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Determining LoA between Left Ventricular EF estimated from Abarquez Formula and Left Ventricular EF measured by 2D Echo

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ABSTRACT

Background: The Abarquez formula (aVR QRS amplitude x 2.264) + (age x 0.645) has been offered to provide an estimate for LVEF measured by 2D Echo. However, studies aiming to establish agreement between the Abarquez formula and LVEF measured by 2D Echo are lacking. **Aims and Objectives:** The aim of this study was to compare the LVEF estimated from 12-lead ECG using the Abarquez formula with the LVEF measured using the 2DED in the following subpopulations: 18-35 years old, 36-60 years old, >60 years old, male, and female patients. To compare these two measurements, the limits of agreement (LoA) by Altman and Bland was used. **Materials and Methods:** Adult patients admitted in the VLMC from January to May 2019 with both a 12-lead ECG and a 2D Echo were included in the study. LVEF from 2D Echo and LVEF estimated using the Abarquez formula were recorded. Comparison of the two measurements was performed by Altman and Bland method using LoA at 95% confidence interval. This analysis was done using Analyse-It Software. Comparison of the mean differences between the two measurement methods was also done using STATA. **Results:** LVEF estimate using the Abarquez formula was found to significantly differ from LVEF measured using 2D Echo. **Conclusions:** The Abarquez formula cannot be used as a surrogate for LVEF measure by 2D Echo.

Key words: Left ventricular ejection fraction; 2D Echocardiogram; Abarquez formula; Limits of agreement

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INTRODUCTION

The most useful index of left ventricular function is the ejection fraction (left ventricular ejection fraction or LVEF), which can be measured through various modalities. Often, the most accessible modality to measure LVEF is the 2-dimensional echocardiogram (2DED), which has been shown to have moderate to strong correlation to LVEF measured through the state of the art technique, cardiac magnetic resonance.[1] Another widely available diagnostic test is the electrocardiogram (ECG), a graphic recording of electric potentials generated by the heart. There are a number of ways by which the LVEF can be estimated from the ECG, including the Palmeri QRS, the QRS score, the sum of R waves in leads aVL, avF, and the precordial leads, and the formula cited by Abarquez[2]: (aVR QRS amplitude X 2.264) + (age X 0.645). This is fortunate, because the ECG is typically even cheaper and more accessible than the echocardiogram.

However, there is a paucity of studies verifying the accuracy of the formula (aVR QRS amplitude x 2.264) + (age x 0.645). In an article by Abarquez[2], a study was cited to establish a correlation between the LVEF estimate using the formula (aVR QRS amplitude x 2.264) + (age x 0.645) and LVEF estimated from the echocardiogram.

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The correlation was 100% specific and 53% sensitive for patients with coronary artery disease, and 100% sensitive and 100% specific for patients with left ventricular hypertrophy. Another study showed that there was a significant difference between 12-lead ECG derived LVEF and LVEF measured from 2D Echo.[3] Furthermore, correlation studies have their limitations. Correlation describes only the linear relationship between two sets of data, and not their agreement.[4] Hence there is a need for further studies looking at the accuracy of 12-lead ECG estimates of LVEF, and a need for studies using analyses other than correlation studies.

In this study, we hope to measure first, the mean difference, and second, the limits of agreement between the LVEF estimated from the ECG using the formula (aVR QRS amplitude in mm X 2.264) + (age in completed years X 0.645) and the LVEF measured using 2D Echo. We also want to conduct the same analyses on the following subgroups: young adult patients 18-35 years old, middle aged patients 36-60 years old, elderly patients >60 years old), male, and female patients.

Aims and objectives

This study aims to determine if the Abarquez formula for estimating left ventricular ejection fraction (aVR QRS amplitude X 2.264) + (age X 0.645) is consistent with left ventricular ejection fraction measured by 2D Echo.

MATERIALS AND METHODS

Consecutive adult patients of the Victoriano Luna Medical Center (VLMC) seen from January to May 2019 with both an official 12-lead ECG and a 2DED were included in the study. Patients with 12-lead ECG that are too blurred to make an accurate measurement of the aVR QRS amplitude (i.e. ECGs where the demarcation of the QRS amplitude is not appreciated). Demographic characteristics of these patients are shown in Table 1.

The minimum number of patients to be included in this study is based on the Bland-Altman plot method and results of Gruszczyńska et al.[1] Using the formula below:

$$1.96\sqrt{\frac{3s^2}{n}} = LoA$$

where: s is the standard deviation, n = sample size and LoA = width of limits of agreement. At 95% level of confidence, assuming s = 5.97[1] and desired LoA is 2%, therefore the minimum sample size is 100. Other options are shown below:

LoA	N
2.1	90
2.3	80
2.4	70
2.62	60
2.87	50

Comparison of two measurement methods (ventricular ejection fraction estimated from electrocardiogram and left ventricular ejection fraction measured from 2D Echo) was performed by Altman and Bland method using limits of agreement at 95% confidence interval. This analysis was done using Analyse-It Software. Comparison of the mean differences between the two measurement methods was also done using STATA. Two sample t-test with equal and unequal variances was performed for this analysis. The research protocol underwent review process of the Armed Forces of the Philippines Health Service Command Research Ethics Committee (AFPHSC REC). The protocol was eventually approved as having minimal risk to patients.

RESULTS

LVEF from 12-lead ECG increased with age, while LVEF from 2DED remained constant, regardless of age or gender (Table 2).

Summary of test for equality of means is show in Table 3. LVEF estimated by the Abarquez formula consistently underestimated LVEF 2DED by a mean difference of 14.54. This trend was observed in all subgroups. At p value of 0.10 or confidence level of 90%, all coefficients by each group suggest rejection of the null hypothesis

Table 1: Demographic characteristics

Characteristics	Results	
	Mean 52.63 Median 51	Min max standard deviation 15.94%
Age, years		
18 to 35	7	11.86
36 to 60	32	54.24
Above 60	20	33.90
Gender		
Male	35	59.32
Female	24	40.68

Table 2: Demographic characteristics versus EF

Characteristics	LVEF from 12-lead ECG	LVEF from 2DED
Age, years		
18 to 35	38.16 ± 8.53	65.71 ± 6.21
36 to 60	48.31 ± 9.16	65.88 ± 8.99
Above 60	60.81 ± 7.43	65.95 ± 9.86
Gender		
Male	52.69 ± 10.73	63.21 ± 9.64
Female	49.37 ± 5.02	68.8 ± 4.93

which states that the mean difference of each group is equal, leading to the conclusion that the mean difference are significantly different at p-value = 0.10. Such confidence level was chosen given the small sample sizes used for each group.

The limits of agreement between LVEF estimated from 12-lead ECG and from 2DED indicate that 12-lead ECG LVEF may measure as much as 42.63 below and 3.8988 above the LVEF measured from the 2DED (Figure 1). These wide intervals are observed in all group analyses. In patients 18-35 years old, LVEF measured from 12-lead ECG underestimate 2DED LVEF by a maximum of 45.27 and a minimum of 9.85 (Figure 2); in patients 35-60 years old, LVEF measured from 12-lead ECG may measure as much as 40.62 below and 5.49 above the LVEF

Table 3: Summary of test for equality of means. Two sample t-test with equal/unequal variances was used.

Subgroup	Equality of Variance	Mean Difference	90% Confidence Interval
Overall (by age group)	Equal variance	-14.54	-17.54 to -11.54 p-value = 0.0000
	Unequal variance	-14.54	-17.54 to -11.54 p-value = 0.0000
Overall (by gender group)	Equal variance	-14.52	-17.58 to -11.46 p-value = 0.0000
	Unequal variance	-14.52	-17.58 to -11.47 p-value = 0.0000
Age group			
18-35	Equal variance	-27.56	-34.55 to -20.57 p-value = 0.0000
	Unequal variance	-27.56	-34.62 to -20.50 p-value = 0.0000
36-60	Equal variance	-17.57	-21.00 to -14.14 p-value = 0.0000
	Unequal variance	-17.57	-21.00 to -14.14 p-value = 0.0000
>60	Equal variance	-5.14	-9.95 to -0.33 p-value = 0.0397
	Unequal variance	-5.14	-9.95 to -0.33 p-value = 0.0398
Gender			
Male	Equal variance	-11.14	-15.39 to -6.88 p-value = 0.0000
	Unequal variance	-11.14	-15.39 to -6.88 p-value = 0.0000
Female	Equal variance	-19.67	-23.73 to -15.62 p-value = 0.0000
	Unequal variance	-19.67	-23.76 to -15.59 p-value = 0.0000

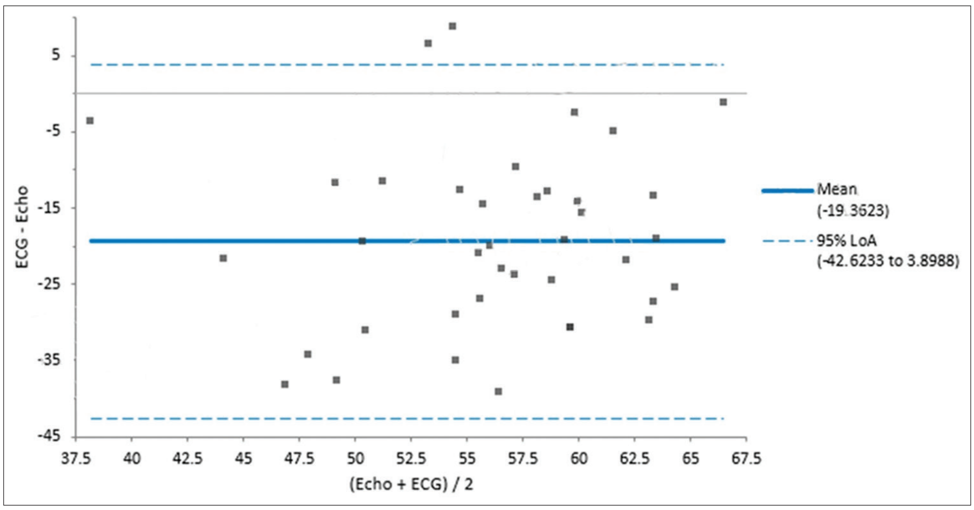

Figure 1: Bland-Altman plot for all measurements of LVEF estimated from 12-lead ECG and from 2DED

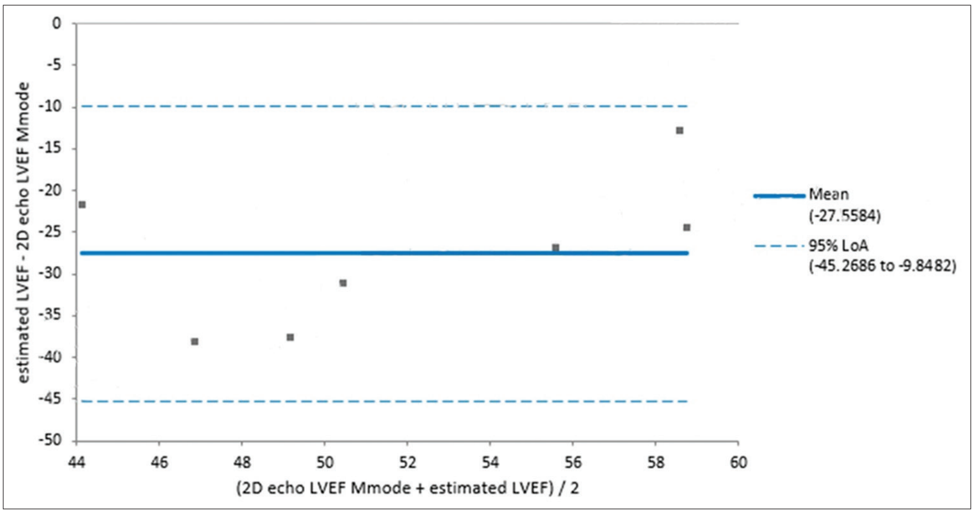

Figure 2: Bland-Altman plot for LVEF estimated from 12-lead ECG and from 2DED in patients 18-35 years old

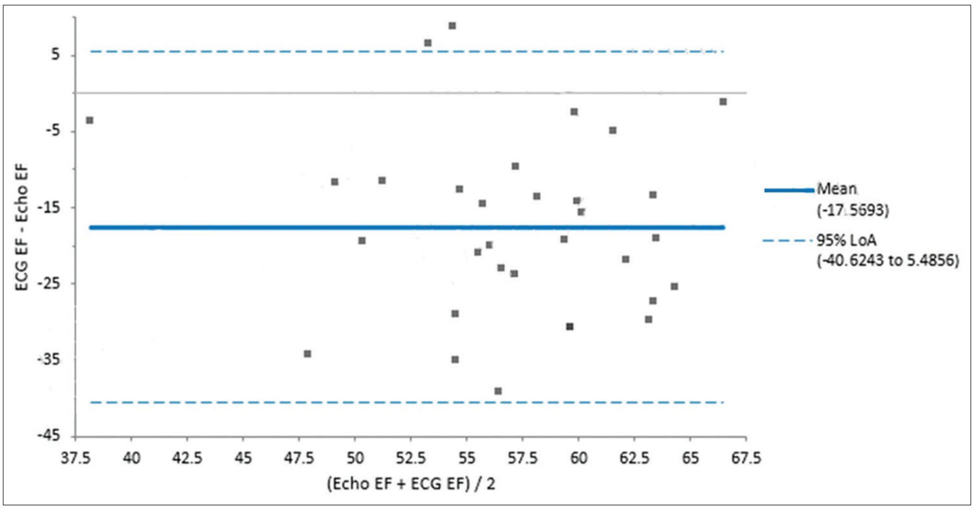

Figure 3: Bland-Altman plot for LVEF estimated from 12-lead ECG and from 2DED in patients 36-60 years old

measured from the 2DED (Figure 3); in patients >60 years old, LVEF measured from 12-lead ECG may measure as much as 29.93 below and 19.65 above the LVEF measured from the 2DED (Figure 4); in male patients, LVEF measured from 12-lead ECG may measure as much as 38.93 below and 16.65 above the LVEF measured from the 2DED (Figure 5), and in women, LVEF measured from 12-lead ECG may measure as much as 43.37 below and 4.02 above the LVEF measured from the 2DED (Figure 6).

DISCUSSION

Although the formula (aVR QRS amplitude in mm x 2.264) + (age x 0.645) has been offered to trainees as a way to estimate LVEF from values measured from the 12-lead ECG, there is a paucity of studies looking at the accuracy and the utility of this formula. In one study, LVEF estimated from the 12-lead ECG using the formula (aVR QRS amplitude in mm x 2.264) + (age x 0.645) was compared to LVEF measured from 2D Echo. The study found a significant difference between 12-lead ECG derived LVEF and LVEF from 2D Echo. However, the study concluded that with age adjustment, the formula (aVR QRS amplitude in mm x 2.264) + (age x 0.645) can be used to estimate LVEF.[3]

In this study, we attempted to verify the accuracy of the formula (aVR QRS amplitude in mm x 2.264) + (age x 0.645) by comparing 12-lead ECG derived LVEF and LVEF measured with 2D Echo by using limits of agreement method of Altman and Bland. Limits of agreement was used instead of doing a correlation study, because according to Giavarina[4], correlation studies the relationship between one variable and another, not the differences, and correlation is not recommended as a

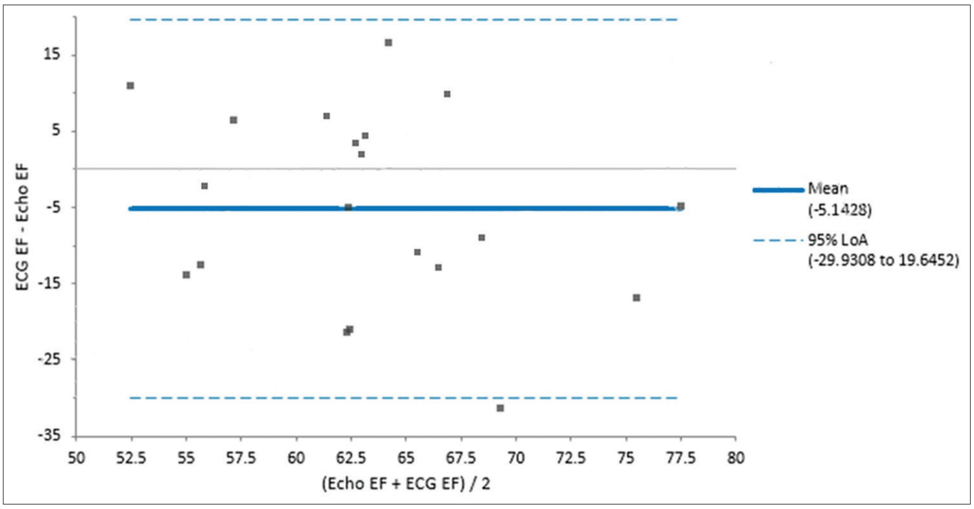

Figure 4: Bland-Altman plot for LVEF estimated from 12-lead ECG and from 2DED in patients >60 years old

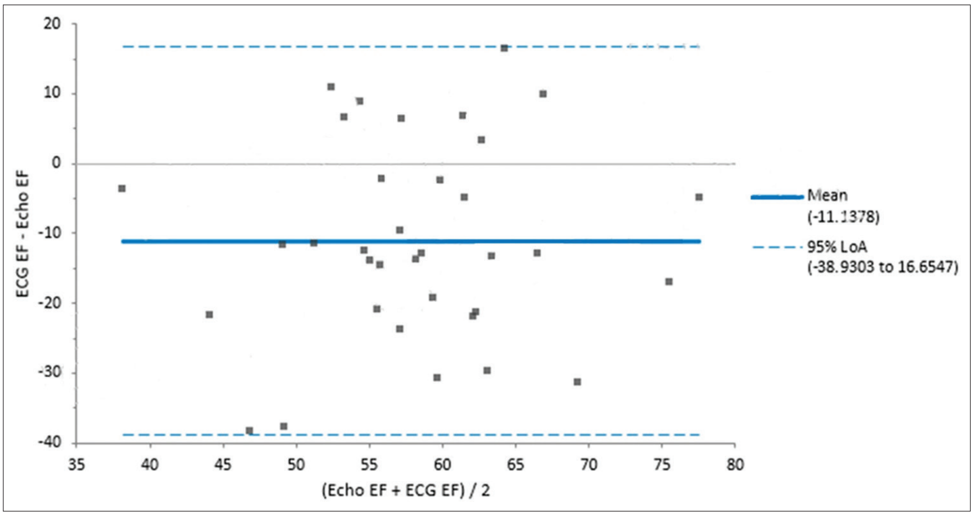

Figure 5: Bland-Altman plot for LVEF estimated from 12-lead ECG and from 2DED in male patients

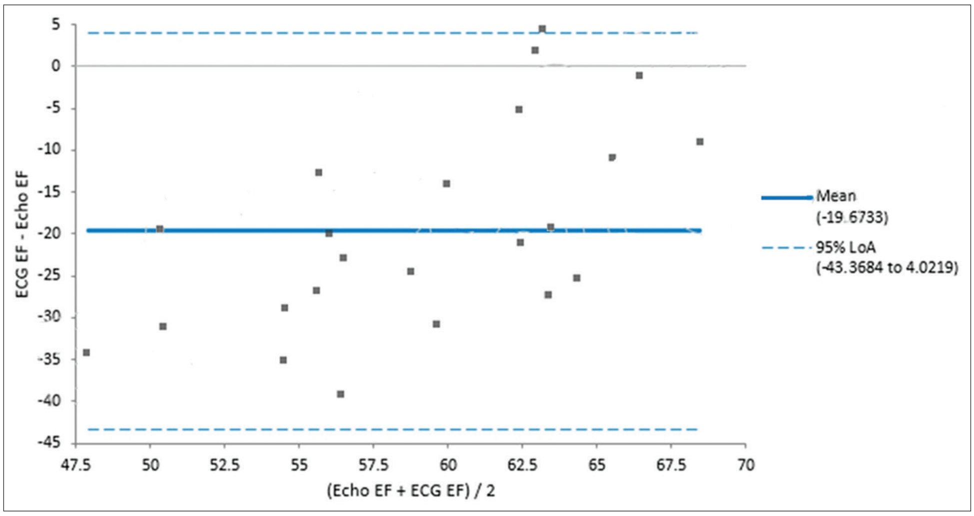

Figure 6: Bland-Altman plot for LVEF estimated from 12-lead ECG and from 2DED in female patients

method for assessing the comparability between methods. To assess the agreement between two quantitative methods of measurement, an alternative analysis is the Bland and Altman plot analysis.[4]

In our study, the limits of agreement of 12-lead ECG and 2DED LVEF estimations were wide (Figure 1-6). The Bland-Altman plot is solely meant to define the intervals of agreement, but does not indicate whether those limits are acceptable or not. The acceptable limits must be defined *a priori,* based on varying factors of clinical, biological, or other considerations (Kalra, 2017).[4,5] The wide limits of agreement found in our study indicate that the formula (aVR QRS amplitude in mm x 2.264) + (age x 0.645) cannot be used clinically to provide a reasonable estimate of the LVEF.

There are many reasons for the wide intervals in limits of agreement in this study. These include the small sample size, large variation in differences, and lack of repeatability of 12-lead ECG and 2DED (since only one ECG and one 2DED was done for every patient). In this regard, future studies should attempt to increase the sample size to at least 100.

Another limitation of this study was that the time during which the 12-lead ECG was taken differs from the time the 2DED was taken. Future studies on this subject should attempt to take the 12-lead ECG immediately before and after the 2DED.

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CONCLUSION

LVEF estimated using Abarquez formula significantly differs from LVEF measured by 2DED. Therefore, the Abarquez formula cannot be used as a surrogate for 2DED. Future studies on this subject should consider the following: 1) increasing the sample size to at least 100; 2) obtaining 12-lead ECG immediately before or after the 2DED; and 3) attempt to determine if the Abarquez formula can reliably predict other cardiac conditions, such as valvular heart disease.

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