# Accuracy of Left Atrial Enlargement Diagnosed by Electrocardiography as Compared to Cardiac Magnetic Resonance in Hypertensive Patients

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***Background:*** *Anatomical left atrial enlargement is associated with significant cardiovascular morbidity and mortality, heart failure, stroke, atrial fibrillation and diastolic dysfunction. This concept is more pronounced in hypertensive population, who have an especially increased risk of LA enlargement from diastolic dysfunction when compared to the general population. However, left atrial enlargement may not be correlated with basic investigation such as electrocardiographic (ECG) criteria. In the past, studies usually correlating ECG criteria with anatomic measures mainly used an inferior M-mode or two-dimensional echocardiography; moreover, these were applied in the general population, not hypertensive patients. In the present study it was sought to determine the accuracy of the ECG criteria to diagnose anatomical left atrial enlargement in a hypertensive population, as determined by volumetric cardiovascular magnetic resonance imaging (CMR).*

***Material and Method:*** *A total of 230 consecutive hypertensive patients referring for CMR (46.2% males, mean age 71.5±10.44 years) were enrolled. The ECG criteria for left atrial enlargement (LAE) was analyzed as well as left atrial volume index using the biplane area-length method from CMR. ECG criteria for LAE were assessed by investigator blinded to CMR data.*

***Results:*** *Mean SBP/DBP at the time of CMR was 140/67±18.5/9.7 mmHg. Mean BMI was 26.8±4.7 kg/m$^2$, co-morbid diseases were as follows; DM, 68 patients (57.1%) and dyslipidemia 67 patients (56.3%). Mean LA volume index was 59.77±17.93 ml/m$^2$ and mean LVEF was 63.18±7.16%. The prevalence of CMR (with the cut-off point of 28 ml/m$^2$) LAE was 98% and by any ECG criteria, was 47%. Sensitivity of individual ECG criteria for LAE, p>120 ms was 49.6%, biphasic P wave in V1 was 30.8%, and P notch >40 ms was 9.7%. If combined, ECG criteria p>120 ms and biphasic P wave in V1, sensitivity increased to 58.1%, that was higher than individual criteria. Specificity of individual ECG criteria for LAE was 100%.*

***Conclusion:*** *In the LAE from ECG criteria, at least one criteria is not sensitive for anatomical LAE but for specificity in hypertensive population. For individual criteria, p>120 ms had the highest sensitivity. These findings from our study emphasized the lack of sensitivity of LAE by ECG criteria in hypertensive patients. Therefore, LAE by ECG criteria might be discovered too late to be the prognosticator in hypertensive patients.*

***Keywords:*** *Left artrial enlargement, ECG, MRI*

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Left atrial (LA) size is one important part of cardiac remodeling in a varietyof cardiovascular diseases[1-3]. Strong evidence suggests that, increased left atrial size has been associated with severity and duration of diastolic dysfunction, atrial fibrillation (AF), predictor of stroke once atrial fibrillation is manifest, congestive heart failure (CHF), incidence and survivalafter myocardial infarction[11] and a strong predictor of cardiovascular morbidity and mortality. This is especially true in the hypertensive population, who are at increased risk of cardiovascular complications as compared to general population. Hypertension (HT) is common health problem, with a prevalence of 20% in Thailand and up to 30-40% in the western countries[5]. Systemic HT is the leading cause of left ventricular hypertrophy (LVH). The ongoing process of pressure overload results in impaired left ventricular (LV) relaxation, reduced distensibility of LV and lastly LA enlargement (LAE). Therefore, LAE in hypertensive population is more excessive than in the general population[4].

Basic investigation for diagnostic LAE is

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chest X-ray and electrocardiography (ECG) but limited by accuracy of the tests. However, echocardiography plays a key role to determine LA size, which is represented more accurately with LA volume than M-mode LA dimensions[2]. Nevertheless, echocardiographic measurement is subject to error due to variability in the attainment of appropriately aligned images, limitations in acoustic windows, and other causes of technical variation. LA size is not of spherical shape and of constant radius but usually asymmetrical dimensional enlargement; therefore, the LA size by echocardiography may be smaller or bigger than its true value. Cardiovascular magnetic resonance (CMR) imaging, which is a new modality for the evaluation of anatomical and functional of cardiac and vascular structures, provides the images in standardized planes, thereby providing a more correct volumetric assessment of LA size. The authors sought to determine the accuracy of the ECG for the detection of LAE in hypertensive population compared with gold standard of volumetric CMR by the biplane, area length method.

In review literature, there is only one study[2] about determining accuracy of electrocardiographic (ECG) criteria for atrial enlargement validation with cardiovascular magnetic resonance (CMR) in general population. A total of 275 patients went for CMR and were evaluated with a prevalence of LAE of 82% and of 21% by any ECG criteria and CMR, respectively. Hypertensive population in the present study was 34% and the prevalence of LAE was similar to general population, which was 30%. Sensitivity and specificity of any ECG criteria were 90% and 21% respectively.

The authors sought to determine the accuracy of the ECG for detection of LAE in hypertensive population compared with gold standard of volumetric CMR by the biplane, area length method. The end point of the present study was accuracy from any ECG criteria for LAE. The result from our study will be useful to diagnose this condition, as well as for follow up and to predict prognosis of the patients.

## Material and Method

Study design was cross sectional study in single center. Two hundred thirty hypertensive subjects with age >18 year, referred for CMR between May 2011 to December 2012 were enrolled. Baseline characteristics, including sex, age, height, weight, body mass index (BMI), body surface area (BSA), blood pressure (BP), underlying diseases, and medications were recorded. Subjects were excluded if they were not insinus rhythm or had any significant valvular heart disease.

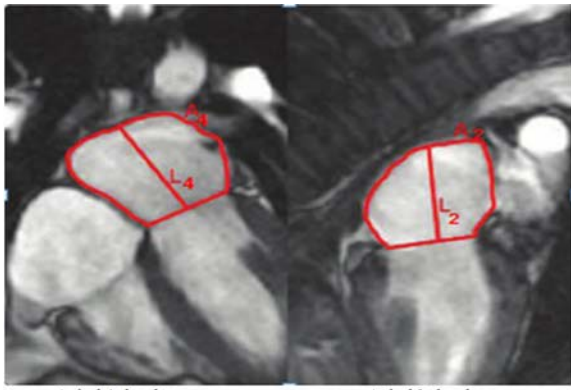
### *ECG*

Standard 12-lead ECG was performed on the same day of CMR. LAE was defined by any one of the following three criteria: 1) P wave in lead II, III, aVF >120 ms, 2) biphasic P wave in V1 by P terminal force >0.04/sec, 3) Notched P wave with interpeak duration >40 ms (P mitrale). All ECG determinations were made by one investigator blinded to other results.

### *CMR imaging analysis*

Images from CMR were transferred to the work station (Easy Vision; Philips Medical Systems). LA length was measured from posterior wall to the plane of mitral annulus, parallel to long-axis of the heart, in 2-chamber and 4-chamber view orientations on cine acquisitions at maximum a trial diastole (Fig. 1). Maximum atrial diastole was defined as the image immediately preceding the opening of mitral and tricuspid valves. LA area in apical 2-chamber and 4-chamber orientation were planimetered by tracing the endocardial border in maximum atrial diastole, excluding the confluence of the pulmonary veins and LA appendage. Atrial volumes were calculated according to the biplane area-length method, and then indexed for body surface area (BSA). Reference of LAE was LA volume index >28 ml/m$^2$. CMR analyses were performed by one investigator blinded to other results.

The following formula was applied for the calculation of LA volume and LA volume index.




Apical 4 chamber Apical 2 chamber

LA volume (ml) by biplane area-length method = $0.85 \times \frac{A2 \times A4}{L}$

(L = shortest of these 2 length ,L4 or L2)
LA volume index (ml/m$^2$) = LA volume/BSA

**Fig. 1** measurement of left atrial volume by biplane area-length method.

LA volume (ml) by biplane area-length method = [0.85xA2xA4]/L (A2 = area from 2-chamber view, A4 = area from 4-chamber view, L = the shortest of these 2 lengths from 2-chamber or 4-chamber views) LA volume index (ml/m$^2$) = LA volume/BSA.

***Statistical analysis***

Category data are presented as counts and percentages. Continuous data are presented as mean ± SD. The difference in categorical measurements between subject subgroups and the prevalence of LAE among the subject subgroups were assessed using Chi-square test or Fisher's exact test. The difference in continuous measures between subject subgroups was assessed using unpaired t-test. The accuracy of LAE from any ECG criteria was compared with CMR measurement presented by ROC curve, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) with 95% confidence interval (CI). A p-value of ≤0.05 was considered statistically significant. All statistical analyses were performed using SPSS version 16.

**Results**

A total of 230 consecutive hypertensive patients (50% male, age 71.5±10.44 years) were enrolled. Mean SBP/DBP at the time of CMR was 139/69±20.1/11.4 mmHg. Mean BMI was 26.5±4.8 kg/m$^2$, co-morbid diseases were as follows: DM in 125 patients (45.7%), dyslipidemia in 207 patients (90%), CAD in 96 patients (41.7%) and CKD in 42 patients (18.3%) (Table 1). Mean LA volume index was 57.05±18.08 ml/m$^2$ and mean

**Table 1.** Baseline characteristics

| Demographic data | Total (n = 230) | LA volume index >28 ml/m$^2$ (n = 223) | LA volume index ≤28 ml/m$^2$ (n = 7) | p-value |
|---|---|---|---|---|
| Male gender (n %) | 115 (50) | 114 (99.1) | 109 (94.8) | 0.119 |
| Age (year) (mean ± SD) | 71±9.92 | 71.50±9.96 | 77.14±7.38 | 0.139 |
| BW (kg) (mean ± SD) | 64.95±2.77 | 64.94±12.84 | 65.28±11.11 | 0.944 |
| Height (cm) (mean ± SD) | 156.51±8.28 | 156.49±8.11 | 157.14±13.39 | 0.839 |
| BMI (kg/m$^2$) (mean ± SD) | 26.52±4.88 | 26.52±4.91 | 26.50±3.70 | 0.857 |
| BSA (m$^2$) (mean ± SD) | 1.67±0.18 | 1.67±0.18 | 1.68±0.19 | 0.992 |
| SBP (mmHg) (mean ± SD) | 139.14±20.13 | 139.33±19.87 | 133.14±28.49 | 0.424 |
| DBP (mmHg) (mean ± SD) | 68.96±11.41 | 69.18±11.15 | 62.00±17.65 | 0.325 |
| Comorbidity | | | | |
| DM (n %) | 125 (45.7) | 101 (96.2) | 4 (3.8) | 0.705 |
| DLP (n %) | 207 (90.0) | 200 (96.6) | 7 (3.4) | 1 |
| CAD (n %) | 96 (41.7) | 94 (97.9) | 2 (2.1) | 0.702 |
| CKD (n %) | 42 (18.3) | 41 (97.6) | 1 (2.4) | 1 |
| CVA (n %) | 9 (3.9) | 9 (100) | 0 (0) | 1 |
| Medication | | | | |
| ASA (n %) | 165 (71.7) | 159 (96.4) | 6 (3.6) | 0.676 |
| Clopidogrel (n %) | 48 (20.9) | 47 (97.9) | 1 (2.1) | 1 |
| Beta-blocker (n %) | 153 (66.5) | 147 (96.1) | 6 (3.9) | 0.429 |
| CCB (n %) | 118 (51.3) | 114 (96.6) | 4 (3.4) | 1 |
| ACEI (n %) | 48 (20.9) | 45 (93.8) | 3 (6.3) | 0.16 |
| ARB (n %) | 89 (38.7) | 86 (96.6) | 3 (3.4) | 1 |
| MRA (n %) | 6 (2.6) | 6 (100) | 0 (0) | 1 |
| Nitrate (n %) | 59 (25.7) | 56 (94.9) | 3 (5.1) | 0.377 |
| Statin (n %) | 190 (82.6) | 184 (96.8) | 6 (3.2) | 1 |
| Oral hypoglycemic drugs (n %) | 87 (37.8) | 84 (96.6) | 3 (3.4) | 1 |
| Insulin (n %) | 20 (8.7) | 18 (90) | 2 (10) | 0.117 |

LA = left atrium; BW = body weight; BMI = body mass index; BSA = body surface area; SBP = systolic blood pressure; DBP = diastolic blood pressure; DM = diabetes mellitus; DLP = dyslipidemia; CAD = coronary artery disease; CKD = chronic kidney disease; CVA = cerebrovascular disease; CCB = calcium channel blocker; ACEI = angiotensin coverting enzyme inhibitor; ARB = angiotensin receptor blocker; MRA = minerocorticoid receptor antagonist

LVEF was 63.99±16.04%. The prevalence of LAE by CMR (with the cut-off point of >28 ml/m$^2$) was 97% and by any ECG criteria it was only 48.7% (Table 2). LAE by any ECG criteria was correlated with mean LA volume index of 61.37±20.07 ml/m$^2$ by CMR (Fig. 2).

## Discussion

In a hypertensive population, who are at increased risk of LAE, the diagnosis LAE from any ECG criteria has low sensitivity and specificity. The prevalence of LAE detected from ECG in the present study was only 48.7% as compare with 97% from CMR. The study indicate that using a combination of ECG criteria could increase sensitivity and specificity for the detection of LAE.

### *LAE and hypertension*

Systemic hypertension is the leading cause of left ventricular (LV) hypertrophy and is related to increased total peripheral resistance. Although concentric LV hypertrophy maintains systolic function at a near-normal level, LV relaxation is impaired with long-standing pressure overload, reflecting reduced distensibility of the left ventricle and impaired early diastolic filling without systolic dysfunction and leading to left atrial enlargement (LAE). In other words, left atrial (LA) size is determined by integration of LA relaxation and left ventricular (LV) systolic function. LAE is a marker of hypertensive heart disease and associated with significantly increased cardiovascular morbidity and mortality.

### *CMR and LA assessment*

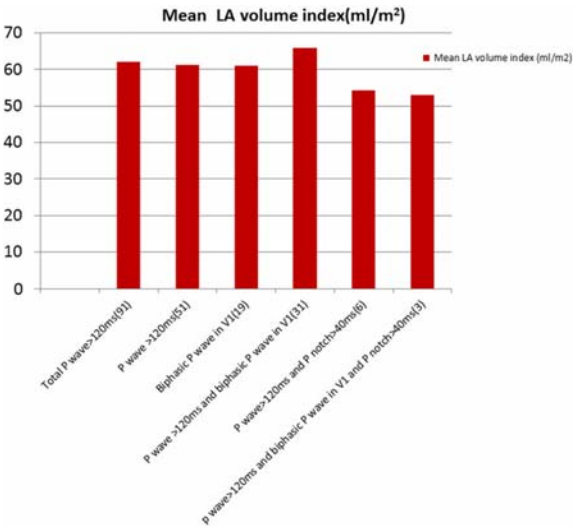
Cardiovascular magnetic resonance imaging is a promising modality for the evaluation of both anatomical and functional of cardiac and vascular structures .The left atrium can be readily imaged using standard CMR techniques, providing greater anatomical detail and information[7,10], and, ultimately providing more precise volumetric assessment of LA size, which is usually asymmetrical dimensional enlargement. Therefore, early detection of LAE is easier with CMR as compared to other investigations. Furthermore, CMR has no limitation of acoustic window and technical variation.

### *ECG and LA assessment*

ECG is basic investigation for providing electrical activities of the heart muscle as it changes with time. It is used to detect anatomical enlargement of cardiac chambers, but it is usually done too late because anatomical changes need to progress to the sufficient size until they affect the summation of electrical activity; earlier then the authors could only

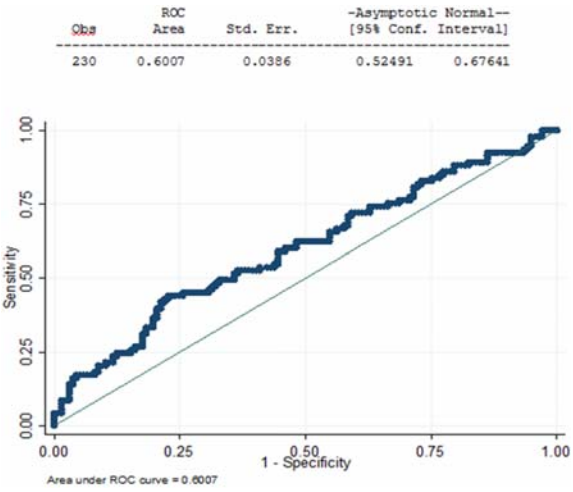
**Table 2.** Prevalence of LAE by ECG and CMR

| | Total (n = 230) | LA volume index >28 ml/m$^2$ (n = 223) | LA volume index ≤28 ml/m$^2$ (n = 7) | p-value |
|---|---|---|---|---|
| Electrocardiography | | | | |
| P wave >120 ms (n %) | 53 (23.04) | 51 (96.22) | 2 (3.77) | 0.013 |
| Biphasic P wave in V1 (n %) | 19 (8.26) | 19 (100) | 0 | |
| P notch >40 ms (n %) | 0 | 0 | 0 | |
| P wave >120 ms and biphasic P wave in V1(n %) | 31 (13.47) | 31 (100) | 0 | |
| P wave >120 ms and P notch >40 ms (n,%) | 6 (2.60) | 6 (100) | 0 | |
| Biphasic P wave in V1 and P notch >40 ms (n %) | 0 (0) | 0 | 0 | |
| P wave >120 ms and biphasic P wave in V1 and P notch >40 ms (n %) | 3 (1.30) | 3 (100) | 0 | |
| CMR | | | | |
| LA volume (ml) (mean ± SD) | 95.08±29.98 | 96.72±28.95 | 42.69±3.04 | 0 |
| LA volume index (ml/m$^2$) (mean ± SD) | 57.05±18.08 | 58.04±17.45 | 25.45±1.46 | 0 |
| LVEDV (ml) (mean ± SD) | 140.07±57.72 | 141.81±57.71 | 84.55±15.28 | 0.009 |
| LVESV (ml) (mean ± SD) | 57.65±54.69 | 58.80±55.13 | 20.90±8.92 | 0.001 |
| LVEF (%) (mean ± SD) | 63.99±16.04 | 63.62±16.11 | 75.90±6.71 | 0.046 |




( ) = number of subjects in each criteria

**Fig. 2** The correlation of mean LA volume index (ml/m$^2$) by any ECG criterias.




From any ECG criteria, P wave >120 ms is only significant correlate with LAE from CMR (p 0.013)at mean LA volume index 61.30 ml/m$^2$ . The sensitivity is 47.3% (95% CI: 36.9-57.9), specificity is 67.9% (95% CI: 59.4-75.6), positive predictive value (PPV) is 50% and negative predictive value (NPV) 65.5%. The accuracy of P wave >120 ms criteria could detect LAE by CMR in only 41.74%

**Fig. 3** ROC curve between ECG criteria P >120 ms and LA volume index(ml/m$^2$) by CMR.

detect abnormalities from ECG.

***Study limitation***

The prevalence of normal LA size when used the standard cut-off was very low in the present study. The authors used only ECG as the basic investigative test for LA assessment. The combined common basic modalities such as ECG and chest X-ray may increase the accuracy of basic test.

**Conclusion**

The LAE diagnosed from ECG criteria was correlated with marked LA enlargement that was at LA volume index of 61.37$\pm$20.07 ml/m$^2$ in hypertensive population. These findings from our study emphasized the lack of sensitivity of LAE by ECG criteria in hypertensive patients. Therefore, LAE by ECG criteria might be too late to be the prognosticator in hypertensive patients.

**Acknowledgement**

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**Potential conflicts of interest**

None.

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# ความแม่นยำของการวินิจฉัยภาวะหัวใจห้องบนซ้ายโตจากการตรวจคลื่นหัวใจเมื่อเทียบกับการตรวจด้วยคลื่นแม่เหล็กไฟฟ้าในกลุ่มผู้ป่วยโรคความดันโลหิตสูง

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***วัตถุประสงค์:*** *ภาวะหัวใจห้องบนซ้ายโตเป็นความผิดปกติที่มีความสำคัญ เนื่องจากสัมพันธ์กับผลลัพธ์ ทางด้านหัวใจและหลอดเลือด ไม่ว่าจะเป็นในแง่ของการเสียชีวิตจากโรคหัวใจและหลอดเลือด การเกิดภาวะหัวใจล้มเหลว การเกิดโรคหลอดเลือดสมองจากลิ่มเลือดอุดตัน การเกิดหัวใจเต้นผิดจังหวะ และสมรรถภาพการคลายตัว ของหัวใจลดลงในกลุ่มประชากรทั่วไป ภาวะดังกล่าวจะยิ่งเพิ่มสูงขึ้น ในกลุ่มประชากรความดันโลหิตสูงซึ่งมีแนวโน้ม ที่หัวใจห้องบนซ้ายโต โดยผ่านกลไกการคลายตัวของกล้ามเนื้อหัวใจที่ผิดปกติอยู่แล้ว การตรวจวินิจฉัยหัวใจ ห้องบนซ้ายโตในอดีตที่ผ่านมามักเปรียบเทียบระหว่างการตรวจด้วยคลื่นหัวใจ (Electrocardiography; ECG) และการตรวจคลื่นเสียงสะท้อนความถี่สูง (Echocardiography) และเป็นการศึกษาในประชากรทั่วไป สำหรับการศึกษานี้ต้องการศึกษาความแม่นยำของการวินิจฉัยภาวะหัวใจห้องบนซ้ายโตจากการตรวจคลื่นหัวใจเมื่อเทียบกับการตรวจด้วยคลื่นแม่เหล็กไฟฟ้า (cardiovascular magnetic resonance imaging; CMR) ซึ่งมีมีความแม่นยำสูงกว่าและเป็นการศึกษาในกลุ่มผู้ป่วยโรคความดันโลหิตสูง*

***วัสดุและวิธีการ:*** *การศึกษานี้เป็นการศึกษาแบบ cross sectional ทำในผู้ป่วยความดันโลหิตสูงที่มารับการตรวจหัวใจ ด้วยคลื่นแม่เหล็กไฟฟ้าที่โรงพยาบาลศิริราช โดยการประเมินขนาดหัวใจห้องบนซ้ายใช้วิธีการวัด biplane area length ในมุมมองของ 2-chamber และ 4 chamber ขณะที่การตรวจคลื่นหัวใจจะทำในวันเดียวกันนั้น และอ่านผลจากโปรแกรมแสดงผลการตรวจคลื่นหัวใจโดยผู้ทำการศึกษา ที่ไม่ทราบผลตรวจอื่น*

***ผลการศึกษา:*** *มีผู้ป่วยในการศึกษาทั้งหมด 230 ราย อายุเฉลี่ย 71±9.92 ปี ความดันโลหิตเฉลี่ย ขณะมารับการตรวจคลื่นแม่เหล็กไฟฟ้า 139/69±20.1/11.4 มิลลิเมตรปรอท ดัชนีมวลกาย 26.5±4.8 กิโลกรัม/เมตร$^2$ ค่า LVEF เฉลี่ย 63.99±16.04% โดยการศึกษาพบว่าความชุกของหัวใจห้องบนซ้ายโตจากการตรวจด้วยคลื่นแม่เหล็กไฟฟ้าสูงถึง 97% ในขณะที่การตรวจจากคลื่นหัวใจพบเพียง 48.7% และสัมพันธ์กับค่าเฉลี่ยของขนาดของหัวใจห้องบนซ้ายที่ LA volume index 61.37±20.07 มิลลิลิตร/ตารางเมตร ความแม่นยำจากการใช้เกณฑ์การวินิจฉัยคลื่นหัวใจที่ P wave >120 ms ซึ่งเป็นเกณฑ์ที่สัมพันธ์กับการวินิจฉัยขนาดหัวใจห้องบนซ้ายโตจากวิธีตรวจด้วยคลื่นแม่เหล็กไฟฟ้า อย่างมีนัยสำคัญทางสถิติ (p 0.013) เท่ากับ 41.74%*

***สรุป:*** *เกณฑ์หัวใจห้องบนซ้ายโตที่วินิจฉัยจากคลื่นหัวใจสัมพันธ์กับขนาดหัวใจห้องบนซ้ายที่ใหญ่กว่าเกณฑ์ที่กำหนด ไว้ถึงสองถึงสามเท่าในกลุ่มประชากรความดันโลหิตสูง ดังนั้นการใช้คลื่นหัวใจเป็นตัววินิจฉัยขนาดหัวใจห้องบนซ้ายโต เพื่อบอกพยากรณ์โรค และป้องกันภาวะแทรกซ้อนต่างๆ ที่เกิดขึ้นจึงอาจเป็นการล่าช้าเกินไป*