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SHORT REPORT

Artificial intelligence-enabled reconstruction of the right ventricular pressure curve using the peak pressure value: a proof-of-concept study

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Abstract

Aims

Conventional echocardiographic parameters of right ventricular (RV) function are afterload-dependent. Therefore, incorporating RV pressures may enable the formulation of new parameters that reflect intrinsic RV function accurately. Accordingly, we sought to develop an artificial intelligence–based method to reconstruct the RV pressure curve based on the peak RV pressure.

Methods and Results

We invasively acquired RV pressure in 29 heart failure patients before and after implanting a left ventricular (LV) assist device. Using these tracings, we trained various machine learning models to reconstruct the RV pressure curve of the entire cardiac cycle based on the peak value of the curve. The best-performing model was compared with two other methods that estimated RV pressures based on a reference LV and RV pressure curve, respectively. Seventeen consecutive patients from another centre who underwent right heart catheterization and simultaneous echocardiography served as an external validation cohort. Among the evaluated algorithms, multilayer perceptron (MLP) achieved the best performance with an R^2 of 0.887 (0.834–0.941). The RV and LV reference curve–based methods achieved R^2 values of 0.879 (0.815–0.943) and 0.636 (0.500–0.771), respectively. During external validation, MLP exhibited similarly good performance [R^2 0.911 (0.873–0.948)], which decreased only modestly if the echocardiography-derived peak RV pressure was used instead of the invasively measured peak RV pressure [R^2 0.802 (0.694–0.909)].

Conclusions

The proposed method enables the reconstruction of the RV pressure curve using only the peak value as input. Thus, it may serve as a fundamental component for developing new echocardiographic tools targeting the afterload-adjusted assessment of RV function.

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Structured Graphical Abstract

Key question

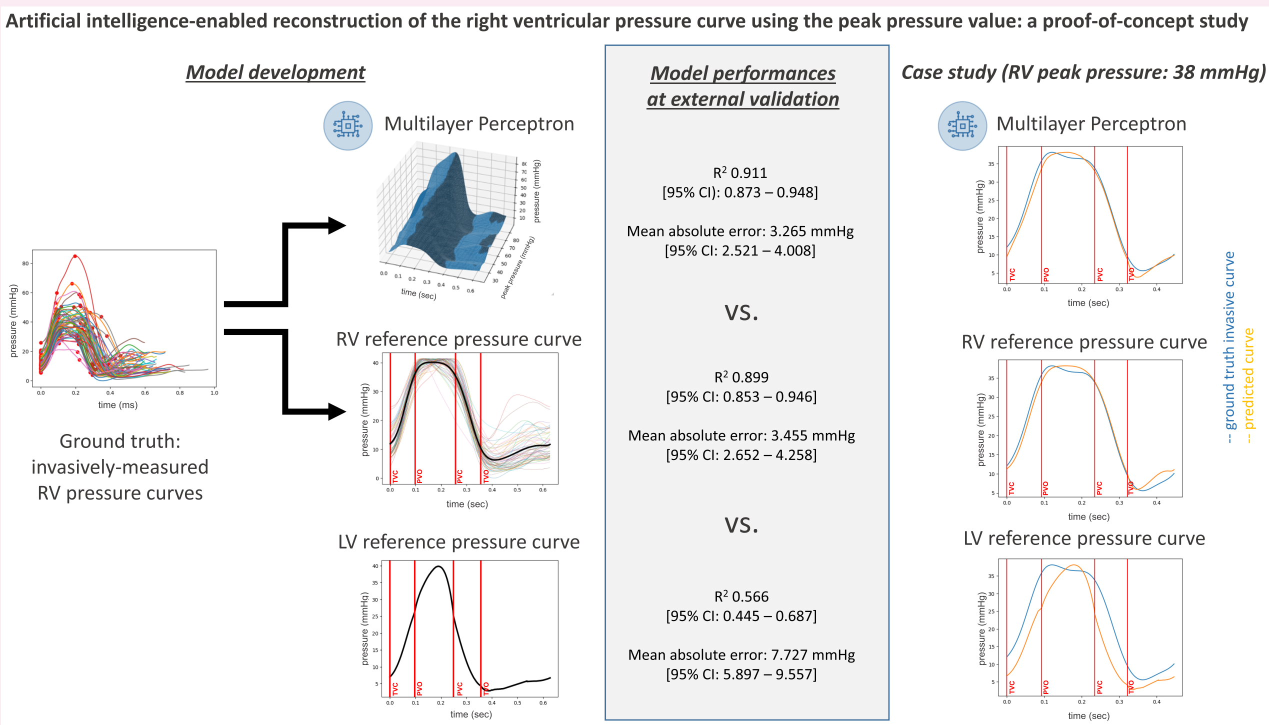
Can artificial intelligence be useful in reconstructing the right ventricular pressure curve of the entire cardiac cycle using only the peak pressure value as input?

Key findings

A multilayer perceptron model predicted pressure values with a balanced, low bias throughout the cardiac cycle, even slightly outperforming the reference curve–based methods at both internal and external validations.

Take-home message

The accurate prediction of the right ventricular pressure curve may enable the formulation of new echocardiographic parameters targeting the afterload-adjusted assessment of right ventricular function.



LV, left ventricular; PVC, pulmonary valve closure; PVO, pulmonary valve opening; RV, right ventricular; TVC, tricuspid valve closure; TVO, tricuspid valve opening.

Keywords right ventricle • right ventricular dysfunction • pulmonary hypertension • artificial intelligence • pressure • pressure curve • myocardial work

Introduction

Echocardiography is the prime imaging modality to assess ventricular systolic function. However, most conventional parameters (i.e. ejection fraction, EF; global longitudinal strain, GLS) depend heavily on the actual afterload; thus, they reflect ventriculo-arterial coupling rather than intrinsic myocardial contractility.[1] To create less load-dependent metrics that reflect myocardial contractility and energetics more accurately, the concept of myocardial work calculation has been recently introduced, and the added clinical value of the newly derived myocardial work parameters has been well established concerning the left ventricle (LV).[2–4] A key step in myocardial work analysis is the non-invasive estimation of the LV pressure curve by rescaling a reference LV pressure curve (derived from LV pressure curves of several patients) based on a single, cuff-based measurement of systolic blood pressure.[2] However, no dedicated solution exists for the right ventricle (RV) despite its function being even more dependent on afterload.[5] Moreover, due to the different haemodynamic characteristics of the pulmonary vascular bed and the RV contraction pattern, the morphology of the RV pressure curve varies significantly between normal, mildly, or severely elevated pulmonary pressures.[6] Thus, instead of deriving a single reference curve, a more sophisticated approach would be required that also considers the changes in the morphology of the RV pressure curve across the entire spectrum of peak RV pressures.

Accordingly, the aims of our proof-of-concept study were (i) to develop and externally validate an artificial intelligence–based method that enables the estimation of the RV pressure curve based on the peak RV pressure value and (ii) to compare the reconstructed pressure curves with those created using other pre-existing approaches.

Methods

Derivation cohort

End-stage heart failure patients over 18 years of age were enrolled in a prospective study and underwent durable LV assist device implantation at the Duke University Medical Center (patients provided written informed consent; IRB approval no. Pro00107652). Exclusion criteria were the exchange of a previously implanted assist device, presence of a percutaneous RV assist device or extracorporeal membrane oxygenator, history of heart transplantation, prior or concomitant tricuspid valve repair/replacement, and contraindication for performing transoesophageal echocardiography. In our current study, we analysed 29 patients who also underwent pressure conductance catheterization. After the induction of general anaesthesia and the institution of mechanical ventilation, a 7 Fr high-fidelity pressure conductance catheter (CD Leycom, Zoetermeer, The Netherlands) that was connected to a signal processor with a dedicated software solution (Inca, CD Leycom) was advanced into the RV. The catheter was positioned in the RV apex under echocardiographic guidance and adjusted until signals derived from the individual electrode pairs were in phase. RV pressure tracings were obtained before skin incision (beginning-of-procedure examination) and after skin closure (end-of-procedure examination). A pressure tracing containing 10 stable separated cardiac cycles per examination was exported with a 250 Hz sampling rate (29 patients × 2 examinations × 10 cardiac cycles = a total of 580 cardiac cycles). Comprehensive 2D and 3D transoesophageal echocardiography was performed during the operation to quantify RV volumes and RVEF (EPIQ CVx system, X8-2t transducer, Philips Healthcare, Best, The Netherlands; and 4D RV-Function 2, TomTec, Unterschleissheim, Germany).

Reference pressure curve–based methods

The exported RV pressure tracings were processed using a custom software solution (implemented in Python v3.9) to identify dedicated cardiac cycle events (i.e. tricuspid valve closure, TVC; pulmonary valve opening, PVO; pulmonary valve closure, PVC; tricuspid valve opening, TVO) using the second derivative squared method by expert consensus reading.[7] These annotated pressure tracings were split into segments, each containing the pressure curve of exactly one cardiac cycle (from TVC to TVC), which were then processed using a previously described method.[2] Briefly, the curves were adjusted in two ways. First, sections of the curves between cardiac cycle events were stretched or compressed along the time axis so that the corresponding events of all curves would align in time. Second, they were scaled vertically (along the pressure axis) to ensure they all had the same peak value. After these adjustments, the pressure curves from the same examination were averaged to create a single examination-level pressure curve. The reference RV pressure curve was generated by normalizing and averaging all examination-level curves using the method described above. Individual pressure curves were reconstructed by scaling this reference curve vertically based on the peak RV pressure and horizontally based on the timings of the cardiac cycle events.

We also evaluated the performance of the LV reference pressure curve–based estimation applied in a commercially available software solution (EchoPAC v204, GE Healthcare, Horten, Norway) for LV myocardial work calculation.

Development and internal validation of a machine learning model

To enable a more accurate estimation of the RV pressure curve that respects the individual characteristics of the curve shape and dynamics along the scale of elevated pressures, we need to consider the effect of the peak RV pressure value. To this end, instead of simply averaging the temporally and vertically normalized curves, we opted for a machine learning–based method. Accordingly, we defined the task for the machine learning models to predict pressure values throughout the cardiac cycle for a given peak RV pressure value. In other words, the task was to fit a continuous 3D surface to all available examination-level pressure curves plotted as a function of the peak pressure values (*Figure 1A*). To reconstruct a patient's pressure curve with a given peak RV pressure value, we ran the model on all normalized time points, resulting in a temporally normalized curve. Finally, the curve was de-normalized along the time axis using the original timings of the cardiac cycle events. We experimented with several machine learning models (linear regression, K-nearest neighbours, support vector machines, random forest, multilayer perceptron—MLP). As internal validation, leave-one-examination-out cross-validation was performed to quantify the models' prediction accuracy (values averaged over all time points of the cardiac cycle), and the coefficient of determination (R^2) was used as the performance metric. We also calculated the mean squared error (MSE) and the mean absolute error (MAE). The performance of the best-performing machine learning model was also compared with the performance of the LV and RV reference pressure curve–based estimation methods. We used the invasively measured, examination-level peak pressures during internal validation to reconstruct the curves using the three different methods.

External validation

To validate the proposed method externally, consecutive patients from another centre (Ospedale San Luca, IRCCS Instituto Auxologico Italiano, Milano, Italy) undergoing a clinically indicated right heart catheterization were also evaluated. Exclusion criteria were the absence of tricuspid regurgitation (TR) or the presence of trace TR with a non-measurable jet or severe TR. Right heart catheterization was conducted in the supine position in a non-fasting state. A 7 F Swan–Ganz catheter with an RV side port was inserted through the internal jugular vein. An RV pressure tracing containing 10 stable consecutive cardiac cycles per examination was exported with a 240 Hz sampling rate and processed as described above to identify valvular events. Simultaneously with catheterization, transthoracic echocardiography was also performed by experienced cardiologists to measure RV volumes, RVEF, and TR peak velocity (Vivid E95, 4Vc-D transducer, GE Vingmed Ultrasound, Horten, Norway). Non-invasively derived RV peak systolic pressure was estimated as $4 \times (\textit{TR peak velocity})^2$. The performance of the best-performing machine learning model was also compared with the performance of the LV and RV reference curve–based estimation methods using both the invasively and the non-invasively measured RV peak systolic pressures.

Statistical analysis

The normal distribution of variables was assessed using the Shapiro–Wilk test. As the vast majority of the variables showed non-normal distribution, continuous variables were expressed as median (interquartile range), whereas categorical variables were reported as frequencies and percentages. Pre-operative and post-operative values of echocardiographic parameters were compared using Wilcoxon signed-rank test. Results from different pressure estimation methods were compared with the invasively measured pressure curves (i.e. the ground truth) using Wilcoxon signed-rank tests and agreement plots. A two-sided $P < 0.05$ was considered statistically significant.

Results

Internal validation

Among the 29 patients undergoing LV assist device implantation, 22 (76%) were male, the median age of the population was 61 (54–71) years, and 10 patients (34%) were of non-ischaemic aetiology. Before the implantation, 1 patient (3%) had trace, 18 (62%) had mild, 9 (31%) had moderate, and 1 (3%) had severe TR. RV end-diastolic [median pre-op vs. post-op: 172 (128–200) vs. 138 (110–168) mL, $P < 0.001$] and end-systolic volumes [122 (86–170) vs. 112 (73–133) mL, $P < 0.001$], along with RVEF [27 (21–33) vs. 25 (20–28)%, $P < 0.05$) decreased after the procedure. The median RV peak systolic pressure of all examinations was 39.9 (34.6–46.0) mmHg, ranging from 21.2 to 84.9 mmHg.

Among the evaluated machine learning algorithms (*Table 1*), MLP achieved the best performance with an R^2 of 0.887 [95% confidence interval (CI) 0.834–0.941], an MSE of 14.398 (95% CI 10.644–18.151) $mmHg^2$, and an MAE of 2.885 (95% CI 2.520–3.249) mmHg during internal validation. The RV reference curve–based estimation method achieved an R^2 of 0.879 (95% CI 0.815–0.943), an MSE of 15.625 (95% CI 10.919–20.329) $mmHg^2$, and an MAE of 2.959 (95% CI 2.555–3.363) mmHg, whereas the LV reference curve–based approach had an R^2 of 0.636 (95% CI 0.500–0.771), an MSE of 51.499 (95% CI 37.875–65.124) $mmHg^2$, and an MAE of 5.251 (95% CI 4.539–5.963) mmHg.

We investigated the differences between the invasively measured pressures and the predicted values at the valvular events (*Table 2*). For the MLP

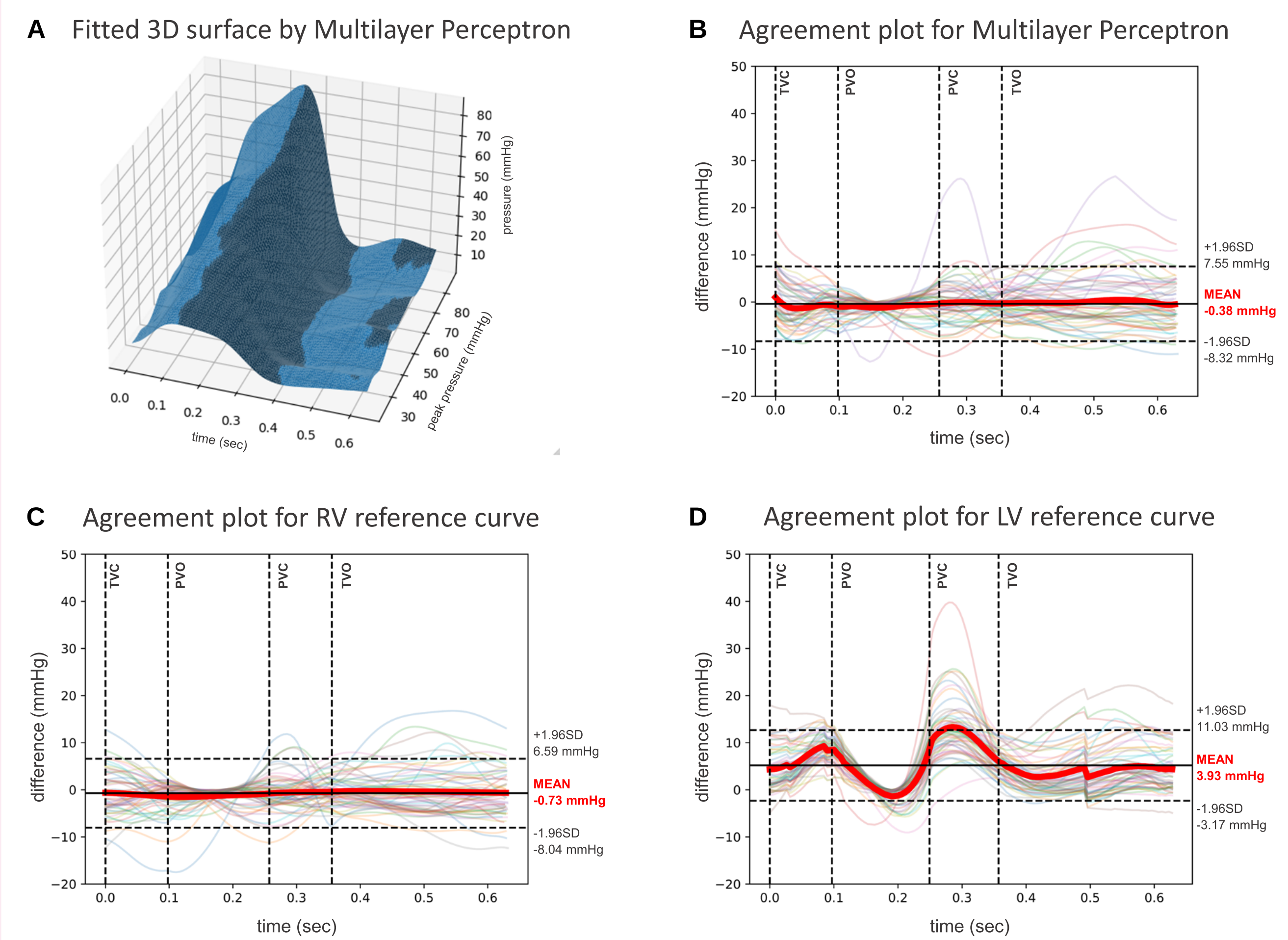


Figure 1 Results of the internal validation. **(***A***)** The 3D continuous surface fitted by the multilayer perceptron to the examination-level normalized RV pressure curves plotted as a function of the peak pressure values. **(***B–D***)** Agreement between the invasively measured ground truth and the pressure curves predicted by the three investigated methods at internal validation. The thick red line indicates the mean difference. LV, left ventricular; PVC, pulmonary valve closure; PVO, pulmonary valve opening; RV, right ventricular; TVC, tricuspid valve closure; TVO, tricuspid valve opening.

and the RV reference curve–based method, the estimated pressures did not differ significantly from the invasively measured ground-truth values at TVC, PVC, and TVO (with the RV reference curve having a borderline non-significant overestimation at PVC). At PVO, both the MLP and the RV reference curve–based method significantly overestimated the RV pressure. The LV reference curve–based method significantly underestimated the pressure values at all dedicated time points. Agreement plots showed similar results (*Figure 1B–D*): whereas the MLP and the RV reference curve–based estimation had a low, balanced bias throughout the cardiac cycle (with MLP exhibiting a slightly lower mean bias), the LV reference curve–based method showed the worst agreement with the ground truth.

External validation

The external validation cohort consisted of 17 patients: 8 (47%) were male, and the median age was 75 (70–80) years. The clinical indication for right heart catheterization was heart failure with preserved EF in 7 (41%), pulmonary artery hypertension in 5 (29%), mitral regurgitation in 3 (18%), and cardiomyopathy in 2 (12%) cases. Median RV end-diastolic volume was 151 (108–207) mL, end-systolic volume was 89 (48–118) mL, and RVEF was 44 (41–57)%. The invasively measured median RV peak systolic pressure was 49.0 (32.3–60.6) mmHg, ranging from 18.6 to 101.8 mmHg. The non-invasively (TR peak velocity) estimated median RV peak systolic pressure was 44.4 (37.9–54.8) mmHg, ranging from 18.8 to 112.8 mmHg.

Using the invasively derived peak pressures, MLP achieved an R^2 of 0.911 (95% CI 0.873–0.948), an MSE of 19.625 (95% CI 9.537–29.714) mmHg^2, and an MAE of 3.265 (95% CI 2.521–4.008) mmHg, whereas the RV reference curve–based estimation method achieved an R^2 of 0.899 (95% CI 0.853–0.946), an MSE of 20.249 (95% CI 11.696–28.803) mmHg^2, and an MAE of 3.455 (95% CI 2.652–4.258) mmHg, and the LV reference curve–based approach had an R^2 of 0.566 (95% CI 0.445–0.687), an MSE of 113.925 (95% CI 57.357–170.492) mmHg^2, and a MAE of 7.727 (95% CI 5.897–9.557) mmHg.

Using the non-invasive (TR peak velocity derived) peak RV pressures, MLP achieved an R^2 of 0.802 (95% CI 0.694–0.909), an MSE of 39.108 (95% CI 22.999–55.216) mmHg^2, and an MAE of 5.004 (95% CI 3.778–6.231) mmHg, whereas the RV reference curve–based estimation method achieved an R^2 of 0.789 (95% CI 0.682–0.897), an MSE of 40.102 (95% CI 23.920–56.283) mmHg^2, and an MAE of 5.163 (95% CI 3.945–6.381) mmHg, and the LV reference curve–based approach had an R^2 of 0.479 (95% CI 0.337–0.622), an MSE of 138.193 (95% CI 78.730–197.654) mmHg^2, and an MAE of 9.159 (95% CI 6.926–11.393) mmHg.

Agreement plots (*Figure 2*) of the external validation set showed similar results to the internal validation: whereas the MLP and the RV

Table 1 Performance of the evaluated machine learning algorithms with optimized hyper-parameters during internal validation

Model	Optimal hyper-parameters	R^2	MSE	MAE
Multilayer perceptron	Hidden layers: [128, 128] Learning rate: 0.001 Batch size: 200 Alpha (for L2 regularization): 0.0001	**0.887 (0.834–0.941)**	**14.398 (10.644–18.151)**	**2.885 (2.520–3.249)**
Support vector machines	Kernel: RBF Kernel coefficient: scaled by the inverse of the variance of the data C (for L2 regularization): 1 Epsilon: 0.1	0.850 (0.773–0.926)	36.627 (−5.784–79.038)	3.458 (2.449–4.467)
Random forest	Number of estimators: 100 Criterion: squared error Min sample split: 2 Min sample leaf: 1	0.767 (0.661–0.872)	30.558 (20.881–40.235)	3.941 (3.343–4.540)
K-nearest neighbours	Neighbours: 15 Weight: uniform Distance: Euclidean	0.856 (0.784–0.928)	19.607 (13.900–25.314)	3.253 (2.796–3.710)
Linear regression	NA	0.275 (0.231–0.319)	135.985 (107.688–164.281)	8.996 (8.243–9.749)

MAE, mean absolute error; MSE, mean squared error; R^2, coefficient of determination with 95% CI. Best results in bold.

Table 2 The invasively measured ground truth and the pressure values estimated by the three methods at internal validation

	Invasively measured pressures	MLP	RV reference curve–based estimation	LV reference curve–based estimation
Pressure at TVC, mmHg	10.48 (8.02–14.87)	10.26 (9.11–11.89)	11.84 (10.32–13.72)	7.02 (6.10–8.10)
Pressure at PVO, mmHg	35.76 (30.73–42.18)	36.59 (31.43–41.95)	36.53 (31.63–42.07)	27.08 (23.53–31.26)
Pressure at PVC, mmHg	34.26 (28.31–39.84)	34.27 (29.84–40.60)	34.76 (30.48–40.29)	25.16 (21.87–29.05)
Pressure at TVO, mmHg	10.37 (7.97–13.70)	10.10 (8.97–12.88)	10.68 (9.59–12.28)	4.35 (3.78–5.02)
Pressure difference at TVC, mmHg	NA	0.03 (−2.48 to 5.16)	−0.70 (−3.76 to 2.22)	3.46 (0.99–7.50)
Pressure difference at PVO, mmHg		−0.56 (−2.28 to 0.64)	−0.35 (−2.39 to 0.76)	7.27 (5.83–9.03)
Pressure difference at PVC, mmHg		−0.73 (−2.48 to 2.06)	−0.68 (−2.86 to 0.91)	8.58 (6.27–10.61)
Pressure difference at TVO, mmHg		−0.73 (−2.34–1.73)	−0.97 (−2.36–1.50)	5.56 (3.62–7.80)
P-value at TVC	NA	0.254	0.289	**<0.001**
P-value at PVO		**0.001**	**0.009**	**<0.001**
P-value at PVC		0.389	0.060	**<0.001**
P-value at TVO		0.367	0.223	**<0.001**

LV, left ventricular; MLP, multilayer perceptron; PVC, pulmonary valve closure; PVO, pulmonary valve opening; RV, right ventricular; TVC, tricuspid valve closure; TVO, tricuspid valve opening. Statistically significant results in bold.

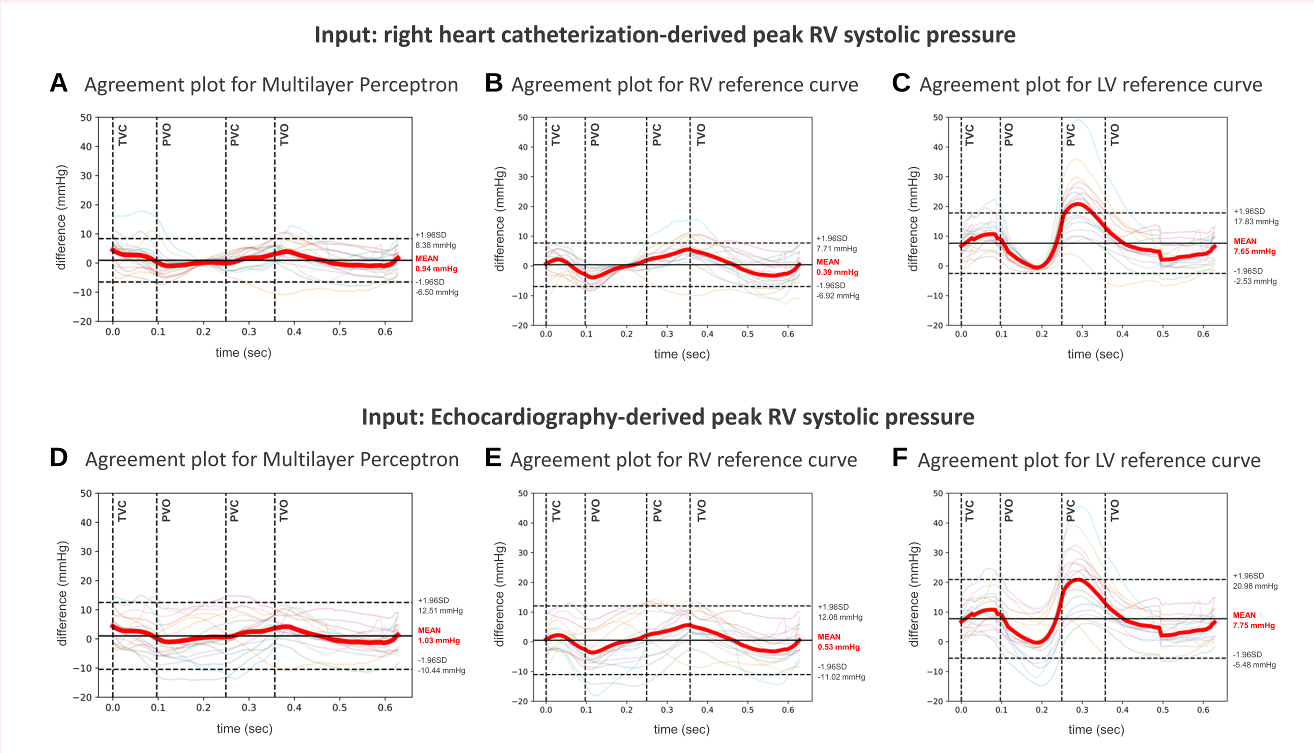


Figure 2 Results of the external validation. **(***A*–*C***)** Agreement between the invasively measured pressure curves (i.e. ground truth) and those predicted by the three investigated methods using the invasively derived peak systolic pressure as input. **(***D*–*F***)** Agreement between the invasively measured pressure curves (i.e. ground truth) and those predicted by the three investigated methods using the non-invasively derived peak systolic pressure (i.e. the peak RV pressure estimated from the Doppler echocardiography–derived peak velocity of the tricuspid regurgitation jet) as input. The thick red line indicates the mean difference. LV, left ventricular; PVC, pulmonary valve closure; PVO, pulmonary valve opening; RV, right ventricular; TVC, tricuspid valve closure; TVO, tricuspid valve opening.

reference curve–based estimation had a low bias throughout the cardiac cycle, the LV reference curve–based method showed worse agreement with the ground truth.

Discussion

Our proof-of-concept study aimed to propose an artificial intelligence–based solution to reconstruct individual RV pressure curves with high fidelity using the peak pressure value as input. The proposed machine learning model showed promising results: it predicted RV pressure values with a balanced, low bias throughout the cardiac cycle, even slightly outperforming the RV reference curve–based method at both internal and external validations. As the morphology of the RV pressure curve can change markedly along the spectrum of elevated pressures (i.e. early systolic peaking transitions to a late peaking, notching pattern as pressure rises), a reconstruction that respects the actual peak RV pressure would be highly advantageous compared with a simple 'averaging'. Due to its favourable attributes, MLP achieved the best performance among the evaluated algorithms. MLP is a feedforward artificial neural network comprising fully connected layers of neurons with a non-linear activation function and is particularly effective at differentiating data points that cannot be separated linearly.[8] A physiologically more realistic curve for the given clinical scenario can have downstream consequences on RV function quantification by myocardial work or other methods relying on RV pressure curves.[9,10] Doppler-based measurement of peak RV pressure is feasible using the jet of tricuspid or pulmonary valve regurgitation by echocardiography; thus, the proposed method can be easily translated to a widely available, non-invasive tool. In an external validation cohort, we also proved that estimating the peak RV systolic pressure based on the TR peak velocity measurement results only in a minor drop in the performance of the proposed MLP. It is important to emphasize that according to our results, the LV pressure reference curve–based estimation significantly underestimates RV pressures throughout the cardiac cycle. This fact questions whether the available dedicated LV solution can be reliably used for RV myocardial work calculations.

Some limitations of our study have to be acknowledged. The performance of the proposed model is specific to the patient cohort from which it was derived; thus, RV pressure curves of patients with other disease aetiologies should be incorporated to create a more comprehensive model. We hypothesize that by investigating more patients and various cardiopulmonary disease aetiologies and stages, the added value of our method would be even more pronounced. The non-invasive pathway by TR peak velocity measurement cannot be performed in patients with no (or not measurable) TR jet or severe TR (significant underestimation of RV peak pressures). Quantifying the pulmonary regurgitation peak velocity and derived peak RV pressure may be an alternative that remains to be tested. Further studies should be conducted to assess the impact of these differences in pressure curve reconstruction on the values of RV functional parameters (e.g. myocardial work indices).

Conflict of interest: Z.T. is one of the founders and the chief technical officer of Argus Cognitive and receives financial compensation for his work. A.K. is the chief medical officer of Argus Cognitive and receives financial compensation for his work. Á.Sz. and A.Sá. are employees of Argus Cognitive and receive financial compensation for their work. A.F. and B.L. report personal fees from Argus Cognitive, Inc. M.T. reports personal fees from CardioSight, Inc., outside the submitted work. All other authors have no competing interests to disclose.

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Data availability

Data will be made available by the corresponding author for reasonable requests.

Lead author biography

Attila Kovács is a clinician–scientist and medical device developer. Attila is the head of Echocardiography Research and Core Laboratory at Semmelweis University Heart and Vascular Center, Budapest. He has special interests in 3D echocardiography, right ventricular function, athlete's heart, and machine learning. Attila is co-inventor of ReVISION, an award-winning, FDA-cleared software medical device for comprehensive right ventricular function characterization. He is a fellow of the American Society of Echocardiography and the European Society of Cardiology.

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