Circulation: Cardiovascular Imaging

ORIGINAL ARTICLE

Deep Learning–Enabled Assessment of Right Ventricular Function Improves Prognostication After Transcatheter Edge-to-Edge Repair for Mitral Regurgitation

Mark Lachmann, MD*; Vera Fortmeier, MD*; Lukas Stolz, MD; Márton Tokodi, MD, PhD; Attila Kovács, MD, PhD; Amelie Hesse, MS; Antonia Leipert, MD; Elena Rippen, MD; Héctor Alfonso Alvarez Covarrubias, MD; Moritz von Scheidt, MD; Jule Tervooren, MS; Ferdinand Roski, MD; Michelle Fett, MS; Muhammed Gerçek, MD; Tibor Schuster, PhD; Gerhard Harmsen, PhD; Shinsuke Yuasa, MD, PhD; N. Patrick Mayr, MD; Adnan Kastrati, MD; Heribert Schunkert, MD; Michael Joner, MD; Erion Xhepa, MD, PhD; Karl-Ludwig Laugwitz, MD; Jörg Hausleiter, MD; Volker Rudolph, MD; Teresa Trenkwalder, MD

BACKGROUND: Right ventricular (RV) function has a well-established prognostic role in patients with severe mitral regurgitation (MR) undergoing transcatheter edge-to-edge repair (TEER) and is typically assessed using echocardiography-measured tricuspid annular plane systolic excursion. Recently, a deep learning model has been proposed that accurately predicts RV ejection fraction (RVEF) from 2-dimensional echocardiographic videos, with similar diagnostic accuracy as 3-dimensional imaging. This study aimed to evaluate the prognostic value of the deep learning–predicted RVEF values in patients with severe MR undergoing TEER.

METHODS: This multicenter registry study analyzed the associations between the predicted RVEF values and 1-year mortality in patients with severe MR undergoing TEER. To predict RVEF, 2-dimensional apical 4-chamber view videos from preprocedural transthoracic echocardiographic studies were exported and processed by a rigorously validated deep learning model.

RESULTS: Good-quality 2-dimensional apical 4-chamber view videos could be retrieved for 1154 patients undergoing TEER between 2017 and 2023. Survival at 1 year after TEER was 84.7%. The predicted RVEF values ranged from 26.6% to 64.0% and correlated only modestly with tricuspid annular plane systolic excursion (Pearson R=0.33; P<0.001). Importantly, predicted RVEF was superior to tricuspid annular plane systolic excursion levels in predicting 1-year mortality after TEER (area under the curve, 0.687 versus 0.625; P=0.029). Furthermore, Kaplan-Meier survival analysis revealed that patients with reduced RV function (n=723; defined as a predicted RVEF of <45%) had significantly worse 1-year survival rates than patients with preserved RV function (n=431; defined as a predicted RVEF of ≥45%; 80.3% [95% CI, 77.4%–83.3%] versus 92.1% [95% CI, 89.5%–94.7%]; hazard ratio for 1-year mortality, 2.67 [95% CI, 1.82–3.90]; P<0.001).

CONCLUSIONS: Deep learning–enabled assessment of RV function using standard 2-dimensional echocardiographic videos can refine the prognostication of patients with severe MR undergoing TEER. Thus, it can be used to screen for patients with RV dysfunction who might benefit from intensified follow-up care.

GRAPHIC ABSTRACT: A graphic abstract is available for this article.

Key Words: deep learning ■ echocardiography ■ mitral valve ■ prognosis ■ survival analysis

See Editorial by Anand and Nkomo

Correspondence to: Mark Lachmann, MD, First Department of Medicine, Klinikum rechts der Isar, Technical University of Munich, Ismaninger Straße 22, 81675 Munich, Germany. Email mark.lachmann@hhu.de
*M. Lachmann and V. Fortmeier contributed equally to this work.
Supplemental Material is available at https://www.ahajournals.org/doi/suppl/10.1161/CIRCIMAGING.124.017005.
Continuing medical education (CME) credit is available for this article. Go to http://cme.ahajournals.org to take the quiz.
For Sources of Funding and Disclosures, see page 36.

Circulation: Cardiovascular Imaging is available at www.ahajournals.org/journal/circimaging

CLINICAL PERSPECTIVE

In patients with severe mitral regurgitation undergoing transcatheter edge-to-edge repair, right ventricular (RV) function has a crucial role in prognostication. This multicenter study evaluated the prognostic value of a rigorously validated deep learning model predicting RV ejection fraction from 2-dimensional echocardiographic videos. Notably, predicted RV ejection fraction values correlated only modestly with tricuspid annular plane systolic excursion and were superior in predicting 1-year mortality after transcatheter edge-to-edge repair (area under the curve, 0.687 versus 0.625, P=0.029). Moreover, patients with reduced RV ejection fraction (<45%) demonstrated significantly worse 1-year survival rates (80.3% versus 92.1%; hazard ratio for 1-year mortality, 2.67 [95% CI, 1.82–3.90]; P<0.001). Thus, deep learning–based RV ejection fraction assessment can potentially refine the prognostication of these patients and identify those requiring intensified follow-up after transcatheter edge-to-edge repair.

Nonstandard Abbreviations and Acronyms

2D	2-dimensional
3D	3-dimensional
AUC	area under the curve
IQR	interquartile range
LVEF	left ventricular ejection fraction
MR	mitral regurgitation
MV	mitral valve
OR	odds ratio
RV	right ventricle/right ventricular
RVEF	right ventricular ejection fraction
TAPSE	tricuspid annular plane systolic excursion
TEER	transcatheter edge-to-edge repair
TR	tricuspid regurgitation

A growing body of scientific evidence emphasizes the clinical relevance of the right ventricle (RV) across a broad spectrum of cardiac diseases, both from symptomatic and prognostic perspectives.[1] In patients with severe mitral regurgitation (MR) undergoing mitral valve (MV) transcatheter edge-to-edge repair (TEER), RV function is a critical determinant of prognosis[2–5]; thus, accurately assessing RV performance is indispensable in these patients. Although conventional 2-dimensional (2D) echocardiography has remained the most frequently used cardiovascular imaging modality, it has substantial limitations in quantifying RV performance because of the RV's intricate geometry and retrosternal position. Tricuspid annular plane systolic excursion (TAPSE) is one of the oldest echocardiographic indices used for assessing RV function. TAPSE measures the displacement of the tricuspid annular plane toward the apex during systole, serving as a surrogate parameter for longitudinal fiber shortening. However, in cases where the RV has undergone pathological remodeling because of increased afterload, leading to ventricular dilatation and elevated wall stress, longitudinal contraction diminishes while circumferential and radial contractions increase.[6,7] Consequently, TAPSE is not suitable for the comprehensive assessment of RV function under these conditions.[8,9] In addition, in patients with more than moderate tricuspid regurgitation (TR), TAPSE can seem pseudo-normalized, further limiting its clinical utility.[10]

In contrast, cardiac magnetic resonance imaging provides a comprehensive 3-dimensional (3D) view of the RV, establishing itself as the gold standard for right heart assessments, such as the quantification of RV volumes and RV ejection fraction (RVEF). However, the high cost, long scan times, and limited accessibility of cardiac magnetic resonance imaging present significant hurdles, restricting its utilization in clinical routine. Deep learning holds the promise of extracting in-depth clinical insights from simpler imaging modalities like 2D echocardiography. Tokodi et al[11] recently developed a deep learning model in a diverse patient population, including individuals with various cardiovascular disorders, healthy volunteers, and elite athletes, to estimate RVEF based on 2D apical 4-chamber view echocardiographic videos. The model was trained using 3D echocardiography–derived RVEF as the ground truth. Although the model was also validated internally and externally, further studies are required to demonstrate its clinical utility in additional patient cohorts.

Acknowledging the potential arising from the convergence of human and artificial intelligence to improve patient care (eg, disease diagnosis, risk stratification, and assessment of treatment response), this study aims to evaluate the prognostic significance of the aforementioned deep learning model for RVEF assessment in patients diagnosed with severe MR. When compared with conventional echocardiographic metrics of RV performance, such as TAPSE, the central research question emerges: does deep learning–derived RVEF predict survival after MV TEER more accurately in these patients? Therefore, this study represents the first attempt to validate the clinical utility of the deep learning model of Tokodi et al[11] in a large multicenter registry of patients with severe MR undergoing MV TEER.

METHODS

The data that support the findings of this study are available from the corresponding author on reasonable request. All requests for raw and analyzed data and related materials will be

reviewed by the Ethics Committee at the Technical University of Munich, Germany. Any data and materials that can be shared will be released via a Material Transfer Agreement.

Study Sample

This is a post hoc, multicenter analysis of prospectively and systematically collected data from patients who underwent MV TEER for symptomatic moderate-to-severe or severe MR at 3 high-volume tertiary care centers in Germany between 2017 and 2023. Baseline demographic and clinical characteristics were obtained from registry data or clinical records as appropriate. All patients underwent transthoracic as well as transesophageal echocardiography before MV TEER. The number of devices implanted was determined by the discretion of the treating physician. In addition, this multicenter registry is device-agnostic, enrolling all patients who underwent MV TEER, irrespective of the specific device used. As an elderly patient population was studied, postprocedural 1-year all-cause mortality was defined as a clinically meaningful primary outcome measure. Survival data were obtained from routine clinical follow-ups, general practitioners, hospitals, and practice cardiologists or the German Civil Registry. The local ethics committee at each participating center approved the collection and analysis of data in accordance with the Declaration of Helsinki, and all patients gave their written informed consent to be enrolled in an observational registry.

Transthoracic Echocardiography

All echocardiographic studies were performed by experienced institutional cardiologists during clinical routine with commercially available equipment (Philips Medical [EPIQ CVx, X5-1 probe] and General Electric [E9, E95, 4Vc-D probe] systems). Echocardiographic measures were assessed according to the current guideline recommendations,[12] and classification of MR severity was performed using an integrative, multiparametric 4-group approach ([1] mild, [2] moderate, [3] severe, and [4] massive). In addition, the cause of MR was defined as either primary (MV prolapse with or without flail leaflet), secondary (ventricular dilatation, atrial dilatation, or both) or mixed. TAPSE was assessed in an apical 4-chamber echocardiographic view by placing the M-mode line at the lateral tricuspid valve annulus and measuring the movement of the tricuspid annulus toward the apex during systole. For the purpose of this study, all echocardiographic studies were retrospectively reviewed, and measurements of RV fractional area change, as well as RV free wall longitudinal strain, were additionally conducted using commercially available software packages, namely EchoPAC BT12 and TomTec Imaging, across different centers. Furthermore, RV function was visually assessed and graded using a qualitative 5-grade scheme: (1) normal, (2) mildly reduced, (3) moderately reduced, (4) moderately to severely reduced, and (5) severely reduced.

Transcatheter Edge-to-Edge Repair

In all patients, the indication for MV TEER was symptomatic moderate-to-severe or severe MR, and the local heart teams approved all procedures. Procedures were performed under general anesthesia with 3D transesophageal echocardiographic and fluoroscopic guidance. Details of the procedures have been described previously.[13]

Deep Learning–Based RVEF Assessment

Experienced echocardiographers reviewed all preprocedural videos in each patient's echocardiographic study and identified suitable 2D apical 4-chamber view recordings (either standard or RV focused, without color Doppler). After the manual identification of suitable 4-chamber views, these videos were exported as deidentified Digital Imaging and Communications in Medicine files and were processed using a previously published deep learning pipeline, coded in Python (Python Software Foundation, Wilmington, DE). Although the deep learning pipeline was originally coded in Python version 3.8.6 using PyTorch version 1.12.1+cu116, we also tested it in Python version 3.12.6 using PyTorch version 2.4.1+cu118 without encountering any issues. The architecture and design of the deep learning model for predicting RVEF have been previously described,[11] and the deep learning pipeline, along with its requirements and instructions, is publicly available at https://github.com/rvenet/RVENet-Demo. In brief, the model comprises an ensemble of 3 spatiotemporal convolutional networks that were trained to predict 3D echocardiography–derived RVEF from 2D apical 4-chamber view echocardiographic videos. Importantly, the model processes multiple cardiac cycles, and the final predicted RVEF is calculated as the average of the predictions derived from all analyzed cardiac cycles within the video to account for beat-to-beat variability. Furthermore, the model provided accurate predictions during both internal and external validation, identified RV dysfunction (ie, an RVEF of <45%) with similar accuracy but higher sensitivity than expert human readers, and provided the same prognostic information as 3D echocardiography. Based on threshold definitions from 3D echocardiography guidelines, we defined preserved RV function as a predicted RVEF of ≥45%.[8]

MitraScore Assessment

The MitraScore was assessed as described by Raposeiras-Roubin et al.[14] The MitraScore was derived by assigning 1 point to each of the following criteria: age ≥75 years, left ventricular ejection fraction (LVEF) <40%, anemia, glomerular filtrate rate <60 mL/min per 1.73 m^2, peripheral artery disease, chronic obstructive pulmonary disease, high dose of diuretics, and no therapy with renin-angiotensin system inhibitors. It is important to note that the MitraScore was only calculated for patients with available data for all these parameters. The MitraScore could not be computed for patients with missing data; thus, those patients were excluded from these subanalyses.

Statistical Analysis

All statistical analyses were performed in R (R version 4.3.2; R Foundation for Statistical Computing, Vienna, Austria).

Categorical data are presented as numbers and frequencies (%), whereas continuous data are expressed as median and interquartile range (IQR). χ^2 or Fisher exact test was used to evaluate the association between categorical variables and independent-sample Wilcoxon tests were used to compare continuous variables.

Survival was plotted using the Kaplan-Meier method, and the log-rank test was applied to compare survival.

Receiver operating characteristic curves and the corresponding areas under the curve (AUCs) were calculated

to assess the performance of RV function metrics to predict 1-year mortality after MV TEER. To statistically compare the AUC from deep learning–based RVEF assessment against that of the established metrics of RV performance, we applied the roc.test function, which compares 2 receiver operating characteristic curves based on the method proposed by DeLong et al.[15]

Univariable logistic regression analyses were conducted to identify clinical and echocardiographic predictors of discrepancy between predicted RVEF and traditional RV function metrics. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated for each variable.

A *P* value of ≤0.05 was considered to indicate statistical significance.

RESULTS

Clinical Characteristics of the Study Sample

A total of 1366 patients who underwent MV TEER for moderate-severe and severe MR between 2017 and 2023 were initially considered for this multicenter analysis. This study focused on echocardiographic videos recorded before MV TEER; hence, only patients with comprehensive and high-quality 2D apical 4-chamber views were selected for further analysis (subsequently referred to as study sample). Images exemplifying adequate and inadequate apical 4-chamber views are provided in Figure 1A. Of the initial cohort, 212 patients (15.5%) were excluded because of technical issues or suboptimal image quality (Figure 1B). The remaining 1154 patients, who form the basis of all subsequent analyses, constitute the final study sample. To evaluate potential selection bias related to the availability and quality of echocardiograms, we compared the baseline characteristics of included and excluded patients. Importantly, both groups were largely similar across key characteristics, including the prevalence of chronic obstructive pulmonary disease—a crucial determinant of imaging quality and a significant factor in right heart failure and subsequent mortality (Tables S1 and S2), emphasizing that our study sample is representative of the entire cohort of patients undergoing MV TEER. Baseline demographic, clinical, and echocardiographic data regarding the final study sample (N=1154 patients) are presented in Tables 1 and 2; Tables S3 and S4 for complete lists of devices utilized). The median age was 79.7 (IQR, 74.2–83.4) years, and 55.9% of patients were male (Table 1). Most patients reported severe exertional dyspnea corresponding to the New York Heart Association functional classes III (72.0%) and IV

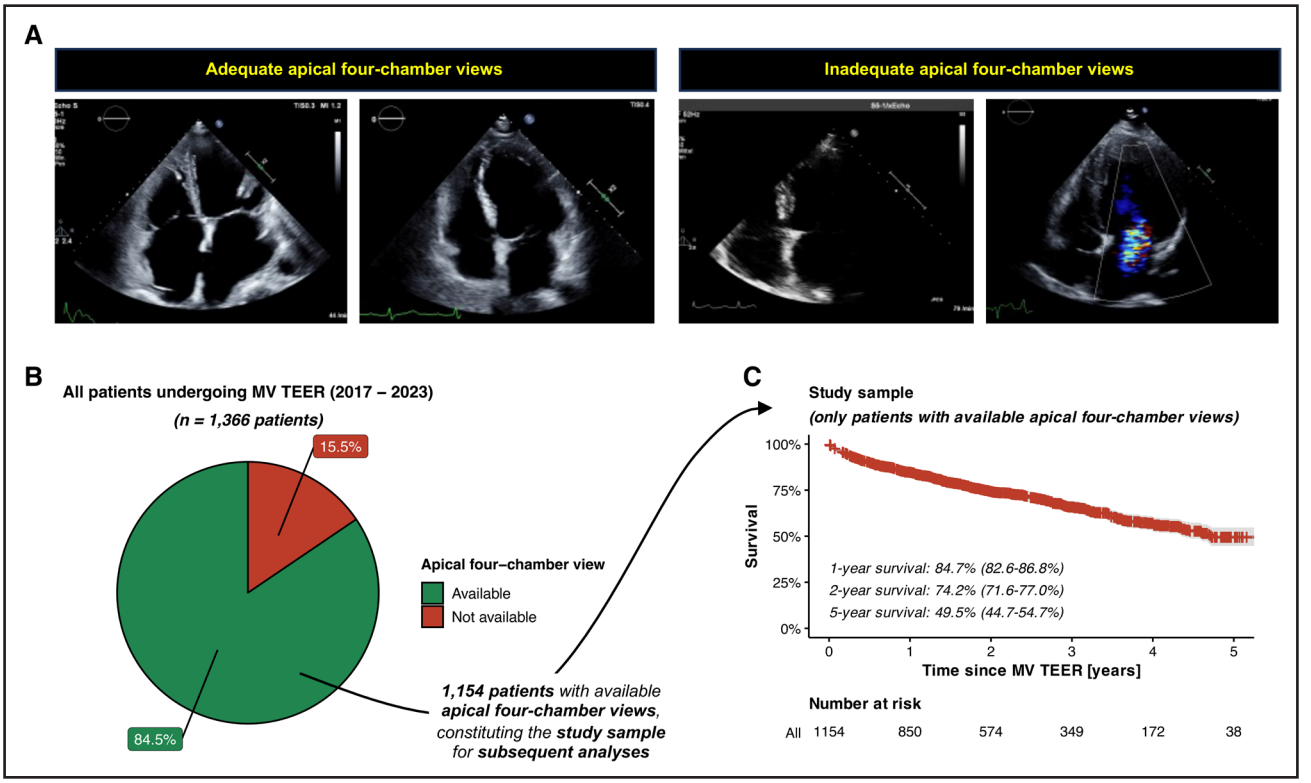

Figure 1. General information about the study sample and the availability of apical 4-chamber views suitable for analysis by the deep learning model.

A, Representative examples of apical 4-chamber views considered either suitable or unsuitable for deep learning analysis (notably, apical 4-chamber views with color Doppler signals were excluded). **B**, Pie chart illustrating the proportion of patients with apical 4-chamber views suitable for analysis using the deep learning model. **C**, Kaplan-Meier curve of the study sample with available apical 4-chamber views from their preprocedural transthoracic echocardiographic studies. MV indicates mitral valve; and TEER, transcatheter edge-to-edge repair.

Table 1. Demographics and Preprocedural Clinical Characteristics.

	All patients (N=1154)	$RVEF_{predicted}$		*P* value
		Preserved (n=431)	Reduced (n=723)	
Age, y	79.7 (74.2–83.4)	80.9 (76.1–84.2)	79.0 (73.3–82.7)	1.1×10^{-5}
Men, n (%)	645 (55.9%)	226 (52.4%)	419 (58.0%)	0.078
BMI, kg/m^2	24.8 (22.4–27.8)	24.7 (22.4–27.7)	24.9 (22.4–27.8)	0.276
Arterial hypertension, n (%)	951 (82.4%)	357 (82.8%)	594 (82.2%)	0.833
Diabetes, n (%)	284 (24.6%)	88 (20.4%)	196 (27.1%)	0.013
History of CAD, n (%)	637 (55.2%)	229 (53.1%)	408 (56.4%)	0.304
History of COPD, n (%)	210 (18.2%)	77 (17.9%)	133 (18.4%)	0.883
History of atrial fibrillation, n (%)	837 (72.5%)	270 (62.6%)	567 (78.4%)	9.4×10^{-9}
NYHA ≤II, n (%)	127 (11.0%)	54 (12.5%)	73 (10.1%)	0.238
NYHA III, n (%)	831 (72.0%)	320 (74.2%)	511 (70.7%)	0.216
NYHA IV, n (%)	196 (17.0%)	57 (13.2%)	139 (19.2%)	0.011
EuroSCORE II, %	4.76 (2.85–8.02)	4.24 (2.57–6.66)	5.08 (3.12–9.04)	$9.8\text{x}10^{-6}$
eGFR, mL/min	49 (36–65)	49 (38–67)	48 (34–64)	0.038
NT-proBNP, pg/mL	3180 (1510–6900)	2626 (896–5216)	3779 (1826–8130)	3.3×10^{-9}
Hemoglobin, g/dL	12.3 (10.8–13.6)	12.2 (10.8–13.5)	12.4 (10.8–13.7)	0.288
Cause, n (%)				
Primary	411 (35.6%)	208 (48.3%)	203 (28.1%)	6.8×10^{-12}
Secondary	610 (52.9%)	178 (41.3%)	432 (59.8%)	1.8×10^{-9}
Mixed	133 (11.5%)	45 (10.4%)	88 (12.2%)	0.426

Categorical data are presented as numbers and frequencies (%), whereas continuous data are expressed as median and interquartile range. EuroSCORE II is a refined risk model used to estimate the mortality risk for patients undergoing cardiac surgery. BMI indicates body mass index; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate; EuroSCORE II, European System for Cardiac Operative Risk Evaluation II; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; and RVEF, right ventricular ejection fraction.

(17.0%). Moreover, patients presented with a median NT-proBNP (N-terminal pro-B-type natriuretic peptide) level of 3180 pg/mL (IQR, 1510–6900 pg/mL). During the study period, 374 deaths were documented among the enrolled patients. The remaining participants were followed for a median duration of 2.41 years (IQR, 1.38–3.77 years). Accordingly, the 1-year survival rate for all patients was 84.7% (95% CI, 82.6%–86.8%; Figure 1C). A comparison of patients undergoing MV TEER between 2017 and 2019 and 2020 to 2023 revealed similar postprocedural gradients across the MV. However, the later treatment period showed better procedural outcomes in terms of residual MR (Figure S1A and S1B). In addition, survival rates were significantly better in patients treated later than those treated earlier (*P*=0.002; Figure S1C).

Comparing the Prognostic Value of the Deep Learning–Predicted RVEF Versus the Established Metrics of RV Performance

Predicted RVEF values ranged from 26.6% to 64.0% (median, 43.0; IQR, 39.1–47.4) and correlated only modestly with TAPSE (Pearson *R*=0.33; $P<2.2\times10^{-16}$; Figure 2). Notably, when predicting 1-year mortality after MV TEER, predicted RVEF outperformed TAPSE, as indicated by their respective AUCs of 0.687 (95% CI, 0.642–0.731) for predicted RVEF versus 0.625 (95% CI, 0.576–0.674) for TAPSE (*P*=0.029; Figure 2). Moreover, predicted RVEF was also superior to RV fractional area change and RV free wall longitudinal strain in predicting 1-year mortality after MV TEER ($P=2.6\times10^{-7}$ and 9.7×10^{-4}, respectively). In terms of visual assessment, most patients (63.7%) presented with normal or mildly reduced RV function (Figure 3A); importantly, the risk of 1-year mortality increased with higher grades of RV dysfunction as evaluated by visual assessment (Figure 3B). Nonetheless, predicted RVEF values were still superior to qualitative grading of RV function using the aforementioned 5-grade scheme in predicting 1-year mortality after MV TEER (*P*=0.041; Figure 3C).

Importantly, not all patients with a history of atrial fibrillation (837 out of 1154 patients; 72.5%) were in atrial fibrillation at the time of the echocardiographic study. In fact, only 566 patients (49.0%) were in atrial fibrillation during the examination, whereas the remaining patients were either in sinus rhythm (49.5%) or under pacemaker stimulation (1.5%). As shown in Figure S2, the predicted RVEF was the highest in patients with sinus rhythm and significantly reduced in those with atrial fibrillation (median predicted RVEF: 44.3% [IQR, 39.9%–49.0%] versus 42.2% [IQR, 38.5%–45.8%]; $P=5.1\times10^{-9}$).

Table 2. Preprocedural Echocardiographic Characteristics

		$RVEF_{predicted}$		
	All patients (N=1154)	Preserved (n=431)	Reduced (n=723)	*P* value
LVEF, %	50 (36–58)	55 (47–61)	45 (32–55)	$<2.2\times10^{-16}$
LVEDD, mm	56 (50–62)	53 (48–59)	57 (51–64)	6.7×10^{-10}
LVESD, mm	43 (36–51)	39 (33–45)	46 (38–54)	$<2.2\times10^{-16}$
LVEDV, mL	139 (98–189)	123 (92–164)	151 (102–205)	2.3×10^{-8}
LVESV, mL	68 (43–119)	54 (36–79)	82 (48–137)	6.6×10^{-15}
MV EROA, cm^2	0.29 (0.20–0.41)	0.30 (0.20–0.50)	0.28 (0.20–0.39)	9.2×10^{-6}
MR vena contract width, cm	0.69 (0.59–0.87)	0.70 (0.60–0.91)	0.67 (0.58–0.85)	0.037
MV regurgitation volume, mL	42 (29–63)	50 (35–73)	39 (27–56)	2.9×10^{-9}
LA volume, mL	122 (88–162)	111 (82–146)	128 (94–171)	1.6×10^{-5}
sPAP, mm Hg	45 (35–56)	46 (35–55)	45 (35–57)	0.984
Right midventricular diameter, mm	33 (29–39)	32 (28–38)	34 (29–40)	0.002
TAPSE, mm	18 (14–21)	19 (16–23)	17 (13–20)	1.3×10^{-14}
RA area, cm^2	25 (19–32)	23 (18–29)	26 (20–33)	7.0×10^{-8}
TAPSE/sPAP ratio, mm/mm Hg	0.385 (0.284–0.531)	0.436 (0.324–0.580)	0.358 (0.271–0.487)	2.6×10^{-8}
MR II and II+/IV°, n (%)	41 (3.55%)	8 (1.86%)	33 (4.56%)	0.025
MR III and III+/IV°, n (%)	666 (57.7%)	228 (52.9%)	438 (60.6%)	0.013
MR IV/IV°, n (%)	447 (38.7%)	195 (45.2%)	252 (34.9%)	0.001
TR ≥III/IV°, n (%)	297 (25.7%)	96 (22.3%)	201 (27.8%)	0.045

Categorical data are presented as numbers and frequencies (%), whereas continuous data are expressed as median and interquartile range. LA indicates left atrial; LVEDD, left ventricular end-diastolic diameter; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic diameter; LVESV, left ventricular end-systolic volume; MR, mitral regurgitation; MV EROA, MV effective regurgitant orifice area; MV, mitral valve; RA, right atrial; RVEF, right ventricular ejection fraction; sPAP, systolic pulmonary artery pressure; TAPSE, tricuspid annular plane systolic excursion; and TR, tricuspid regurgitation.

Notably, the performance of predicted RVEF levels to anticipate survival outcomes was equally good irrespective of the underlying MR cause (Figure 4). Kaplan-Meier survival analysis finally showed that patients with reduced RV function (defined as predicted RVEF <45%) had significantly worse 1-year survival compared with those with preserved RV function (80.3% [95% CI, 77.4%–83.3%] versus 92.1% [95% CI, 89.5%–94.7%]; hazard ratio for 1-year mortality, 2.67 [95% CI, 1.82–3.90]; *P*<0.001; Figure 5). Such a poor survival was only observed in patients who met at least 3 out of 4 conventional criteria for RV dysfunction (ie, TAPSE <17 mm, RV fractional area change <35%, RV free wall longitudinal strain >–20%, and qualitative grade of RV dysfunction from third to fifth grade; Figure 3D).

Notably, for patients who met a maximum of 2 out of 4 criteria for RV dysfunction and were thus not unambiguously categorized as having either preserved or reduced RV function, the additional assessment of predicted RVEF proved to be prognostically relevant. This assessment stratified these patients into low-risk and high-risk groups, with a hazard ratio of 7.16 ([95% CI, 1.65–31.2] *P*=0.009) for 1-year mortality after MV TEER (Figure 6).

Overall, only 3.7% of patients were identified as having a discrepancy between their predicted RVEF (≥45%) and traditional metrics of RV dysfunction (defined as meeting at least 3 out of 4 traditional criteria for RV dysfunction). To identify the predictors of this discrepancy, we performed univariable logistic regression analysis for several clinical and echocardiographic variables (Table S5). The analysis revealed that atrial fibrillation was the only significant predictor of discrepancy between predicted RVEF and traditional metrics of RV dysfunction, with an OR of 3.40 ([95% CI, 1.20–14.29] *P*=0.045). Other factors, including age (OR, 0.99 [95% CI, 0.96–1.03]; *P*=0.696), body mass index (OR, 0.96 [95% CI, 0.89–1.04]; *P*=0.332), and comorbidities, such as chronic obstructive pulmonary disease (OR, 1.75 [95% CI, 0.76–3.72]; *P*=0.162), were not significant predictors.

In addition, stratification into low-risk and high-risk groups based on the predicted RVEF was effective for patients regardless of the treatment period (Figure S1D).

Comparing the Functional and Morphological Characteristics of Patients With Preserved Versus Patients With Impaired RV Function

Figure 7 illustrates the functional and morphological characteristics of patients with either preserved or impaired RV function. Secondary MR was the predominant cause in 59.8% of patients with impaired RV

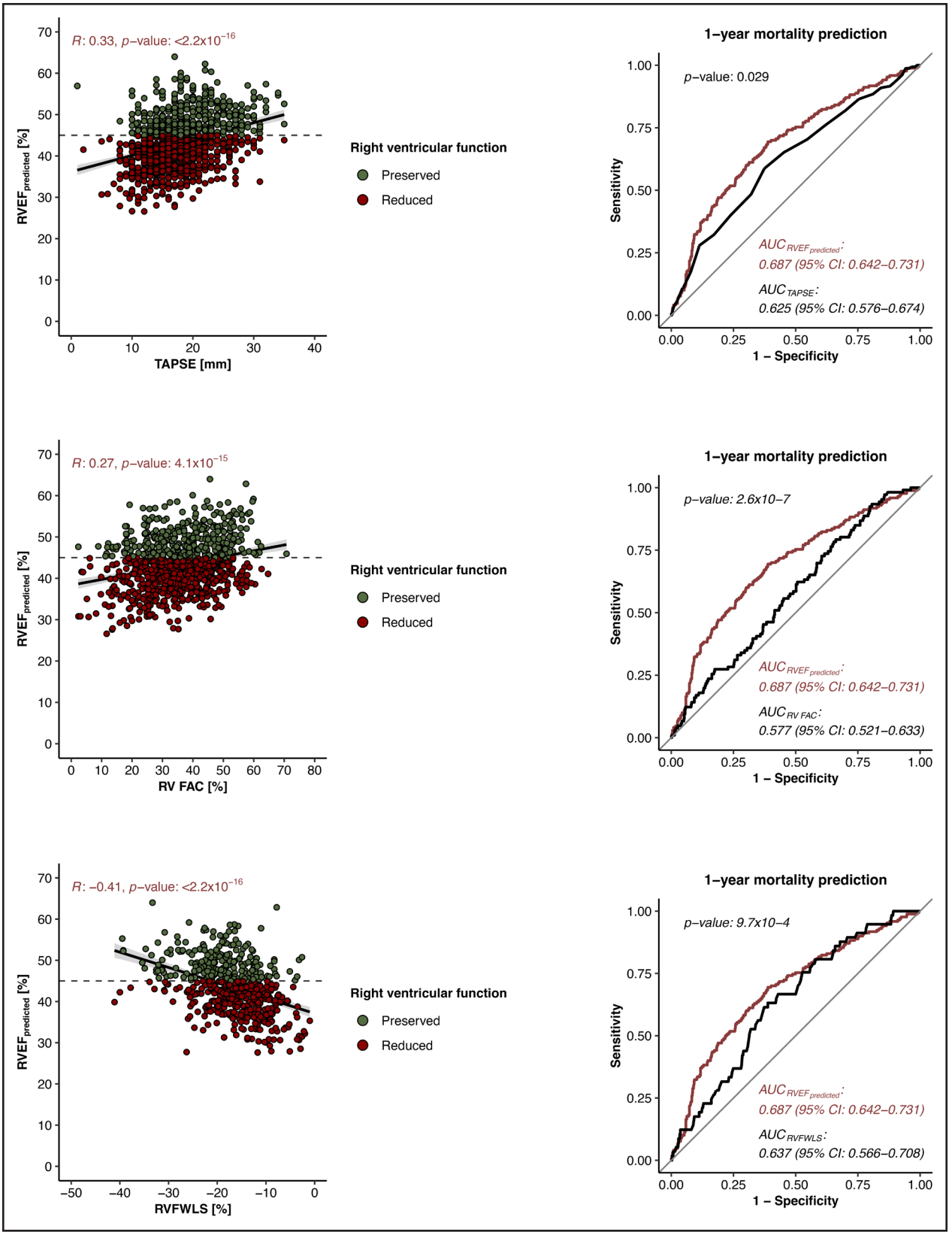

Figure 2. Correlation plots and receiver operating characteristic analyses for deep learning–predicted right ventricular (RV) ejection fraction (RVEF) values vs tricuspid annular plane systolic excursion (TAPSE), RV fractional area change (FAC), and RV free wall longitudinal strain (RVFWLS) measurements.

The black line indicates the linear regression line, whereas the gray area denotes the 95% confidence band. The availability of TAPSE, RV FAC, and RVFWLS measurements was 1012/1154 (87.7%), 829/1154 (71.8%), and 559/1154 (48.4%), respectively. AUC indicates area under the curve.

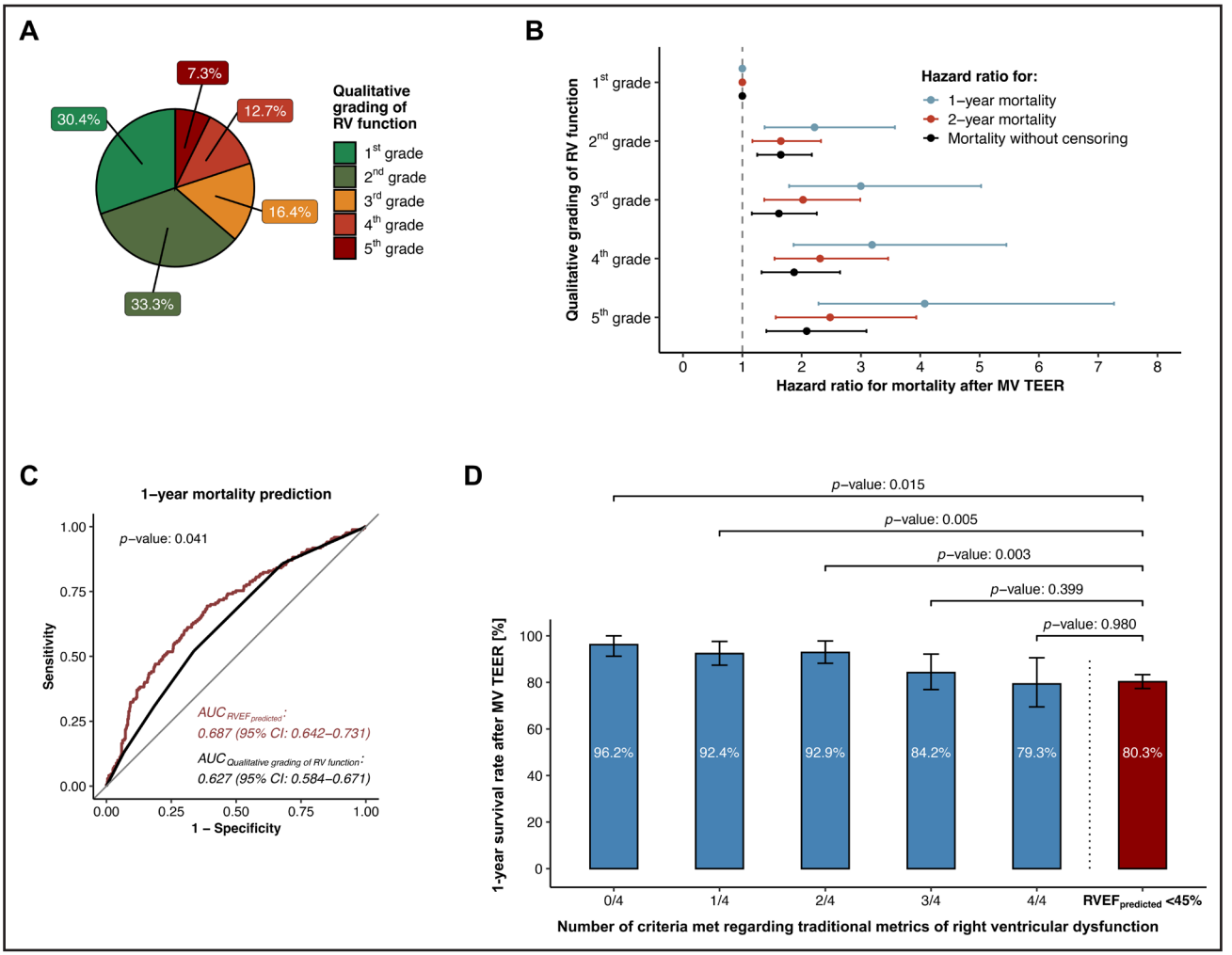

Figure 3. Visual assessment of right ventricular (RV) function and a combination of traditional metrics of RV function to identify high-risk patients for mortality after mitral valve (MV) transcatheter edge-to-edge repair (TEER).
A, Pie chart to illustrate the distribution of qualitative grades of RV function as visually assessed (qualitative 5-grade scheme: normal [first grade], mildly reduced [second grade], moderately reduced [third grade], moderately to severely reduced [fourth grade], and severely reduced [fifth grade]). **B**, Hazard ratios for mortality after MV TEER per qualitative grade of RV function. **C**, Receiver operating characteristic analysis comparing qualitative grades of RV function against deep learning–predicted RV ejection fraction (RVEF) values. **D**, Comparison of 1-year survival rates in patients meeting up to 4 criteria for RV dysfunction as evaluated using traditional metrics (ie, tricuspid annular plane systolic excursion <17 mm, RV fractional area change <35%, RV free wall longitudinal strain >−20%, and qualitative grade of RV dysfunction from third to fifth grade). AUC indicates area under the curve.

function, whereas primary MR was the predominant cause in 48.3% of patients with preserved RV function (Table 1). Compared with patients with preserved RV function, those with impaired RV function exhibited lower LVEF (median, 45% [IQR, 32%–55%] versus 55% [IQR, 47%–61%]; $P<2.2\times10^{-16}$) and larger left ventricular end-systolic volumes (median, 82 mL [IQR, 48–137 mL] versus 54 mL [IQR, 36–79 mL]; $P=6.6\times10^{-15}$; Table 2). Notably, LVEF and predicted RVEF were significantly correlated (Pearson $R=0.42$; $P<2.2\times10^{-16}$; Figure S3). Furthermore, the prevalence of coronary artery disease and chronic obstructive pulmonary disease was similar between the 2 groups. However, atrial fibrillation was more frequently diagnosed in patients with impaired RV function compared with those with preserved RV function (78.4% versus 62.6%, $P=9.4\times10^{-9}$; Table 1). In addition, patients with impaired RV function exhibited biatrial dilation, despite having comparable values of systolic pulmonary artery pressure (median, 45 mm Hg [IQR, 35–57 mm Hg] versus 46 mm Hg [35–55 mm Hg]; $P=0.984$) and were more likely to suffer from concomitant severe TR (27.8% versus 22.3%; $P=0.045$).

Performance of the Deep Learning–Predicted RVEF Versus the MitraScore in Predicting Mortality After MV TEER

The computation of the MitraScore was feasible in 1055 out of 1154 patients (91.4%) because of the missing data in 109 out of 9232 data points (1.18%). The

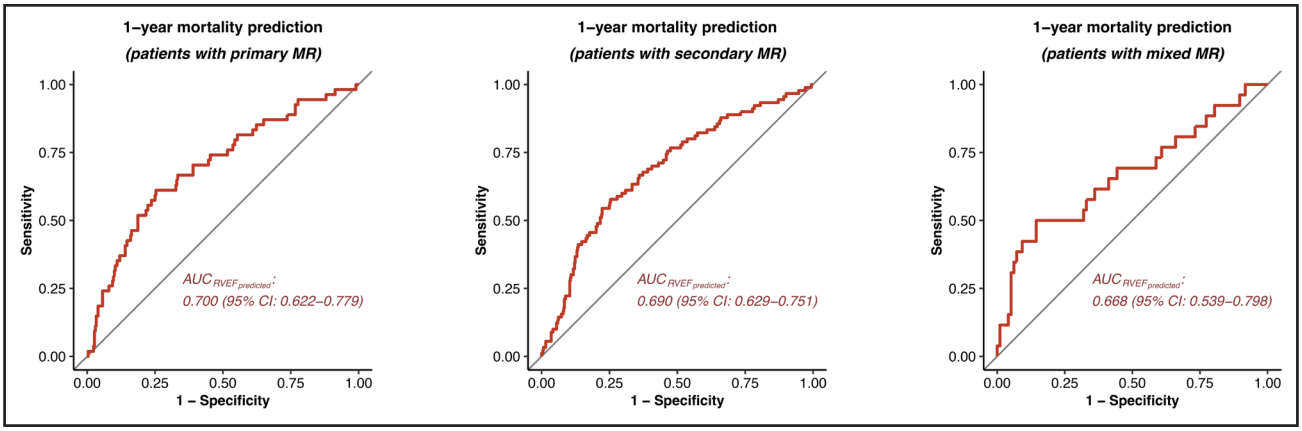

Figure 4. Receiver operating characteristic analyses for deep learning–predicted right ventricular ejection fraction (RVEF) values in accordance with underlying mitral regurgitation (MR) cause.
AUC indicates area under the curve.

most frequently missing variable was medication data regarding the usage of renin-angiotensin system inhibitors (absent in 4.68% of cases). The majority of patients presented with a MitraScore of 4 (out of 8) points (326 patients; 30.9%; Figure 8A). Furthermore, higher scores were associated with a greater hazard ratio for 1-year mortality after MV TEER (Figure 8B). Importantly, the prognostic value of the deep learning–predicted RVEF alone was found to be statistically similar and numerically superior to that of the comprehensive MitraScore (AUC, 0.687 [95% CI, 0.642–0.731] for predicted RVEF versus 0.662 [95% CI, 0.618–0.706] for the MitraScore; P=0.284; Figure 8C). Although the P value of 0.284 indicates that the difference is not statistically significant, the higher numerical AUC of deep learning–predicted RVEF suggests potential clinical relevance. Therefore, extending the MitraScore with the evaluation of RV dysfunction, defined as a predicted RVEF of <45%, significantly enhanced its performance in predicting 1-year mortality after MV TEER (AUC, 0.699 [95% CI, 0.656–0.741]; P=2.8×10^{-6}; Figure 8D and 8E).

DISCUSSION

Advancing RV Function Assessment With Deep Learning: Steps Toward Clinical Integration

To the best of our knowledge, this is the first study employing a deep learning model to improve the assessment of the historically difficult-to-image RV in patients with severe MR and proving that the deep learning–based prediction of RVEF can refine

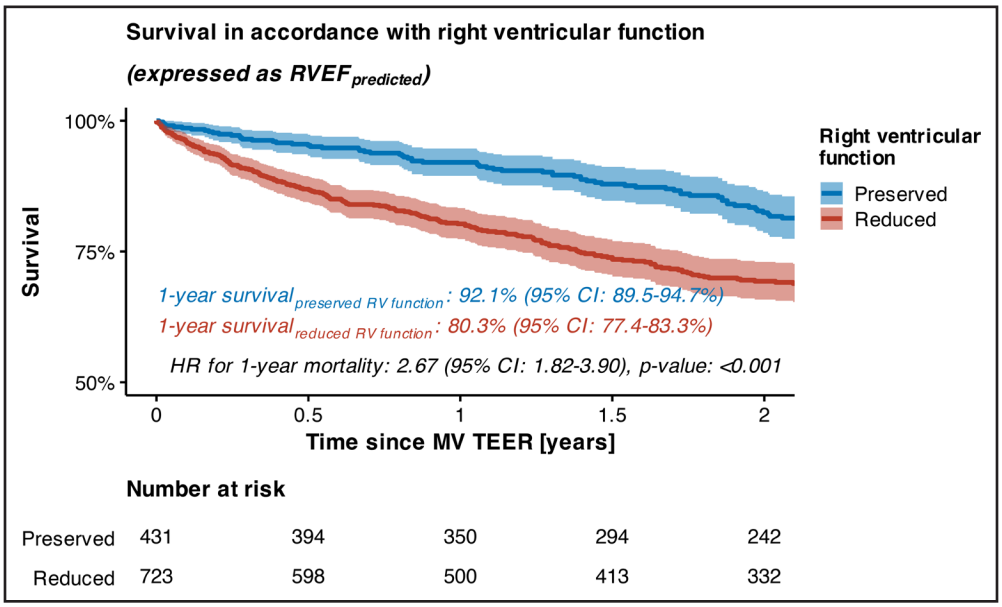

Figure 5. Kaplan-Meier survival plot in accordance with right ventricular (RV) function expressed as deep learning–predicted RV ejection fraction (RVEF).
HR indicates hazard ratio; MV, mitral valve; and TEER, transcatheter edge-to-edge repair.

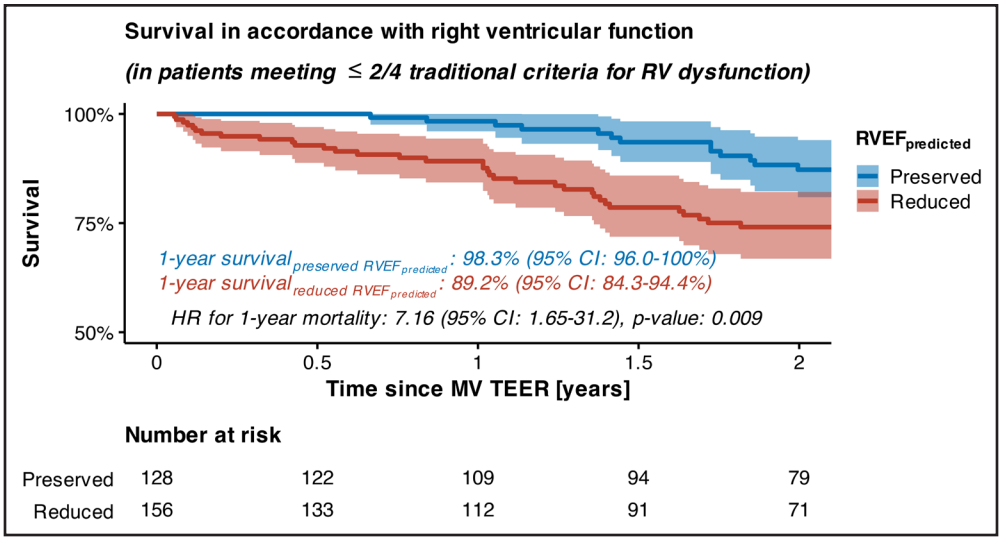

Figure 6. Kaplan-Meier survival plot in accordance with right ventricular (RV) function expressed as deep learning–predicted RV ejection fraction (RVEF) in patients meeting a maximum of 2 of 4 traditional criteria for RV dysfunction (ie, tricuspid annular plane systolic excursion <17 mm, RV fractional area change <35%, RV free wall longitudinal strain >−20%, and qualitative grade of RV dysfunction from third to fifth grade).
HR indicates hazard ratio; MV, mitral valve; and TEER, transcatheter edge-to-edge repair.

prognostication after MV TEER. Importantly, this approach achieves a level of accuracy comparable to that of the multiparametric MitraScore, which incorporates a plethora of individual factors such as age, left ventricular function, comorbidities like renal impairment and chronic obstructive pulmonary disease, and medication data. Although the critical role of right heart integrity is well-established in patients with severe

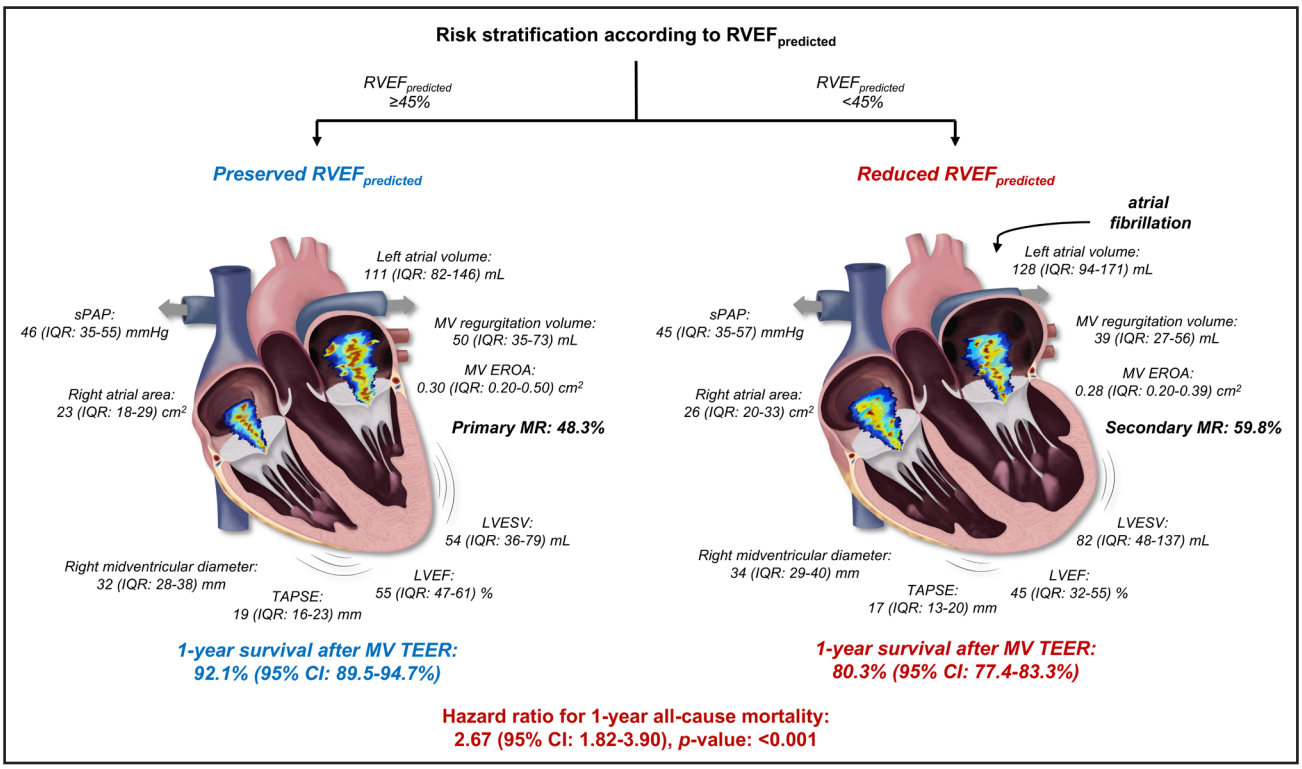

Figure 7. Schematic illustration of the heart of patients with either preserved or reduced right ventricular (RV) function.
Categorical data are presented as frequencies (%), whereas continuous data are expressed as median and interquartile range (IQR). LVEF indicates left ventricular ejection fraction; LVESV, left ventricular end-systolic volume; MR, mitral regurgitation; MV EROA, MV effective regurgitant orifice area; MV, mitral valve; RVEF, RV ejection fraction; sPAP, systolic pulmonary artery pressure; TAPSE, tricuspid annular plane systolic excursion; and TEER, transcatheter edge-to-edge repair.

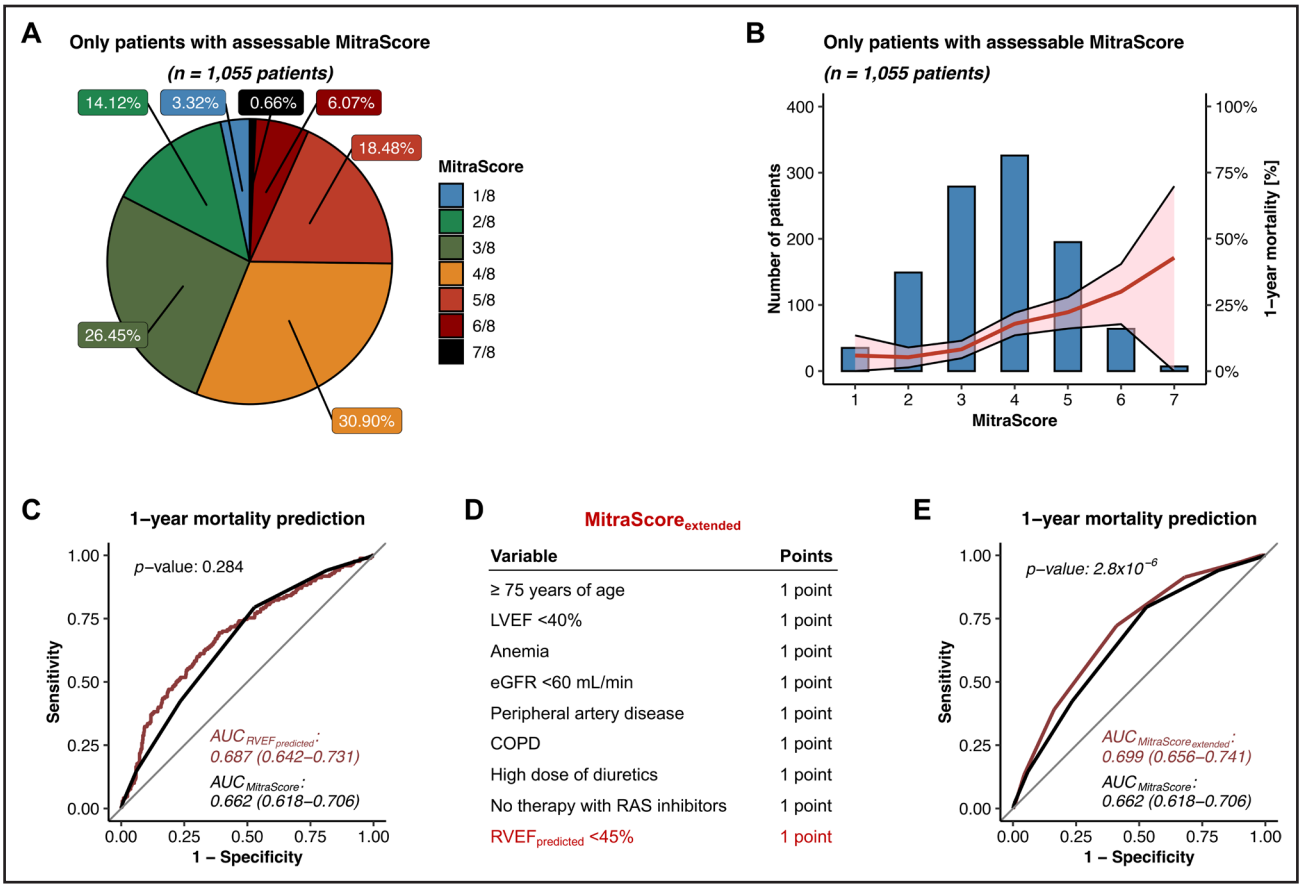

Figure 8. Placing right ventricular (RV) dysfunction into context with the multiparametric MitraScore to predict 1-year mortality after mitral valve (MV) transcatheter edge-to-edge repair (TEER).
A, Pie chart illustrating the proportion of patients per MitraScore rank. **B**, Number of patients and their corresponding 1-year mortality rates after MV TEER per MitraScore rank. **C**, Receiver operating characteristic (ROC) analysis comparing the performance of the deep learning–predicted RV ejection fraction (RVEF) vs the original MitraScore to predict 1-year mortality after MV TEER. **D**, The proposed extended MitraScore that uses the original MitraScore scoring system while also considering RV dysfunction (defined as deep learning–predicted RVEF of <45%). **E**, ROC analysis comparing the performance of the extended MitraScore vs the original MitraScore to predict 1-year mortality after MV TEER. AUC indicates area under the curve; COPD, chronic obstructive pulmonary disease; and eGFR, estimated glomerular filtration rate.

MR,[16–18] RV function has not been included in the MitraScore as an independent predictor variable. It is plausible that RV function did not emerge as an independent predictor in the original study by Raposeiras-Roubin et al[14] because they had already included chronic obstructive pulmonary disease and the usage of diuretics as predictor variables. Despite the appreciation for deep learning to solve complex tasks such as RV function assessment,[19] the implementation success for most deep learning applications in medicine is still limited.[20] In addition to demonstrating their clinical utility, as we have done in this study, deep learning models must move beyond the developer's hard drive and be implemented into clinical practice, thus making them available and usable for both tertiary care centers and frontline healthcare providers, where they can make a real difference. In the future, we envision our model being integrated into ultrasound systems, allowing for real-time automated estimation of RVEF without requiring time-consuming export-import steps or a cost-intensive 3D echocardiography–capable ultrasound machine with inherent practical limitations, particularly in the peri-procedural setting.

On the Evolution of RV Dysfunction and Its Prognostic Implications in Patients With Severe MR

Notably, markers indicating MR severity, such as MV effective regurgitant orifice area, MR vena contracta width, and MV regurgitation volume, were significantly higher in patients with preserved RV function than in those with reduced RV function (Table 2). Despite this, patients with preserved RV function had more favorable outcomes. This observation aligns well with the growing body of evidence suggesting that not merely the MV damage but, more critically, the potentially irreversible extra-MV cardiac damage determines prognosis after MV TEER.[2,4,21] Importantly, the extra-MV cardiac damage does not necessarily occur in a sequential

fashion, progressing from left heart dysfunction to pulmonary hypertension and culminating in RV failure, but can also be exacerbated by concurrent comorbidities. The multifactorial cause of RV dysfunction and the nonsequential nature of coexistent cardiac lesions are typical observations in the elderly, who often suffer from multiple pathologies at the same time. Initially, one might have anticipated that patients with more severe MR (ie, those with mainly primary MR and preserved RV function) would also have a larger left atrium and elevated systolic pulmonary artery pressure. Contrary to this expectation, our study found that patients with reduced RV function (diagnosed with secondary cause in 59.8% of the cases) had an enlarged left atrium, whereas systolic pulmonary artery pressure remained comparable between the 2 groups. The finding that LVEF and predicted RVEF were significantly correlated suggests that biventricular failure caused by hemodynamic interdependence can indeed occur without pulmonary hypertension as the linking pathology. The prevalence of atrial fibrillation was also higher in those with reduced RV function, potentially contributing to the vicious circle of left atrial enlargement, mitral annulus dilatation, and progression of MR. Furthermore, atrial fibrillation itself has been linked to the deterioration of RV function,[22] partially explaining why cardiovascular death is the leading cause of death in anticoagulated patients with atrial fibrillation.[23] Ultimately, atrial fibrillation might have also caused right atrial enlargement and progression to severe TR,[24] as observed in patients with reduced RV function, and atrial fibrillation-related TR in turn, could further worsen their prognosis, as shown across a broad spectrum of different etiologies of RV dysfunction.[25]

Explaining the Paradox: Reduced Predicted RVEF and Less Severe MR in Patients With MV TEER

Notably, patients with reduced predicted RVEF presented with less severe MR as assessed by MV effective regurgitant orifice area, MR vena contracta width, and MV regurgitation volume (Table 2). However, the grade of cardiac decompensation, as indicated by significantly higher NT-proBNP levels, was more severe in these patients compared with those with preserved predicted RVEF. In addition, worse dyspnea, expressed as New York Heart Association class IV, was more frequent in patients with reduced predicted RVEF. This may be attributed to the fact that patients with reduced predicted RVEF (and also reduced left ventricular function, as evidenced by a median LVEF of 45% [IQR, 32%–55%]) had less capacity to compensate for additional MR and were therefore treated at earlier stages of MR severity, mainly driven by secondary cause (diagnosed in 59.8% of cases). These findings highlight that not only the severity of the valvular defect but also the extent of concomitant extravalvular cardiac damage determines prognosis, similar to observations in patients with severe aortic stenosis undergoing transcatheter aortic valve implantation.[26,27]

How to Further Improve the Survival of Patients With Reduced Predicted RVEF: Is Severe TR a Prognostically Relevant Interventional Target in Patients With Reduced RV Function?

Given the retrospective nature of this study, it is advisable to view some of the results as hypotheses that warrant further investigation. The observation that patients without RV dysfunction exhibited superior survival suggests that intervention as early as possible in patients with severe MR might be beneficial, ideally before the manifestation of RV dysfunction. At the same time, a conservatively managed control group of patients with severe MR would be required to determine the net benefit of MV TEER among those with RV dysfunction. Drawing conclusions about futility is impossible from this retrospective registry study, and outcomes among patients with severe MR and RV dysfunction might be even worse without MV TEER, as the constant backward transmission of left-sided filling pressures would inevitably accelerate the deterioration of RV function. Although the direct treatment of RV dysfunction bears challenges (as the pharmacological armamentarium is mainly limited to diuretics), addressing concurrent severe TR has received increased attention lately. In our cohort of 1154 patients, 297 (25.7%) were diagnosed with severe TR at baseline (Table 2). Advanced age, long-standing atrial fibrillation, RV dysfunction, and limited procedural MR reduction are established independent predictors for the persistence of severe TR after MV TEER.[28] Notably, those without an improvement in severe TR after MV TEER had suboptimal survival and an increased risk of heart failure re-hospitalizations.[28,29] Retrospective data from 2 large registries showed that combined transcatheter mitral and tricuspid valve repair correlated with a 2-fold higher 1-year survival rate than isolated MV TEER in patients with coexisting MR and TR.[30] However, the first randomized trial on transcatheter tricuspid valve repair plus optimized medical therapy versus medical therapy alone highlighted the importance of adequate patient selection, as a reduction in the severity of TR and an associated improvement in quality of life, but no survival benefit at 1 year after intervention could be observed in the former group.[31] Employing the RV to pulmonary artery coupling concept, as outlined by Brener et al,[32] could be instrumental in identifying patients who might benefit the most from transcatheter tricuspid valve repair. Among the 723 patients with reduced predicted RVEF in our study, 201 patients presented with severe TR at baseline (27.8%; Table 2). Their median RV to pulmonary artery coupling index (calculated as TAPSE/systolic pulmonary artery

pressure) was 0.358 mm/mm Hg (IQR, 0.271–0.487 mm/mm Hg) before MV TEER. Nevertheless, follow-up data would be required to investigate whether these indices will improve after MV TEER, potentially making these patients ideal candidates for further tricuspid valve intervention.

Limitations

Being a retrospective, observational, nonrandomized register study with inherent weaknesses, 3 major limitations of our analysis merit consideration.

1. Image quality of the input data: 212 of the 1366 echocardiographic videos (15.5%) were omitted from our analysis because of suboptimal image quality or unavailability of the video as raw data—for instance, when patients underwent transthoracic echocardiography at a referring hospital. When encountering videos of suboptimal image quality, the physician's expertise in assessing RV function remains indispensable.
2. Model specificity: Our results are specifically related to the deep learning model proposed by Tokodi et al,[11] which was trained on a dataset including patients with various cardiovascular diseases, healthy subjects, and elite athletes.[33] Future endeavors should focus on refining this algorithm or exploring alternative solutions like the LVivoRV artificial intelligence software, which can also evaluate RV fractional area change and RV free wall longitudinal strain.[34] Moreover, validating the predicted RVEF against RVEF from gold standard MRI in our cohort would have been desirable.
3. Need for prospective validation: This is a retrospective analysis, and the benefit of using artificial intelligence for better patient care is yet to be demonstrated in a prospective setting. The key questions are as follows: Will patients identified with RV dysfunction (defined as RVEF <45%) truly experience better outcomes with more frequent follow-ups? And will the application of artificial intelligence emerge as the optimal strategy to identify high-risk patients?

Conclusions

In this multicenter study evaluating the prognostic significance of a previously published deep learning model for RVEF assessment in patients with severe MR, the predicted RVEF exhibited a prognostic power superior to TAPSE and comparable to the multiparametric MitraScore, emphasizing the crucial role of right heart function in left-sided heart disease. Utilizing deep learning to extract clinically meaningful information from technically simple yet readily available and cost-effective imaging techniques may represent a new, transformative approach to echocardiographic analysis, including the assessment of RV function. Integrating such tools in clinical practice holds promise to improve patient care, allowing more accurate risk stratification and personalized treatment strategies, for example, by recommending more rigorous follow-up and more aggressive treatment of comorbidities in high-risk patients with impaired RV function.

ARTICLE INFORMATION

Received April 30, 2024; accepted October 30, 2024.

Affiliations

First Department of Medicine, Klinikum Rechts der Isar, Technical University of Munich, Munich, Germany (M.L., A.H., E.R., J.T., K.-L.L.). DZHK (German Center for Cardiovascular Research), partner site Munich Heart Alliance (M.L., A.H., E.R., M.v.S., A. Kastrati, H.S., M.J., E.X., K.-L.L., J.H., T.T.). Department of General and Interventional Cardiology, Heart and Diabetes Center Northrhine-Westfalia, Ruhr University Bochum, Bad Oeynhausen, Germany (V.F., M.F., M.G., V.R.). Medizinische Klinik und Poliklinik I, Klinikum der Universität München, Ludwig Maximilians University of Munich, Germany (L.S., J.H.). Heart and Vascular Center, Semmelweis University, Budapest, Hungary (M.T., A. Kovács). Department of Cardiology (A.L., H.A.A.C., M.v.S., F.R., A. Kastrati, H.S., M.J., E.X., T.T.) and Institute of Anesthesiology (N.P.M.), German Heart Center Munich, Technical University of Munich, Munich, Germany. Department of Family Medicine, McGill University, Montreal, Canada (T.S.). Department of Physics, University of Johannesburg, Auckland Park, South Africa (G.H.). Department of Cardiology, Keio University School of Medicine, Tokyo, Japan (S.Y.).

Sources of Funding

Dr Lachmann has received funding from the Technical University of Munich (Clinician Scientist Grant), Else Kröner-Fresenius Foundation (Clinician Scientist Grant), German Center for Cardiovascular Research (Postdoc Start-up Grant on advancing Digital Aspects), and German Heart Foundation (Machine learning in severe mitral regurgitation). Dr Fortmeier has received funding from Ruhr University Bochum (Female Clinician Scientist Grant). Dr Stolz received research honoraria from Edwards Lifesciences. Amelie Hesse received funding from the German Cardiac Society (Otto Hess Doctoral Scholarship). Project number RRF-2.3.1-21-2022-00004 has been implemented with support from the European Union. TKP2021-NVA-12 has been implemented with the support provided by the Ministry of Culture and Innovation of Hungary from the National Research, Development, and Innovation Fund, financed under the TKP2021-NVA funding scheme. Dr Tokodi was supported by the New National Excellence Program (ÚNKP-23-4-II-SE-39) of the Ministry of Culture and Innovation in Hungary from the National Research, Development, and Innovation Fund. Dr Tokodi is also supported by the János Bolyai Research Scholarship of the Hungarian Academy of Sciences. Dr Kovács has received grant support from the National Research, Development, and Innovation Office of Hungary (FK 142573) and is supported by the János Bolyai Research Scholarship of the Hungarian Academy of Sciences. Dr Tokodi reports consulting fees from CardioSight, Inc, outside the submitted work. Dr Kovács reports personal fees from Argus Cognitive, Inc, and CardioSight, Inc, outside the submitted work. Dr Hausleiter received speaker honoraria from and serves as consultant for Edwards Lifesciences. Dr Trenkwalder received funding from the Else Kröner-Fresenius Foundation (Clinician Scientist Grant) and from the German Heart Foundation.

Disclosures

None.

Supplemental Material

Tables S1–S5
Figures S1–S3

REFERENCES

1. Sanz J, Sánchez-Quintana D, Bossone E, Bogaard HJ, Naeije R. Anatomy, function, and dysfunction of the right ventricle. *J Am Coll Cardiol.* 2019;73:1463–1482. doi: 10.1016/j.jacc.2018.12.076
2. Stolz L, Doldi PM, Orban M, Karam N, Puscas T, Wild MG, Popescu A, Von Bardeleben RS, Iliadis C, Baldus S, et al; EuroSMR Investigators. Staging

heart failure patients with secondary mitral regurgitation undergoing transcatheter edge-to-edge repair. *JACC Cardiovasc Interv*. 2023;16:140–151. doi: 10.1016/j.jcin.2022.10.032
3. Shamekhi J, Sugiura A, Spieker M, Iliadis C, Weber M, Öztürk C, Becher MU, Tiyerili V, Zimmer S, Horn P, et al. A staging classification of right heart remodelling for patients undergoing transcatheter edge-to-edge mitral valve repair. *EuroIntervention*. 2021;18:43–49 . doi: 10.4244/EIJ-D-21-00667
4. Trenkwalder T, Lachmann M, Stolz L, Fortmeier V, Covarrubias HAA, Rippen E, Schürmann F, Presch A, von Scheidt M, Ruff C, et al. Machine learning identifies pathophysiologically and prognostically informative phenotypes among patients with mitral regurgitation undergoing transcatheter edge-to-edge repair. *Eur Heart J Cardiovasc Imaging*. 2023;24:574–587. doi: 10.1093/ehjci/jead013
5. Stolz L, Doldi PM, Weckbach LT, Trimborn F, Orban M, Stocker TJ, Wild MG, Massberg S, Näbauer M, Hausleiter J. Right ventricular contraction patterns in patients undergoing mitral valve transcatheter edge-to-edge repair. *JACC Cardiovasc Interv*. 2023;16:242–244. doi: 10.1016/j.jcin.2022.09.034
6. Tolvaj M, Kovács A, Radu N, Cascella A, Muraru D, Lakatos B, Fábián A, Tokodi M, Tomaselli M, Gavazzoni M, et al. Significant disagreement between conventional parameters and 3D echocardiography-derived ejection fraction in the detection of right ventricular systolic dysfunction and its association with outcomes. *J Am Soc Echocardiogr*. 2024;37:677–686. doi: 10.1016/j.echo.2024.04.005
7. Kovács A, Lakatos B, Tokodi M, Merkely B. Right ventricular mechanical pattern in health and disease: beyond longitudinal shortening. *Heart Fail Rev*. 2019;24:511–520. doi: 10.1007/s10741-019-09778-1
8. Hahn RT, Lerakis S, Delgado V, Addetia K, Burkhoff D, Muraru D, Pinney S, Friedberg MK. Multimodality imaging of right heart function: JACC scientific statement. *J Am Coll Cardiol*. 2023;81:1954–1973. doi: 10.1016/j.jacc.2023.03.392
9. Sayour AA, Tokodi M, Celeng C, Takx RAP, Fábián A, Lakatos BK, Friebel R, Surkova E, Merkely B, Kovács A. Association of right ventricular functional parameters with adverse cardiopulmonary outcomes: a meta-analysis. *J Am Soc Echocardiogr*. 2023;36:624.e8–633.e8. doi: 10.1016/j.echo.2023.01.018
10. Grapsa J, Zancanaro E, Enriquez-Sarano M. Welcome to the exciting world of the right ventricle. *Eur Heart J*. 2024;45:3100–3102. doi: 10.1093/eurheartj/ehae377
11. Tokodi M, Magyar B, Soós A, Takeuchi M, Tolvaj M, Lakatos BK, Kitano T, Nabeshima Y, Fábián A, Szigeti MB, et al. Deep learning-based prediction of right ventricular ejection fraction using 2D echocardiograms. *JACC Cardiovasc Imaging*. 2023;16:1005–1018. doi: 10.1016/j.jcmg.2023.02.017
12. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, Flachskampf FA, Foster E, Goldstein SA, Kuznetsova T, 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. *J Am Soc Echocardiogr*. 2015;28:1.e14–39.e14. doi: 10.1016/j.echo.2014.10.003
13. Feldman T, Wasserman HS, Herrmann HC, Gray W, Block PC, Whitlow P, St. Goar F, Rodriguez L, Silvestry F, Schwartz A, et al. Percutaneous mitral valve repair using the edge-to-edge technique. *J Am Coll Cardiol*. 2005;46:2134–2140. doi: 10.1016/j.jacc.2005.07.065
14. Raposeiras-Roubin S, Adamo M, Freixa X, Arzamendi D, Benito-González T, Montefusco A, Pascual I, Nombela-Franco L, Rodes-Cabau J, Shuvy M, et al. A score to assess mortality after percutaneous mitral valve repair. *J Am Coll Cardiol*. 2022;79:562–573. doi: 10.1016/j.jacc.2021.11.041
15. DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. *Biometrics*. 1988;44:837–845.
16. Tokodi M, Németh E, Lakatos BK, Kispál E, Tősér Z, Staub L, Rácz K, Soltész A, Szigeti S, Varga T, et al. Right ventricular mechanical pattern in patients undergoing mitral valve surgery: a predictor of post-operative dysfunction? *ESC Heart Fail*. 2020;7:1246–1256. doi: 10.1002/ehf2.12682
17. Karam N, Stolz L, Orban M, Deseive S, Praz F, Kalbacher D, Westermann D, Braun D, Näbauer M, Neuss M, et al. Impact of right ventricular dysfunction on outcomes after transcatheter edge-to-edge repair for secondary mitral regurgitation. *JACC Cardiovasc Imaging*. 2021;14:768–778. doi: 10.1016/j.jcmg.2020.12.015
18. Doldi PM, Stolz L, Kalbacher D, Köll B, Geyer M, Ludwig S, Orban M, Braun D, Weckbach LT, Stocker TJ, et al; EuroSMR and PRIME-MR Investigators. Right ventricular dysfunction predicts outcome after transcatheter mitral valve repair for primary mitral valve regurgitation. *Eur J Heart Fail*. 2022;24:2162–2171. doi: 10.1002/ejhf.2661
19. Ouyang D, Cheng S. Revival and revision of right ventricular assessment by machine learning. *JACC Cardiovasc Imaging*. 2022;15:780–782. doi: 10.1016/j.jcmg.2022.01.019
20. Van Smeden M, Heinze G, Van Calster B, Asselbergs FW, Vardas PE, Bruining N, De Jaegere P, Moore JH, Denaxas S, Boulesteix AL, et al. Critical appraisal of artificial intelligence-based prediction models for cardiovascular disease. *Eur Heart J*. 2022;43:2921–2930. doi: 10.1093/eurheartj/ehac238
21. van Wijngaarden AL, Mantegazza V, Hiemstra YL, Volpato V, van der Bijl P, Pepi M, Palmen M, Delgado V, Ajmone Marsan N, Tamborini G, et al. Prognostic impact of extra–mitral valve cardiac involvement in patients with primary mitral regurgitation. *JACC Cardiovasc Imaging*. 2022;15:961–970. doi: 10.1016/j.jcmg.2021.11.009
22. Reddy YNV, Obokata M, Verbrugge FH, Lin G, Borlaug BA. Atrial dysfunction in patients with heart failure with preserved ejection fraction and atrial fibrillation. *J Am Coll Cardiol*. 2020;76:1051–1064. doi: 10.1016/j.jacc.2020.07.009
23. Gómez-Outes A, Lagunar-Ruíz J, Terleira-Fernández AI, Calvo-Rojas G, Suárez-Gea ML, Vargas-Castrillón E. Causes of death in anticoagulated patients with atrial fibrillation. *J Am Coll Cardiol*. 2016;68:2508–2521. doi: 10.1016/j.jacc.2016.09.944
24. Patlolla SH, Schaff HV, Nishimura RA, Stulak JM, Chamberlain AM, Pislaru SV, Nkomo VT. Incidence and burden of tricuspid regurgitation in patients with atrial fibrillation. *J Am Coll Cardiol*. 2022;80:2289–2298. doi: 10.1016/j.jacc.2022.09.045
25. Padang R, Chandrashekar N, Indrabhinduwat M, Scott CG, Luis SA, Chandrasekaran K, Michelena HI, Nkomo VT, Pislaru SV, Pellikka PA, et al. Aetiology and outcomes of severe right ventricular dysfunction. *Eur Heart J*. 2020;41:1273–1282. doi: 10.1093/eurheartj/ehaa037
26. Lachmann M, Rippen E, Rueckert D, Schuster T, Xhepa E, von Scheidt M, Pellegrini C, Trenkwalder T, Rheude T, Stundl A, et al. Harnessing feature extraction capacities from a pre-trained convolutional neural network (VGG-16) for the unsupervised distinction of aortic outflow velocity profiles in patients with severe aortic stenosis. *Eur Heart J Digit Health*. 2022;3:153–168. doi: 10.1093/ehjdh/ztac004
27. Lachmann M, Rippen E, Schuster T, Xhepa E, von Scheidt M, Pellegrini C, Trenkwalder T, Rheude T, Stundl A, Thalmann R, et al. Subphenotyping of patients with aortic stenosis by unsupervised agglomerative clustering of echocardiographic and hemodynamic data. *JACC Cardiovasc Interv*. 2021;14:2127–2140. doi: 10.1016/j.jcin.2021.08.034
28. Meijerink F, Koch KT, De Winter RJ, Robbers-Visser D, Boekholdt SM, Holierook M, Baan J, Bouma BJ. Tricuspid regurgitation after transcatheter mitral valve repair: clinical course and impact on outcome. *Catheter Cardiovasc Interv*. 2021;98:E427–E435. doi: 10.1002/ccd.29464
29. Kavsur R, Iliadis C, Spieker M, Brachtendorf BM, Tiyerili V, Metze C, Horn P, Baldus S, Kelm M, Nickenig G, et al. Predictors and prognostic relevance of tricuspid alterations in patients undergoing transcatheter edge-to-edge mitral valve repair. *EuroIntervention*. 2021;17:827–834. doi: 10.4244/EIJ-D-20-01094
30. Mehr M, Karam N, Taramasso M, Ouarrak T, Schneider S, Lurz P, Von Bardeleben RS, Fam N, Pozzoli A, Lubos E, et al; TriValve and TRAMI Investigators. Combined tricuspid and mitral versus isolated mitral valve repair for severe MR and TR. *JACC Cardiovasc Interv*. 2020;13:543–550. doi: 10.1016/j.jcin.2019.10.023
31. Sorajja P, Whisenant B, Hamid N, Naik H, Makkar R, Tadros P, Price MJ, Singh G, Fam N, Kar S, et al; TRILUMINATE Pivotal Investigators. Transcatheter repair for patients with tricuspid regurgitation. *N Engl J Med*. 2023;388:1833–1842. doi: 10.1056/NEJMoa2300525
32. Brener MI, Lurz P, Hausleiter J, Rodés-Cabau J, Fam N, Kodali SK, Rommel K-P, Muntané-Carol G, Gavazzoni M, Nazif TM, et al. Right ventricular-pulmonary arterial coupling and afterload reserve in patients undergoing transcatheter tricuspid valve repair. *J Am Coll Cardiol*. 2022;79:448–461. doi: 10.1016/j.jacc.2021.11.031
33. Magyar B, Tokodi M, Soós A, Tolvaj M, Lakatos BK, Fábián A, Surkova E, Merkely B, Kovács A, Horváth A. RVENet: a large echocardiographic dataset for the deep learning-based assessment of right ventricular function. In: Karlinsky L, Michaeli T, Nishino K, eds. *Computer Vision—ECCV 2022 Workshops*. Springer Nature; 2023:569–583.
34. Hsia BC, Lai A, Singh S, Samtani R, Bienstock S, Liao S, Stern E, LaRocca G, Sanz J, Lerakis S, et al. Validation of American Society of Echocardiography guideline-recommended parameters of right ventricular dysfunction using artificial intelligence compared with cardiac magnetic resonance imaging. *J Am Soc Echocardiogr*. 2023;36:967–977. doi: 10.1016/j.echo.2023.05.015