Predicting Global Longitudinal Strain from Conventional Echocardiographic Measurements in Cancer Patients

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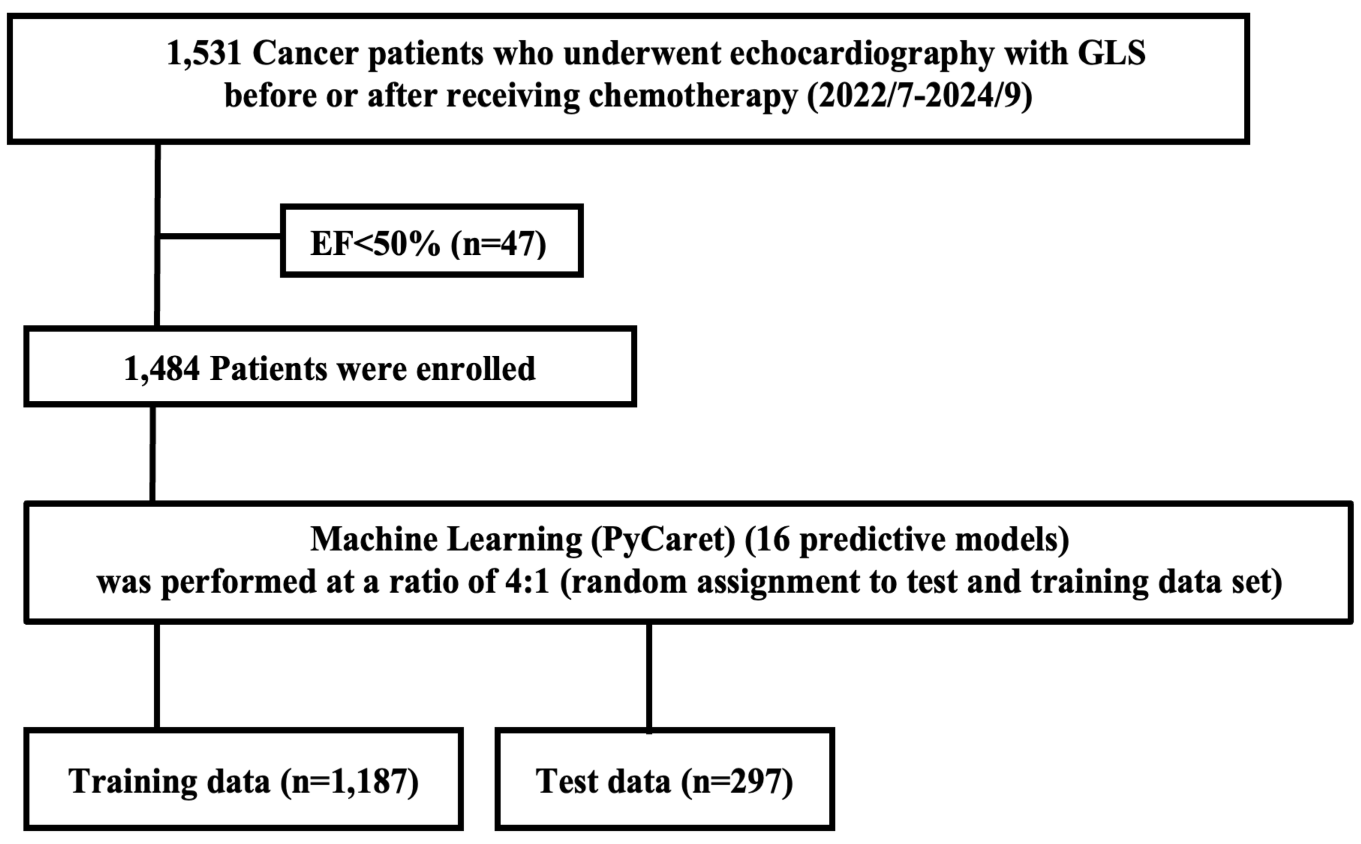
開示すべき利益相反状態はありません

Introduction

Global longitudinal strain (GLS) parameters are more sensitive for detecting decreased left ventricular(LV) function than traditional measures of LV ejection fraction(LVEF)*[1]. GLS has been recommended as a complementary clinical approach that provides additional prognostic information over LVEF in patients with conditions such as cancer-therapy-related cardiac dysfunction(CTRCD), heart failure, valve disease, and cardiomyopathy*[2]. However, Hospitals and clinics equipped to measure GLS are limited. We tested the hypothesis that the reduction of GLS could be predicted using conventional echocardiography through a machine learning (ML) approach.

Methods

Consecutive patients subjected to echocardiographic assessment at our hospital were enrolled in this study (Figure 1).
1,484 patients (64±13 y/o, 69% female) were enrolled for ML model development, excluding the patients with EF<50%. The patients were randomly assigned to the training and test datasets in a 4:1 ratio. Low-GLS was defined as GLS <16*[3].
We constructed ML models to predict our GLS based on standard echocardiographic measurements. The PyCaret library developed and evaluated fifteen ML predictive models based on area under the receiver operating characteristic curve (AUC), accuracy, sensitivity, specificity, Positive predictive value (PPV), Negative predictive value (NPV), and F1 score. PyCaret is a Python library that simplifies the machine learning workflow by offering a cohesive platform for various processes, such as data preprocessing, model training, hyperparameter optimization, and model explanation. Moreover, the Shapley Additive exPlanations (SHAP) method evaluated essential predictors.



GLS, Global Longitudinal Strain; EF, ejection fraction

Figure 1 Study Design

Results

Table 1. Patients Characteristics

	Total (n=1,484)	Low-GLS (n=406)	Normal-GLS (n=1,078)	P-value
Age (y/o)	63.7±13.3	66.5±12.8	62.6±13.4	<.01
Female, n(%)	69.0%	59.1%	72.7%	<.001
BMI (kg/m²)	22.1±3.8	22.5± 4.0	22.0±3.6	<.05
EF (%)	66.0±6.0	64.5±6.5	66.6±5.6	<.001
GLS(%)	17.7±3.2	13.7±2.0	19.1±2.1	N/A
AAD (mm)	20.5±2.2	21.1±2.4	20.3±2.1	<.001
LAD (mm)	31.9±5.5	31.8±6.2	31.9±5.2	0.94
LVDd (mm)	43.0±4.7	42.6±5.2	43.2±4.4	0.02
LVDs (mm)	27.3±3.7	27.5±4.2	27.2±3.5	0.11
IVST (mm)	8.5±1.4	8.8±1.5	8.3±1.4	<.001
PWT (mm)	8.5±1.3	8.8±1.4	8.3±1.2	<.001
E wave (cm/s)	70.2±18.2	65.1±17.3	73.5±18.0	<.001
A wave (cm/s)	75.6±20.1	77.8±20.7	74.8±19.8	<.05
DCT (ms)	225.5±61.2	228.6±66.4	224.8±59.1	0.28
Septal e` (cm/s)	7.0±2.3	6.1± 2.0	7.3± 2.3	<.001
Septal a` (cm/s)	9.2±1.9	9.0± 2.0	9.3± 1.8	<.01
Lateral e` (cm/s)	9.2±2.8	7.9± 2.7	9.5± 2.8	<.001
Lateral a` (cm/s)	9.9±2.5	9.8± 2.4	10.0± 2.5	0.12
E/A	1.0±0.4	0.9±0.3	1.0±0.4	<.001
E/e’	11.0±4.0	11.5±4.3	10.8±3.8	<.01
LVMI (g/m²)	73.6±18.3	75.4±20.4	72.9±17.5	0.07
AV-Vmax (m/s)	1.4±0.4	1.3±0.4	1.4± 0.4	<.001
LVOT-Vmax (m/s)	1.0±0.2	0.9± 0.2	1.0 ± 0.2	<.001

Table 2. Comparison of machine learning predictive models by PyCaret

Model	AUC	ACC	Sensitivity (Recall)	Specificity	PPV (Precision)	NPV	F-1
Training dataset (after fine-tuning)							
CatBoost Classifier	0.7547	0.7709	0.2986	0.9490	0.6794	0.7826	0.4106
Extra Trees Classifier	0.7542	0.7591	0.2187	0.9629	0.6907	0.7658	0.3306
Gradient Boosting Classifier	0.7493	0.7616	0.1788	0.9814	0.7567	0.7604	0.2854
Test dataset							
CatBoost Classifier	0.7481	0.7340	0.2469	0.9167	0.7645	0.5263	0.3361
Extra Trees Classifier	0.7217	0.7508	0.1605	0.9722	0.7554	0.6842	0.2600
Gradient Boosting Classifier	0.7572	0.7374	0.1358	0.9630	0.7482	0.5789	0.2200

Low-GLS patients were 406 (66.5±12.8y/o, 59% female). Several variables, such as EF, E wave, and mitral annular early diastolic velocity (e’), significantly differed between the two groups (**Table 1**). Using 24 conventional echocardiographic measurements, the best models were the CatBoost Classifier (AUC: 0.75, Accuracy: 73%), Extra Trees Classifier (AUC: 0.72, Accuracy: 75%), and Gradient Boosting Classifier (AUC: 0.75, Accuracy: 73%) (**Table 2**).
The confusion matrix (**Figure 2**) shows that 53% of the patients with Low-GLS and 77% of normal GLS in the unseen test set were correctly classified.

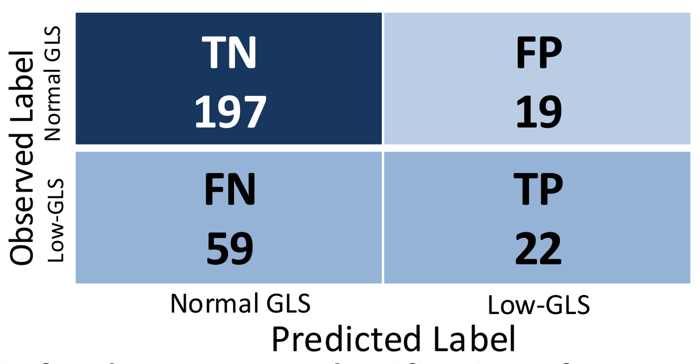


Figure 2. Confusion matrix for the CatBoost classification of Low-GLS versus Normal-GLS

EF: Ejection Fraction, AAD: Aortic Root Diameter, LAD: Left Atrium, LVDd: Left Ventricular Diastolic Diameter, LVDs: Left Ventricular Systolic Diameter, IVST: Interventricular Septal Thickness, PWT: Left Ventricular Posterior Wall Thickness, E_wave: Early Diastolic Wave, A_wave: Atrial Contraction Wave, DCT: Deceleration Time of E wave , e`: Mitral Annular Early Diastolic Velocity, a`: Mitral Annular Atrial Systolic Velocity, med: Septal, lateral: Lateral, LVMI: Left Ventricular Mass Index AV-Vmax: Aortic Valve Peak Velocity , LVOT-Vmax: Left Ventricular Outflow Tract Velocity Maximum, Continuous variables are analyzed with the t-test., Categorical variables are analyzed with the Chi-square test or Fisher's exact test.

Figure 3 shows the most impactful features on prediction (ranked from most to least important). **Figures 4** indicates the Shapley Additive exPlanations (SHAP) model for the CatBoost Classifier and shows the distribution of the impacts of each feature on the model output. Within each row, each dot represents a patient. The colors of the dots represent the feature values: red for larger values and blue for lower ones.

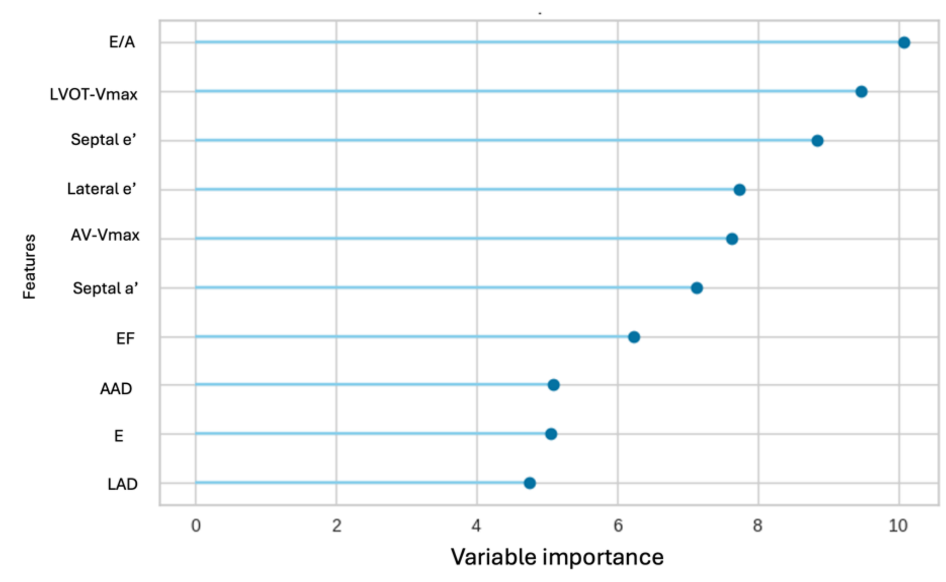


Figure 3. Feature importance of CatBoost Classifier on the training dataset

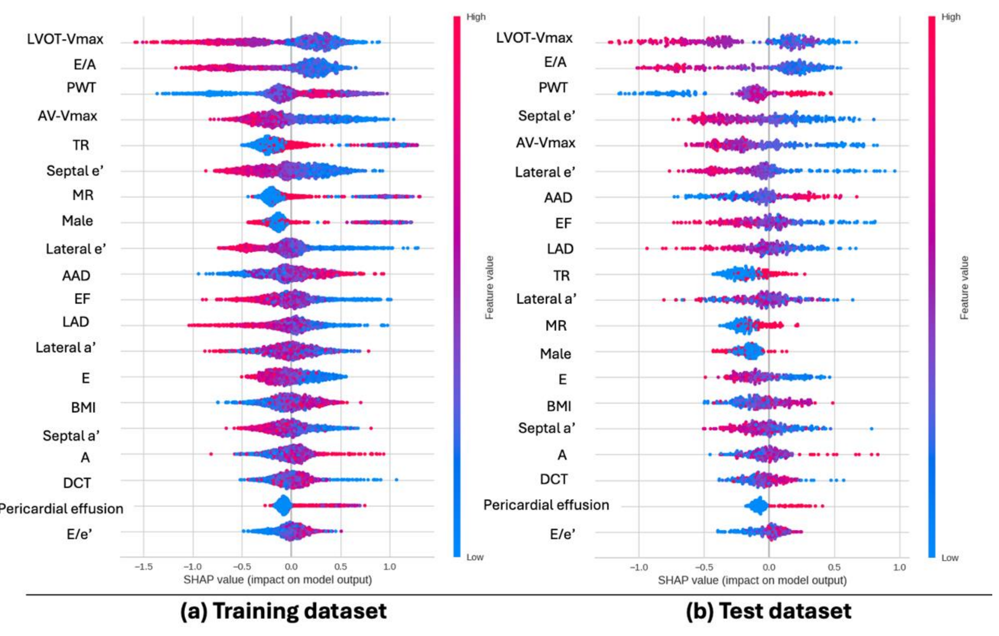


Figure 4. SHAP for CatBoost Classifier

Diastolic dysfunction indices [such as septal/lateral mitral annular early diastolic velocity (e’) and E-wave to atrial contraction filling velocity (E/A)] and peak velocity-related parameters [aortic valve peak velocity (AV-Vmax) and left ventricular outflow tract velocity maximum (LVOT-Vmax)] played essential roles in the Low-GLS prediction model.

Discussion

In the present study, Low-GLS was predicted with high accuracy by machine learning from conventional echocardiographic measurements. Diastolic dysfunction indices and peak velocity-related parameters played essential roles in the model.
The present study has several limitations. First, the sample size was relatively small, and the findings have not been externally validated. Although we demonstrated good diagnostic performance, the machine learning model developed using all 1,484 cases was not tested with patient data from other institutes. Second, due to the cross-sectional nature of the study design, this ML model cannot predict changes in GLS following anticancer drug administration or patient prognosis.

Conclusion

This study indicated the possibility that Low-GLS might be predicted from conventional echocardiography measurements.

Reference

[1] Oikonomou EK, et al. Assessment of Prognostic Value of Left Ventricular Global Longitudinal Strain for Early Prediction of Chemotherapy-Induced Cardiotoxicity: A Systematic Review and Meta-analysis. JAMA Cardiol. 2019;4(10):1007
[2] Potter E, et al. Assessment of Left Ventricular Function by Echocardiography: The Case for Routinely Adding Global Longitudinal Strain to Ejection Fraction. ACC Cardiovasc Imaging. 2018;11(2 Pt 1):260.
[3] Yingchoncharoen T, Agarwal S, Popović ZB, Marwick TH. Normal ranges of left ventricular strain: a meta-analysis. J Am Soc Echocardiogr. 2013 Feb;26(2):185-91. doi: 10.1016/j.echo.2012.10.008.