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Predicting Left Ventricular Mass Using ECG, Demographic and DXA Features

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Abstract

The gold standard for the assessment of cardiac mass is cardiac magnetic resonance imaging (CMR). However, it is costly and requires specific expertise. Electrocardiographic (ECG) criteria could provide a low-cost solution, but have shown to be poorly correlated with LVM in athletes. We hypothesize that this poor correlation could be overcome by taking into account body measurements (length, weight) and composition (fat mass, lean mass and bone mass). The objective was to assess whether adding demographic (Demo) and/or Dual-energy X-ray absorptiometry (DXA) features could improve an ECG-based regression model for the estimation of LVM in athletes. 107 young competitive endurance athletes (19±2 years; 35 female) underwent a 12-lead ECG, a DXA scan and CMRI. We constructed four feature subsets: ECG, ECG+Demo, ECG+DXA and All. The best combination of features from each set, was used to build a Support Vector Machines regression model with 5 features. The ECG model performed significantly worse than all other models (R^2 = 0.28 (0.17), RMSE = 34.33 (5.63) g). The best performing model was constructed with the entire feature set ((R^2 = 0.67 (0.14), RMSE = 23.08 (4.42) g). These results suggest that an ECG based regression model for LVM prediction can be improved by adding demographic and/or body composition features.

1. Introduction

The term "athlete's heart" describes the adaptation of the left ventricle (LV) to long-term, intensive training. Increased wall thickness, LV mass (LVM) and chamber dilation are the primary features of exercise induced cardiac remodeling [1]. Distinguishing this physiological adaptation from concentric hypertrophic cardiomyopathy (HCM) can be challenging [2]. The stakes of resolving such diagnostic ambiguity are high since, on the one hand, false reassurance may lead to an increased risk of sudden cardiac death. On the other hand, a diagnosis of HCM may imply a life-long ban from competitive sports, regular medical follow-up, screening of family members and psychological stress [2]. Hence, accurate phenotyping, including quantification of cardiac dimensions, is crucial to help distinguish normal training adaptation from pathological changes.

The gold standard for the assessment of cardiac volumes and mass is cardiac magnetic resonance imaging (CMR). Structural measures by CMR are both accurate and reproducible [3]. However, cost and operational considerations tend to limit its utility in large-scale population studies and clinical trials [4].

ECG criteria for left ventricle hypertrophy (LVH) provide a low-cost solution, but have low sensitivity in the general population. In an attempt to resolve this issue, the combination of multiple criteria was suggested. This approach increased the sensitivity for detection of LVH, but came at the expense of a lowered specificity [5]. A more sophisticated solution was the use of multivariate statistical models for the estimation of LVM. This way, the LVM could be estimated on a continuous scale, instead of a binary classification. Good results have been obtained in an older population, but this has not been done in a young athlete population [4].

The ECG is measured at the body surface. The conduction of the electrical signal of the heart to the skin is influenced by the composition of the different organ tissues separating the electrodes from the heart. Including body composition to an ECG-based estimation of LVM might therefore improve its accuracy. In this study, we first combined ECG features in a regression model to predict LVM. Hereafter, we added demographic and body composition features. The latter are measured with Dual-energy X-ray absorptiometry (DXA). We hypothesize that adding these features will improve the estimation.

The first objective of this study is to identify features from the different modalities that are highly correlated with LVM. The second objective is to assess whether adding demographic and/or DXA features could improve an ECG-based regression model for the estimation of LVM in athletes.

2. Materials & Methods

2.1. Study population

This study was conducted using data of the Pro@heart study. This is a longitudinal cohort study in elite endurance athletes aiming to phenotype the structural and functional cardiovascular adaptations associated with high volume exercise. 107 young competitive endurance athletes (19±2 years; 35 female), were included in the university of Leuven (Belgium) and the Baker Heart and Diabetes Institute (Australia). The full demographics are shown in Table 1.

2.2. Feature collection

Every athlete underwent a 12-lead ECG, DXA scan and CMR. A subset of features, which have shown potential as single features or as combinations in earlier studies, was selected from each modality for further analysis.

The data from all 12-lead ECGs were automatically processed and measurements of each lead were averaged over the ECG to obtain representative metrics. We selected: SV1, SV3, RV5, RV6, RI, RaVL, SaVL and QRS duration; where S is the absolute value of the S-wave amplitude and R is the R-wave amplitude in the respectively indicated leads. Additionally, we included 4 ECG criteria for LVH: Cornell voltage (CV) and product (CP), Sokolow-Lyon voltage (SLV) and product (SLP). CV is considered the most accurate criterion for LVH. It is computed as the amplitude of R in aVL plus the amplitude of S in V3 (RaVL+SV3). The SLV is computed by the amplitude of S in V1 and the amplitude of R in V5 or V6, whichever is the larger (SV1+RV5/6). Both products are obtained by multiplying the voltages with the QRS duration.

Five demographic variables were used: age, sex, weight (kg), height (m) and body surface area (BSA, m^2). BSA was computed with the Dubois and Dubois equation [2] and was included since its frequent use as a scaling parameter for LVM.

From the DXA scan, we selected: bone mineral content of the trunk (BMCTrunk), fat mass of the trunk (FMTrunk), lean mass of the trunk (LMTrunk), total fat mass (FMTotal) and total lean mass (LMTotal).

For calculation of LVM, the volume of the myocardium measured by CMR was multiplied by the specific gravity of the myocardium (1.05g/mL). The volume of the myocardium was obtained by subtracting the LV end-diastolic volume from the epicardial volume, both drawn from apex to basal short axis views.

2.3. Correlation and regression analysis

We quantified the linear correlation between each of the features and the LVM on the entire dataset using the Pearson correlation coefficient, ρ.

To identify the predictive power of each feature we performed a univariate linear regression analysis. The dataset was randomly split into a training and test set with a 70/30 ratio. The training set was used to build the model, while the performance was assessed on the test set. For statistical robustness, the whole process was repeated 100 times.

Table 1: Demographics. Values are shown as median and interquartile range.

	All	Men	Women
Number	107	72	35
Age (y)	19.00 (2.00)	19.00 (2.00)	18.00 (2.75)
Height (m)	1.78 (0.13)	1.82 (0.10)	1.70 (0.09)
Weight (kg)	66.50 (12.20)	69.33 (10.43)	58.36 (10.01)
LVM (g)	142.80 (54.54)	159.50 (45.80)	106.05 (32.35)

2.4. Feature selection

Features with a non-significant ($p > 0.05$) correlation with the LVM were removed for further analysis.

Hereafter, we created four feature subsets. The first subset consists solely of ECG features (ECG). The second subset is comprised of both ECG and demographic features (ECG+Demo). The third subset consists of both ECG and DXA features (ECG+DXA) and the last subset contains all available features (All).

The selection of the most relevant features from the different subsets was carried out using the least absolute shrinkage and selection operator (LASSO) algorithm [6]. This is a particular case of the penalized least squares regression with L1-penalty function. It has one major drawback however: if there is a group of highly correlated variables, LASSO tends to randomly select only one variable from that group [7]. Therefore, we performed the LASSO algorithm 100 times and sorted each feature based on majority voting.

2.5. Development of LVM estimation model

Since we have only 107 subjects, we opted to keep the model complexity low. Therefore, we constructed a linear support vector machine (SVM) regression model and used only the five highest ranked features from every subset. The latter to avoid overfitting.

To be able to statistically compare the 4 models, we used the same approach as for the univariate regression analysis. We randomly split the dataset 100 times into a

training and test set with a 70/30 ratio. These sets were then used to train and test the model. The hyperparameters were automatically tuned using 5-fold cross-validation and Bayesian optimization.

The coefficient of determination, R^2, and the root-mean-squared-error (RMSE) were used as statistics to measure the goodness of fit of the models. The median and interquartile range of the performance metrics are always reported. Depending on the normality, we tested the difference between models with a one-way ANOVA or with a Kruskal-Wallis test. Normality was tested with the Lilliefors test and a p-value <0.05 was considered significant. All analysis were performed using MATLAB© (MathWorks).

3. Results

The highest correlated variables are SLP, age, sex, height, weight and LMTrunk, LMTotal. In contrast, RaVL, SaVL, SIII, FMTrunk and FMTotal are not significantly correlated to the LVM. Hence, these features were removed before the feature selection (Table 2).

The univariate regression analysis showed that ECG derived features predict LVM rather poorly, compared to features derived from other modalities. The best performing ECG features are SLV and SLP.

The five highest ranked features by the LASSO algorithm are SLP, Age, Sex, Weight and LMTrunk. All of these features were selected at least 83 out of 100 times. The resulting RMSE of the regression models of each of these features separately ranged between 26.66-35.46 g.

The performance of all four models are shown in Figure 1. The best performing model was constructed with the 5 highest ranked features from all modalities (R^2 = 0.67 (0.14), RMSE = 23.08 (4.42) g). The model outperformed the ECG and ECG+DXA based models, but did not differ from the ECG+Demo model.

The ECG based model performed significantly worse compared to all other models (R^2 = 0.28 (0.17), RMSE = 34.33 (5.63) g).

The ECG+Demo (R^2 = 0.65 (0.10), RMSE = 23.56 (3.65) g) and the ECG+DXA model (R2 = 0.61 (0.14), RMSE = 25.21 (4.10) g) performed similarly.

4. Discussion

The first objective was to identify features which correlate well with LVM. LMTrunk and LMTotal correlate best (ρ > 0.7) and have the best goodness of fit (R^2 > 0.5, RMSE < 28 g). This was expected, since the cardiovascular system has to efficiently distribute oxygen to metabolic active tissue such as lean muscle mass, especially during exercise [2].

Table 2: Correlation and regression analysis for each feature. ρ = correlation coefficient; R^2 = coefficient of determination; RMSE = root mean squared error; # LASSO = amount of times each feature was selected by LASSO when taking all features into account.

	ρ	R^2 (IQR)	RMSE (g) (IQR)	# LASSO
SV1	0.26	0.09 (0.12)	37.30 (4.92)	1
SV3	0.32	0.12 (0.09)	35.96 (5.65)	1
RV5	0.43	0.20 (0.17)	34.96 (5.87)	73
RV6	0.24	0.08 (0.13)	37.55 (5.44)	1
RI	0.20	0.05 (0.08)	37.67 (5.25)	1
RaVL	0.04	0.01 (0.03)	38.33 (5.21)	
SaVL	-0.01	0.01 (0.04)	38.45 (4.11)	
SIII	0.09	0.02 (0.04)	38.02 (5.32)	
QRS	0.44	0.21 (0.19)	35.32 (4.74)	32
CV	0.32	0.11 (0.08)	35.94 (5.62)	0
CP	0.37	0.15 (0.10)	35.28 (5.65)	10
SLV	0.47	0.23 (0.14)	34.07 (4.37)	0
SLP	0.54	0.30 (0.19)	32.49 (4.15)	83
Age	0.43	0.19 (0.13)	35.46 (5.78)	95
Sex	-0.61	0.30 (0.15)	30.56 (4.55)	93
Height	0.58	0.33 (0.15)	31.65 (3.88)	2
Weight	0.68	0.46 (0.17)	28.74 (4.26)	86
BSA	0.69	0.48 (0.14)	28.54 (4.16)	7
BMCTrunk	0.60	0.32 (0.18)	31.70 (5.34)	73
FMTrunk	0.09	0.01 (0.04)	38.12 (5.10)	
LMTrunk	0.73	0.55 (0.16)	26.66 (4.66)	99
FMTotal	-0.04	0.01 (0.03)	38.15 (5.33)	
LMTotal	0.72	0.53 (0.17)	27.30 (4.84)	23

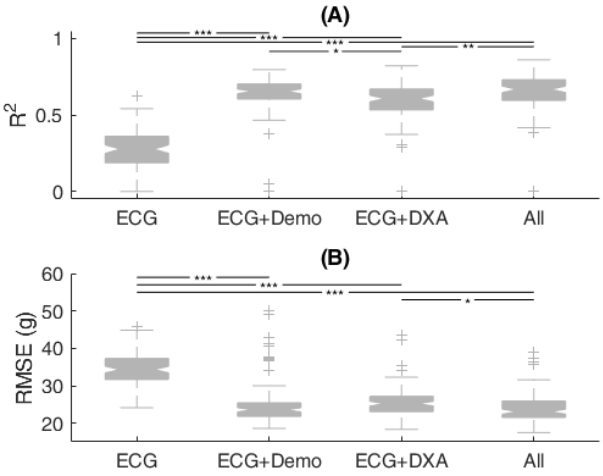


Figure 1: (A) R^2 and (B) RMSE of all 4 models. * = p < 0.05, ** = p < 0.01, *** = p < 0.001

Additionally, this high correlation has also been observed in other studies [2, 8]. Since the metabolic demand of FM is rather low, this could also explain the poor correlation between FM and LVM.

ECG criteria correlate poorly with LVM ($R^2 < 0.3$). The SLV and SLP are the best predicting ECG features with a median R^2 of respectively 0.23 and 0.30.

The best performing model used all possible features. The five highest ranked features which were used for the construction of the model are LMTrunk, Age, Sex, Weight and SLP. The presence of features from all modalities indicates that all modalities contribute for an accurate prediction of LVM. The added value of Sex with LMTrunk has previously been observed where a higher LVM is measured in boys compared to girls [8]. However, sex-specific predictive equations were used for the quantification of lean body mass. We performed a more accurate assessment of LVM using a DXA-scan.

One limitation of this study is the limited number of data points. This prevented the creation of an independent test set. In this study we used all data points for feature selection and again for the learning algorithm design. Ideally, those steps should be performed separately to prevent overfitting. Future research is needed to validate this model in a larger cohort of athletes, as well as to see whether such a model could help differentiate mild concentric left ventricular hypertrophy from physiological adaptions in athletes.

Furthermore the added value of other modalities should be assessed. Maximal oxygen consumption (VO2max) as measure by cardiac pulmonary exercise testing has shown strong correlation with LVM with an R^2 of 0.71 [3], hence could serve as a potential add-on in predictive models for LVM.

5. Conclusion

An ECG-based regression model poorly predicts LVM in endurance athletes. Adding demographic and body composition features significantly improves the model enabling accurate estimation of LVM. Further research is needed to firstly validate the model and secondly assess its discriminative performance between healthy athletes and those with LVH.

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