Original Article

Diagnostic Value of Electrocardiography Compared with Echocardiography in Measuring Left Ventricular Mass Index in Major Thalassemia Patients Over 10 Years of Age

Noormohammad Noori, MD[1], Maziar Mahjoubifard, MD[1*], Seyed Mostafa Alavi, MD[2], Saeid Hosseini, MD[2], Hamidreza Sanati, MD[2], Yalda Mirmesdagh, MD[2]

[1]*Children and Adolescent Health Research Center, Zahedan University of Medical Sciences, Zahedan, Iran.*
[2]*Rajaei Cardiovascular, Medical and Research Center, Tehran University of Medical Sciences, Tehran, Iran.*

Received 08 January 2012; Accepted 05 November 2012

Abstract

Background: *Patients suffering from major beta thalassemia need frequent blood transfusions and, if not treated well, would be at risk of heart dysfunction. This study was performed to determine the diagnostic value of electrocardiography versus echocardiography in measuring the left ventricular mass index in these patients.*

Methods: *Between July 2010 and June 2011, 82 asymptomatic patients over 10 years of age with major thalassemia (42 men with a mean age of 17.65 ± 3.39 years and 40 women with a mean age of 16.9 ± 3.38 years) were enrolled in this study. For all the patients, standard electrocardiography (to measure R in aVL and S in V3 and calculate left ventricular mass index by electrocardiography) and echocardiography (to measure interventricular septum diameter in diastole, left ventricular posterior wall diameter in diastole, and left ventricular diameter in diastole in order to calculate left ventricular mass index by echocardiography) were performed, at least one week after transfusion. The calculated left ventricular mass indices were thereafter compared between the two methods (electrocardiography and echocardiography).*

Results: *Sensitivity, specificity, positive predictive value, and negative predictive value in the two techniques in determining the left ventricular mass index were 67%, 25%, 89%, and 7% in the females, 65%, 33%, 92%, and 6% in the males, and 67%, 14%, 89%, and 3% in the total population, respectively. Furthermore, this study demonstrated that the average left ventricular mass index by echocardiography and electrocardiography was 104.86 ± 21.65 gr/m2 and 91.69 ± 12.03 gr/m2, respectively. Echocardiography was much more accurate than electrocardiography in determining the left ventricular mass index (p value = 0.0001).*

Conclusion: *The findings of this study demonstrated that echocardiography was more accurate and more reliable than electrocardiography in determining the left ventricular mass index in major thalassemia patients.*

J Teh Univ Heart Ctr 2013;8(3):121-126

This paper should be cited as: Noori N, Mahjoubifard M, Alavi SM, Hosseini S, Sanati H, Mirmesdagh Y. Diagnostic Value of Electrocardiography Compared with Echocardiography in Measuring Left Ventricular Mass Index in Major Thalassemia Patients Over 10 Years of Age. J Teh Univ Heart Ctr 2013;8(3):121-126.

Keywords: *Thalassemia • Electrocardiography • Echocardiography*

[*]**Corresponding Author:** ***Maziar Mahjoubifard,*** *Assistant Professor of Anesthesiology, Children and Adolescent Health Research Center, Ali-ebn e-Abitaleb Hospital, Khash Road, Zahedan University of Medical Sciences, Zahedan, Iran. 9816865616. Tel: +98 912 7308089. Fax: +98 21 22663293. E-mail: m_mahgoobifard@yahoo.com.*

Introduction

Major thalassemia is a very common genetic disorder, affecting almost 200 million people all over the world.[1] Although the total incidence of hemoglobinopathies is estimated at 1 in 100,000 the worldwide and 1 in 10,000 people in the European Union, the selective factors that introduce thalassemia as a common disease are yet to be recongized.[2]

Thalassemia is a monogenic disorder which is transferred from parents to children in an autosomal recessive manner and it is also a heterogenic group of hemoglobin synthesis disorder in which the formation of hemoglobin polypeptide chain is impaired and the synthesis rate is decreased.[2] Because of the inevitable side effects (increased iron load), it would usually be fatal until one reaches 30 years of age.[1] The most common cause of death in major thalassemia patients is dilated cardiomyopathy accompanied by left ventricular dysfunction.[2] The study of Schieken and et al.[3] showed that there were no correlations between electrocardiographic measures and blood pressure, left ventricular wall thickness, or left ventricular wall mass. Also they concluded that the echocardiogram was a more sensitive measurement of increased left ventricular mass than the electrocardiogram (ECG) in children with elevated blood pressure. The study of Rijnbeek et al.[4] demonstrated that sensitivities improved better when the ECG parameters were combined, and Reffelmann et al.[5] reported that a combination of the ECG and echocardiography findings on the left ventricular mass identified those in a pediatric group over 5 years at risk for developing a progressive rise in the left ventricular mass.

The left ventricular systolic size and pressure are particularly increased in major thalassemia patients.[6] This increased wall thickness and enlargement of the left ventricle (heart chambers) are diagnosable by the ECG. Echocardiography may be a more sensitive and specific tool for this evaluation, but it is more expensive and the interpretation and analysis are dependent on professional conduct of the operator, whereas the ECG is inexpensive and available everywhere and is less dependent on the experience of the user.

There is currently a dearth of data on a comparison between the diagnostic value of the ECG and echocardiography for this specific reason. The present study was, therefore, performed in order to determine the diagnostic value of these two modalities in measuring the left ventricular muscular mass in patients with major thalassemia over 10 years old.

Methods

This descriptive-analytic study was performed on 82 of 380 major thalassemia patients over 10 years of age who referred to the specialized center of Ali Asghar Hospital in Zahedan between July 2010 and June 2011. The study complies with the current ethical considerations. Informed consent was obtained from each patient or parents of the minors included in the study, and the study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the institution's Human Research Committee.

After history taking, physical examination, chest radiography, and ECG, patients with heart failure, bundle branch block, Wolf-Parkinson-White (WPW), valvular heart disease, structural disorders, and endocrine and metabolic disorders were excluded from the study. The number of the sample population was determined on the basis of a pilot study and literature references.[1] In total, 82 patients were selected. The study was conducted on patients over 10 years of age.

The main characteristics of the patients were comprised of age over 10 years, regular use of Deferoxamine chellator (DFO) from the time of diagnosis (at least 5 times per week with a dose of 50 mg/kg/day), regular referral to blood banks to receive packed cell transfusions, hemoglobin before transfusion of more than 9 g/dl, regular transfusion before age 2 years old, and duration of chelating therapy more than 5 years.

This group of patients was thoroughly investigated by a pediatric cardiologist using echocardiography (challenge 700 manufactured in Italy) with 3.5, 5.2, 5, and 3.5 MHz transducers and with the M-mode, two-dimensional (2D), and Doppler techniques.

The standard twelve-lead ECG was obtained from the patients using FX^{2}III, manufactured in Japan, at a speed of 25 mm/s. The body surface area (BSA) was calculated with the following formula:[7, 8]

$$BSA\ (m^2) = \sqrt{height\ (cm) \times weight\ (kg)/3600}.$$

Echocardiography was obtained in supine position without breathing retention in M-Mode view, parasternally at the tip of the mitral valve. The left interventricular septal diameter in diastole (LVSd), left ventricular end-diastolic diameter (LVEDd), and left ventricular posterior wall diameter in diastole (LVPWd) were obtained in M-mode. The left ventricular mass index (LVMI) was calculated with the following formula:

$$LVMI = 1.04 \times 0.8 \times [(LVSd + PWDd + LVEDd)^3 - LVEDd^3] + 0.6$$

Doppler view and M-Mode were registered at the speed of 50 mm/sec on paper. The ECG leads were located as follows, making sure their correct positions were checked: the red lead (AVR) on the right hand; the yellow lead (AVL) on the left hand; the green lead (AVF) on the left foot; and the black lead (neutral) on the right foot. The parasternal leads were correctly positioned as follows: lead V1 in the 4th intercostal position, on the right side of the sternum; lead V2 in the 4th intercostal position, on the left side of the sternum; lead V3 between leads V2 and V4; lead V4 in the 5th intercostal position, on the left mid clavicle line; lead V5 on the anterior

left axillary line, at the level of lead V4; and lead V6 on the left mid-axillary line, at the same level.

A standard twelve-lead ECG at the speed of 25 mm/sec was obtained, and the LVMI was calculated via the following formulas:[1]

In the male patients, we observed LVMI = [0.026 × (RaVL + SV3)] + (1.25 × weight) + 34.4, whereas in the female patients we had LVMI = [0.020 × (RaVL + SV3)] + (1.12 × weight) + 36.2.

For the statistical analyses, the statistical software SPSS version 13.0 for Windows (SPSS Inc., Chicago, IL) was used.

The independent samples t-test and Pearson correlation coefficient were employed to measure the LVMI in the comparison between the two above-mentioned methods. A p value < 0.05 was considered statistically significant.

Results

The findings of this study on 82 patients, comprising 42 men and 40 women, were as follows:

The mean age of the patients was 16.9 ± 3.38 years in the female patients, 17.65 ± 3.39 years in the male cases, and 17.28± 3.38 years in the total population. The average weight was 45.88 ± 8.91 kilograms in the women, 50.32 ± 10.99 kilograms in the men, and 48.15 ± 10.22 kilograms in the total population (Table 1).

Table 1. General characteristics of the participants*

Age (y)	17.28±3.38
Weight (kg)	48.15±10.22
HR (beat/min)	87.50±12.23
SV (cm^3)	92.60±63.16
CO (l/min)	7.86±2.41
CI ($l/min/m^2$)	7.09±1.80
Systolic BP (mm Hg)	96.95±10.08
Diastolic BP (mm Hg)	70.18±6.75
Hemoglobin (g/dl)	10.16±0.88
Ferritin	3625.12±1821.96

*Data are presented as mean±SD
HR, Heart rate; SV, Stroke volume; CO, Cardiac output; CI, Cardiac index; BP, Blood pressure

Sensitivity, specificity, positive predictive value, and negative predictive value in the ECG method in determining the LVMI compared with echocardiography were 67%, 25%, 89%, and 7% in the females and 65%, 33%, 92%, 6% in the males, and 67%, 14%, 89%, and 3% in the total population, respectively.

The left ventricular diastolic diameter was 50.65 ± 4.06 mm, septal thickness in diastole was 6.87 ± 1.45 mm, and the posterior wall thickness size in diastole was 4.19 ± 0.94 mm (Table 2). The echocardiographic parameters of the right heart are illustrated in Table 3.

Table 2. Echocardiographic parameters of the left heart in the participants*

MPI	0.58±0.12
IRT (ms)	117.04±18.45
AT (ms)	63.08±21.38
DT (ms)	90.45±18.83
PEP (ms)	97.81±14.34
ET (ms)	259.78±24.70
EF (%)	60.82±5.68
FS (%)	32.60±4.44
LVSDD (mm)	6.87±1.45
PWDD (mm)	4.19±0.94
LVDD (mm)	50.65±4.06

*Data are presented as mean±SD
MPI, Myocardial performance index; IRT, Isovolumic relaxation time; AT, Acceleration time; DT, Deceleration time; PEP, Pre-ejection period; ET, Ejection time; EF, Ejection fraction; FS, Fractional shortening; LVSDD, Left ventricular septal diameter in diastole; PWDD, Posterior wall thickness diameter in diastole; LVDD, Left ventricular diameter in diastole

Table 3. Echocardiographic parameters of the right heart in the participants*

MPI	0.67±0.11
IRT (ms)	129.34±18.67
AT (ms)	67.17±20.53
DT (ms)	96.11±15.25
PEP (ms)	95.91±10.08
ET (ms)	260.21±16.03

*Data are presented as mean±SD
MPI, Myocardial performance index; IRT, Isovolumic relaxation time; AT, Acceleration time; DT, Deceleration time; PEP, Pre-ejection period; ET, Ejection time

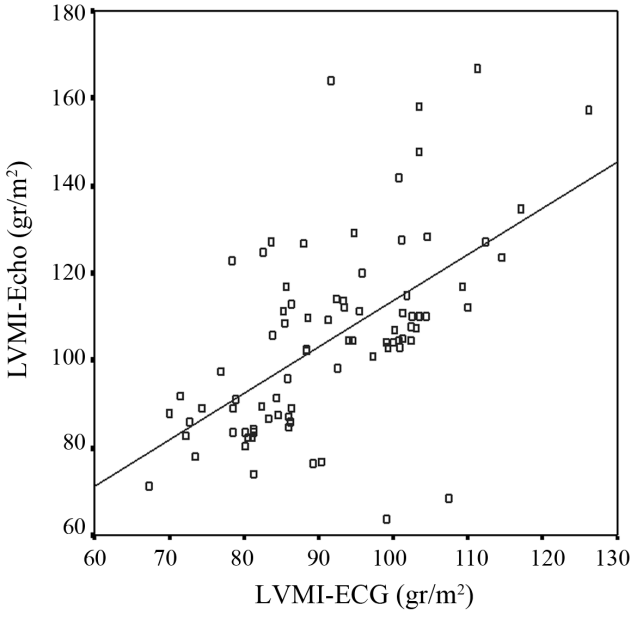

Figure 1. The correlation between echocardiography and electrocardiography in terms of the left ventricular mass index in the participants
LVMI-ECG, Left ventricular mass index by electrocardiography; LVMI-Echo, Left ventricular mass index by echocardiography

In this study, the two methods of echocardiography and the ECG were evaluated for measuring the LVMI (mean ± SD of left ventricular mass index by echocardiography and electrocardiography was 104.86 ± 21.65 gr/m^2 and 91.69 ± 12.03 gr/m^2, respectively): it became clear that there was a significant difference between these two methods (R = 0.598; p value = 0.0001).

The correlation coefficient test demonstrated a correlation between echocardiography and the ECG in determining the LVMI in the major thalassemia patients. Figure 1 depicts the correlation between echocardiography and the ECG in determining the LVMI in our study population.

Discussion

Conventional diagnostic methods for the diagnosis of left ventricular hypertrophy include echocardiography and the ECG. Diagnosis by the ECG is based on voltage and wavelength, particularly QRS complex, in which the absolute value on the standard twelve-lead ECG is expected to rise in left ventricular hypertrophy. The principle of diagnosis by echocardiography is based on the direct observation of the heart via an echocardiograph and measurement of the essential parameters for calculating the LVMI and the left ventricular functional index.

In this study, we evaluated the diagnostic value of the ECG, in comparison with echocardiography, in measuring the LVMI in major thalassemia patients over 10 years old. The LVMI, which is calculated by echocardiography, was considered a gold standard for the comparison of the two methods. Fogel and colleagues[9] considered an ECG study of 12 patients who had undergone surgery because of a significant stenosis in their left ventricular outflow tract and another 12 patients who had undergone heart catheterization or surgery because of ventricular septal defect (VSD) and then compared them with a 21-patient controlled group, whose LVMI had been measured via echocardiography. This comparison showed that the posterior wall septum thickness and the left ventricular chamber size in the AS patients were clearly larger than those of the controlled group. Nevertheless, in the VSD group, only the left ventricular size was larger than that of the controlled group. The authors concluded that using the conventional ECG criteria for diagnosing left ventricular hypertrophy was of the highest sensitivity in the AS group (67%) and of moderate sensitivity in the VSD group (60%). In addition, there was no relation between the ECG voltage and anatomic information or measurable hemodynamic data via echocardiography. The conventional criteria of the ECG in children for diagnosing left ventricular hypertrophy had only a modest sensitivity for this purpose, not taking the pressure or volume overload of the heart into account. Furthermore, since the left ventricular mass is measurable accurately by echocardiography, the ECG criteria should be used with caution. These findings chime in with the results of our study. Tsiachris et al.[10] demonstrated that age should be thought in reserve into consideration when choosing suitable ECG criteria for the recognition of left ventricular hypertrophy. Indexation of the LVMI distinguishes the diagnostic ability of the ECG criteria, especially in older patients. There was a slight correlation between our study and that of Tsiachris et al. Truong et al.[11] showed that not only did these ECG criteria have satisfactory test profiles due to their high specificity and test-positive likelihood ratios when compared to the reference standard of cardiac CT, but also they were associated with CT-based left ventricular hypertrophy and had augmentation predictive values for detecting CT-based left ventricular hypertrophy outside that of the history of hypertension. Of these ECG criteria, the three Cornell-based criteria delivered the greatest test presentation for finding patients with left ventricular hypertrophy. Our study revealed almost similar results to those of the Truong et al. study.

The patients' weight in our study, compared with that of the study of Rautaharju and colleagues, was low. The LVMI in the Rantaharju and colleagues study was more than the calculated index in our study regarding the weight of the patients; this is in direct relation to the left ventricular mass in the calculation formula of the LVMI through the ECG.[12] With respect to the patients' age and weight, the LVMI determined by echocardiography and the ECG in our study was lower than that of the study of Moyosi and colleagues in 2002. In our study, the age and weight of the patients were lower than those in the above-mentioned study; given that the patient's weight is directly related to the LVMI calculation by electrocardiography, an increase in age may be in tandem with a rise in weight. In the Mayosi and colleagues study, the average age was 52.4 ± 13.5 years and the average weight was 76.8 ± 14.8 kilograms, whereas our study population had an average age of 17.28 ± 3.38 years and an average weight of 48.5 ± 10.22 kilograms.[1] Killian et al.[13] showed that the ECG was a poor screening test for the evaluation of left ventricular hypertrophy and concluded that in the pediatric group, the standard twelve-lead ECG had a low sensitivity and low negative predictive value for detecting left ventricular hypertrophy. These findings are useful for physiological left ventricular hypertrophy and should not be extrapolated for the evaluation of hypertrophic cardiomyopathy.

In regard to sensitivity and specificity, there are no comparison studies in these methods on children. Be that as it may, Sau and colleagues in 1993 studied patients with no signs of major thalassemia, who were under regular transfusion and chellator therapy, and observed that in the echocardiographic investigation of LVEDd, the inter ventricular septum and posterior wall size had increased in diastole. All these three parameters were the calculating components of the LV mass and that is why the LV mass in these patients had increased.[14] Also, Favlli et al.[6] in 1993 reported that the LVMI in thalassemia children, compared with a control group, had

a significant increase. In our study, in line with the study of Sau et al.[15] in 1995, clinical investigation, chest X-ray, and the ECG showed no significant changes but similar to the study of Sau and colleagues, echocardiography was more reliable in calculating the LVMI. Magri et al. in 2007[16] demonstrated a weak relationship between the left ventricular mass and QT-changes: this is not compatible with our findings and further research is required in this regard. In the same study, a direct relation was demonstrated between increasing QTC and the LVMI. Rives and colleagues[17] reported that the ECG had a very little diagnostic value in determining left ventricular hypertrophy and that echocardiography would be more accurate for determining left ventricular hypertrophy. Sundstrom and colleagues in 2001[18] argued that echocardiography and the ECG could be utilized to determine left ventricular hypertrophy and prevent mortality caused by non-dependent cardiovascular risk factors; the authors recommended the simultaneous use of both methods. Elsewhere, Buchner and coworkers[19] suggested that the Sokolow-Lyon index was possibly the most widely used ECG score for left ventricular hypertrophy. In the current study, the Sokolow-Lyon index also showed a reasonable relationship with cardiac structural parameters and the LVMI. Nevertheless, the sensitivity and negative predictive value for the Sokolow-Lyon index were relatively poor, whereas the specificity and positive predictive value were rather high. This may be due to the relatively high LVMI of the patients with a positive Sokolow-Lyon index in comparison to the LVMI of the normal subjects.

Conclusion

Echocardiography was a more reliable and accurate method than the ECG in determining the LVMI in our study population of major thalassemia patients. Still, where echocardiography cannot be readily available, the ECG can be drawn upon to determine the LVMI in these patients.

Acknowledgment

This study was approved and supported by Zahedan University of Medical Sciences and Tehran University of Medical Sciences.

References

1. Mayosi BM, Keavney B, Kardos A, Davies CH, Ratcliffe PJ, Farrall M, Watkins H. Electrocardiographic measures of left ventricular hypertrophy show greater heritability than echocardiographic left ventricular mass. Eur Heart J 2002;23:1963-1971.
2. Galanello R, Origa R. Beta-thalassemia. Orphanet J Rare Dis 2010;5:11.
3. Schieken RM, Clarke WR, Prineas R, Klein V, Lauer RM. Electrocardiographic measures of left ventricular hypertrophy in children across the distribution of blood pressure: the Muscatine study. Circulation 1982;66:428-432.
4. Rijnbeek PR, van Herpen G, Kapusta L, Ten Harkel AD, Witsenburg M, Kors JA. Electrocardiographic criteria for left ventricular hypertrophy in children. Pediatr Cardiol 2008;29:923-928.
5. Reffelmann T, Dörr M, Völzke H, Kors J, Ruppert J, Robinson D, Felix SB. Combination of electrocardiographic and echocardiographic information identifies individuals prone to a progressive increase in left ventricular mass over 5 years. J Hypertens 2009;27:861-868.
6. Favilli S, De Simone L, Mori F, Pollini I, Cecchi F, Zuppiroli A, Manetti A. The cardiac changes in thalassemia major: their assessment by Doppler echocardiography. G Ital Cardiol 1993;23:1195-1200.
7. Kim BW, Song MK, Chung S, Kim KS. Evaluation of kidney size in children: a pilot study of renal length as a surrogate of organ growth. Korean J Pediatr 2012;55:54-57.
8. Sharkey I, Boddy AV, Wallace H, Mycroft J, Hollis R, Picton S; Chemotherapy Standardisation group of the United Kingdom Children's Cancer Study Group. Body surface area estimation in children using weight alone: application in paediatric oncology. Br J Cancer 2001;85:23-28.
9. Fogel MA, Lieb DR, Seliem MA. Validity of electrocardiographic criteria for left ventricular hypertrophy in children with pressure- or volume-loaded ventricles: comparison with echocardiographic left ventricular muscle mass. Pediatr Cardiol 1995;16:261-269.
10. Tsiachris D, Chrysohoou C, Oikonomou E, Lazaros G, Dimitriadis K, Maragiannis D, Roussos D, Andreou I, Tsantilas A, Christoforatou E, Pitsavos C, Panagiotakos D, Stefanadis C. Distinct role of electrocardiographic criteria in echocardiographic diagnosis of left ventricular hypertrophy according to age, in the general population: the Ikaria Study. J Hypertens 2011;29:1624-1632.
11. Truong QA, Ptaszek LM, Charipar EM, Taylor C, Fontes JD, Kriegel M, Irlbeck T, Toepker M, Schlett CL, Bamberg F, Blankstein R, Brady TJ, Nagurney JT, Hoffmann U. Performance of electrocardiographic criteria for left ventricular hypertrophy as compared with cardiac computed tomography: from the Rule Out Myocardial Infarction Using Computer Assisted Tomography trial. J Hypertens 2010;28:1959-1967.
12. Rautaharju PM, Park LP, Gottdiener JS, Siscovick D, Boineau R, Smith V, Powe NR. Race- and sex-specific ECG models for left ventricular mass in older populations. Factors influencing overestimation of left ventricular hypertrophy prevalence by ECG criteria in African-Americans. J Electrocardiol 2000;33:205-218.
13. Killian L, Simpson JM, Savis A, Rawlins D, Sinha MD. Electrocardiography is a poor screening test to detect left ventricular hypertrophy in children. Arch Dis Child 2010;95:832-836.
14. Sau F, Lai ME, Seguro C, Onnis E, Figus A, Farci P, Balestrieri A, Cherchi A. Echocardiographic study at rest and during effort in adult asymptomatic thalassemic patients. Cardiologia 1989;34:221-227.
15. Sau F, Lai ME, Pargentino E, Seguro C, Pilloni MI, Lisci V, Guaita B, Naccarato S, Pisanu S, Figus R. Clinical and echocardiographic evaluation of thalassemic cardiomyopathy. Cardiologia 1995;40:307-314.
16. Magrì D, Sciomer S, Fedele F, Gualdi G, Casciani E, Pugliese P, Losardo A, Ferrazza G, Pasquazzi E, Schifano E, Magnanti M, Matera S, Marigliano V, Piccirillo G. Increased QT variability in young asymptomatic patients with beta-thalassemia major. Eur J Haematol 2007;79:322-329.
17. Rivenes SM, Colan SD, Easley KA, Kaplan S, Jenkins KJ, Khan MN, Lai WW, Lipshultz SE, Moodie DS, Starc TJ, Sopko G, Zhang W, Bricker JT; Pediatric Pulmonary and Cardiovascular Complications of Vertically Transmitted HIV Infection Study Group. Usefulness of the pediatric electrocardiogram in detecting

left ventricular hypertrophy: results from the prospective pediatric pulmonary and cardiovascular complications of vertically transmitted HIV infection (P2C2 HIV) multicenter study. Am Heart J 2003;145:716-723.
18. Sundström J, Lind L, Arnlöv J, Zethelius B, Andrén B, Lithell HO. Echocardiographic and electrocardiographic diagnoses of left ventricular hypertrophy predict mortality independently of each other in a population of elderly men. Circulation 2001;103:2346-2351.
19. Buchner S, Debl K, Haimerl J, Djavidani B, Poschenrieder F, Feuerbach S, Riegger GA, Luchner A. Electrocardiographic diagnosis of left ventricular hypertrophy in aortic valve disease: evaluation of ECG criteria by cardiovascular magnetic resonance. J Cardiovasc Magn Reson 2009;11:18.