Machine Learning Enabled ECG Wavelet Analysis as a Gatekeeper for Appropriate Evaluation of Diastolic Function by Echocardiography

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Background

- Population-based studies have recognized left ventricular (LV) diastolic dysfunction (DD) as a strong predictor of cardiovascular and all-cause mortality.
- However, identifying patients with LVDD or deciding which patients need further tests is a challenge.
- We investigated the role of a novel high sensitivity surface electrocardiogram (hs-ECG) as a screening device for appropriate referral for echocardiographic assessment of subclinical LVDD.

Methods

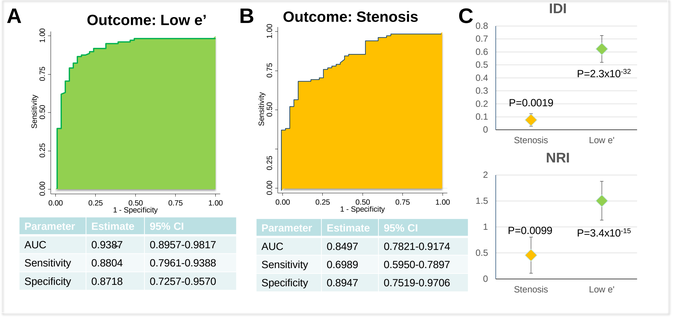
- We conducted a prospective, diagnostic validation study at two institutions, recruiting consequently total 191 patients.
- The presence of diastolic dysfunction was assessed using comprehensive 2-dimensional and Doppler echocardiography with all patients undergoing coronary computed tomography angiography for assessing presence of underlying coronary artery disease.
- The prediction performance of continuous wavelet-transformed 12-lead hs-ECG (Myovista™, HeartSciences) with time–frequency-energy displays (Fig. 1A) for diagnosing the echocardiographic features of diastolic dysfunction was validated using machine-learning approaches with receiver-operating characteristic curves (ROC).

Results

Table 1. Patient Clinical Characteristics

CHARACTERISTIC	DESCRIPTION
Age [mean (SD)] y	57 (12)
Females [n, (%)]	110 (58)
Race [n, (%)]	
White	88 (47)
Black	46 (24)
Hispanic/Mexican American	38 (20)
Asian	16 (9)
BMI [mean (SD)] Kg/m^2 (n=80)	29 (6)
Ever Smokers [n (%)]	79 (42)
NYHA class [n (%)]	
I	121 (66)
II	55 (29)
III	8 (4)
IV	1 (1)
Body surface area [mean (SD)] m^2	1.96 (0.31)
Blood pressure [mean (SD)] mmHg	
Systolic	122.75 (18.82)
Diastolic	71.91 (9.47)
Mean arterial	88.69 (11.52)
Serum creatinine [mean (SD)] mg/dl (n=90)	0.91 (0.21)
Clinical conditions [n, (%)]	
Hypertension	33 (17)
Obesity (BMI >=30 Kg/m^2)	75 (40)
Dyslipidemia (high TSC, high TG or low HDL)	82 (44)
Ever Smokers	79 (42)
Cardiovascular conditions	
Presence of stenosis	104 (55.32)
Presence of severe stenosis (>50%)	28 (14.89)
Low e'	135 (71.81)
Traditional ECG findings	
Abnormal ECG	25 (13.30)
Borderline ECG	55 (29.26)
Normal ECG	108 (57.44)

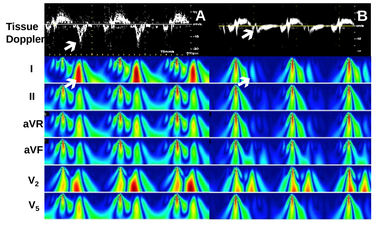
Figure 1. Diagnostic performance of 12 lead hs-ECG.



Parameter	Estimate	95% CI
AUC	0.9387	0.8957-0.9817
Sensitivity	0.8804	0.7961-0.9388
Specificity	0.8718	0.7257-0.9570

Parameter	Estimate	95% CI
AUC	0.8497	0.7821-0.9174
Sensitivity	0.6989	0.5950-0.7897
Specificity	0.8947	0.7519-0.9706

Figure 2. Illustrative examples of a normal and abnormal tests



Normal (a) and reduced (b) early diastolic mitral annular relaxation velocities (e') have been shown along with hs-ECG. Note the normal energy-frequency spectrum of repolarization waves (A, arrow) which are attenuated In the presence of reduced e' (B)

- A machine learning enabled diagnostic classifier developed from Hs-ECG variables showed a high diagnostic value for predicting the presence of early diastolic LV relaxation (e') abnormalities. The ROC curves and Area under the ROC Curves based on the results of Random Forest with Monte-Carlo classification scheme using expanded set (A, 370 input variables) and limited set (B, 7 variables) are shown in Figure 1.
- hs-ECG had higher incremental value over traditional ECG with superior integrated discrimination and net reclassification improvement for predicting low e' with or without coronary stenosis ≥50% (IDI and NRI, P<0.0001 for both, Fig. 1C).

Table 2. Test of moderator effects on the diagnostic performance

Moderator variable and categories	N	AUC (95% CI)	Q (df)*	P_{het}
Overall	188	0.9387 (0.8957 – 0.9817)		---
Age			3.83 (1)	0.0502
<60 years	104	0.9246 (0.8662 – 0.9831)		
≥60 years	84	0.9872 (0.9652 – 1.0000)		
Gender			0.06 (1)	0.8139
Male	78	0.9360 (0.8621 – 1.0000)		
Female	110	0.9467 (0.8977 – 0.9957)		
Race			2.25 (3)	0.5228
White	88	0.9009 (0.8027 – 0.9991)		
Black	46	0.9637 (0.9027 – 1.0000)		
Hispanic / Mexican	38	0.9706 (0.9210 – 1.0000)		
Asian	16	0.8667 (0.6489 – 1.0000)		
Ever smoker			7.33 (1)	0.0068
Yes	79	0.9965 (0.9882 – 1.0000)		
No	109	0.8946 (0.8213 – 0.9679)		
Obesity (BMI ≥30 Kg/m^2)			0.29 (1)	0.5928
Obese	75	0.9571 (0.8927 – 1.0000)		
Non-obese	113	0.9341 (0.8798 – 0.9885)		
Body surface area (BSA ≥2.30 m^2)			0.60 (1)	0.4387
Top quartile	48	0.8795 (0.7077 – 1.0000)		
First to third quartile	140	0.9491 (0.9098 – 0.9884)		
NYHA Class			1.13 (1)	0.2879
I	67	0.9305 (0.8758 – 0.9851)		
II/III/IV	121	0.9706 (0.9209 – 1.0000)		

*, Cochrane Q statistic for test of heterogeneity of diagnostic performance across subgroups

Conclusions

Identification of repolarization abnormalities using hs-ECG provides robust prediction of LVDD in presence or absence of coronary artery disease. If confirmed in a population based-study, primary screening for LVDD using hs-ECG could have a significant impact on optimizing the referral for echocardiography in patients with suspected subclinical LVDD.

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