinically meaningful acute and long-term arrhythmia control with CA due to the competing short-term risk of HF progression and mortality (2). On these premises, a proper pre-procedural risk stratification of patients with NIDCM and VT referred for CA is crucial, as it may improve patient selection; inform referring physicians, patients, and their families on expected outcomes and probability of adverse events; and help develop appropriate procedural and post-procedural treatment pathways (22).

In this study, we systematically evaluated the role of 8 risk stratification tools to predict procedural outcomes in patients with NIDCM and VT undergoing CA. As mentioned, the SHFM and PAINESD scores significantly outperformed other risk stratification tools and demonstrated an acceptable calibration to our sample and a good discrimination for early and long-term mortality and VT recurrence. These findings in a homogeneous population of NIDCM and VT confirm and expand the results of prior observational studies, including the recent multicenter registry by Vergara et al. (23), in which a survival tree statistical analysis has been performed to identify the best variables able to discriminate groups of subjects with homogeneous survival and VT-recurrence rates (2,3). However, at variance with prior investigations that proposed risk stratification algorithms best fitting their specific study population without external validation in independent cohorts, our study systematically compared the predictive role of different established HF risk scores that have all already been validated in different and independent patient cohorts. In addition, our study is specifically focused on a homogenous group of patients with NIDCM to determine what may be the optimal approach to pre-procedural risk stratification in this challenging patient population.

Direct comparison of the SHFM risk score with the PAINESD score failed to find significant differences between the 2 scores, although there was a trend toward improved prognostic performance with the SHFM. In this regard it is important to point out that the SHFM is composed of a large number of parameters that include variables such as lymphocyte count, uric acid, and total cholesterol (5). From a practical perspective and particularly for subjects with NIDCM referred for CA of VT, calculation of the SHFM may be cumbersome and hard to implement in clinical practice. On the other hand, the PAINESD score has significantly fewer readily available variables, making it easier to implement at the bedside.

As expected, the risk of death/transplant and VT recurrence increased with increasing values of scores. In this context, pre-procedural risk stratification is important to provide reliable expectations to patients and their family members and to tailor the best treatment approach taking into account different patient characteristics, clinical presentation, and existence of alternative treatment options. This is especially important when there is a high risk of unfavorable outcomes due to the coexistence of advanced HF or significant comorbidities.

It is important to emphasize that our study does not support the adoption of different pre-procedural risk stratification tools to decide whether a CA procedure should be performed, as also patients with

high values of scores (i.e., SHFM ≥1.9 and PAINESD ≥15) may derive benefit from VT control with CA. However, in these high-risk cases, other considerations beyond control of recurrent VT must be made, including evaluation for advanced HF management (i.e., early referral for heart transplant/mechanical ventricular assistance devices). In this regard, it is important to emphasize that even when high-risk patients with NIDCM and recurrent VT qualify for advanced HF therapies, VT ablation may still represent an important therapeutic option particularly in the setting of poorly controlled arrhythmias with repeated ICD shocks. In these cases, achievement of VT control with ablation is important also when heart transplant is considered and there are no further AAD options (24).

The present study poses the basis for the use of prognostic models for risk stratification of patients with structural heart disease undergoing CA of VT. Further prospective studies on larger populations are needed to evaluate the impact of using such models on guiding clinical practice and decisions for specific therapeutic approaches as compared to the usual care not guided by specific protocols for pre-procedural risk stratification.

STUDY LIMITATIONS. This is a single-center observational study conducted in a tertiary center specialized in the treatment of complex ventricular arrhythmias. Moreover, 16% of the patients were referred after failed attempts of VT ablation in outside institutions and therefore patient's characteristics, incidence of procedural complications, and rate of procedural success may not reflect those of an unselected sample of patients. All variables used for risk calculation were collected at the time of hospital admission, which is in line with prior studies evaluating the performance of different HF risk models (3,25). However, this approach provides a more "static" picture of the patients' status at the time of hospital admission, without accounting for possible longitudinal changes in clinical status and management with potential prognostic impact, such as changes in HF medications or AAD therapy following VT ablation.

CONCLUSIONS

In patients with NIDCM and VT undergoing CA, pre-procedural risk stratification utilizing established HF risk scores is feasible and can provide important prognostic information on the anticipated procedural outcomes. The SHFM and PAINESD scores showed similar performance and appeared to be more accurate than other models in predicting mortality/transplant and acute and long-term CA success. The implementation of these risk stratification tools can help identifying the optimal therapeutic pathways beyond treatment of VT, such as earlier consideration for advanced HF therapies and/or proper discussion with patients and families about the expected procedural outcomes and goals of care.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: The implementation of established HF risk scores such as the SHFM and PAINESD scores in pre-procedural risk stratification of patients with NIDCM undergoing CA of VT can provide important prognostic information on the anticipated procedural outcomes.

TRANSLATIONAL OUTLOOK: Multiparametric prediction models are developed to guide health care professionals in clinical decision-making. Testing a model in different patient populations than those from which it was developed (external validation) is necessary before its application in routine clinical practice. Further validation on large prospective studies assessing the impact of pre-procedural risk stratification on different therapeutic management pathways for patients with NIDCM and VT is needed.

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KEY WORDS **catheter ablation, dilated cardiomyopathy, electroanatomical mapping, heart failure, ventricular tachycardia**

APPENDIX **For supplemental tables and figures, please see the online version of this paper.**