

# Formula to estimate left atrial volume using antero-posterior diameter in patients with catheter ablation of atrial fibrillation

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#### Abstract

In patients undergoing atrial fibrillation (AF) ablation, an enlarged left atrium (LA) is a predictor of procedural failure as well as AF recurrence on long term. The most used method to assess LA size is echocardiography-measured diameter, but the most accurate remains computed tomography (CT).

The aim of our study was to determine whether there is an association between left atrial diameters measured in echocardiography and the left atrial volume determined by CT in patients who underwent AF ablation.

The study included 93 patients, of whom 60 (64.5%) were men and 64 (68.8%) had paroxysmal AF, who underwent AF catheter ablation between January 2018 and June 2019. Left atrial diameters in echocardiography were measured from the long axis parasternal view and the LA volume in CT was measured on reconstructed three-dimensional images.

The LA in echocardiography had an antero-posterior (AP) diameter of  $45.0 \pm 6$  mm (median 45; Inter Quartile Range [IQR] 41–49, range 25–73 mm), longitudinal diameter of  $67.5 \pm 9.4$  (median 66; IQR 56–88, range 52–100 mm), and transversal diameter of  $42 \pm 8.9$  mm (IQR 30–59, range 23–64.5 mm). The volume in CT was  $123 \pm 29.4$  mL (median 118; IQR 103–160; range 86–194 mL). We found a significant correlation (r=0.702; P < .05) between the AP diameter and the LA volume. The formula according to which the AP diameter of the LA can predict the volume was: LA volume=AP diam<sup>3</sup>+45 mL.

There is a clear association between the left atrial AP diameter measured on echocardiography and the volume measured on CT. The AP diameter might be sufficient to determine the increase in the volume of the atrium and predict cardiovascular outcomes.

**Abbreviations:** AF = atrial fibrillation, AP = antero-posterior, CMR = cardiac magnetic resonance, CT = computed tomography, DCM = dilated cardiomyopathy, diam = diameter, HCM = hypertrophic cardiomyopathy, LA = left atrial appendage, LAVI = left atrial volume index, LSPV = left superior pulmonary vein, vol = volume.

Keywords: computed tomography, diameter, echocardiography, left atrium, volume

# 1. Introduction

The size of the left atrium (LA) is an independent predictor of cardiovascular events such as myocardial infarction, heart failure, atrial fibrillation, stroke, and cardiovascular mortality.<sup>[1,2]</sup> It has been also been shown to be predictive of the effectiveness of radiofrequency ablation in terms of acute success and long-term recurrences.<sup>[3,4]</sup> For the evaluation of LA size the most used examination is echocardiography, and the most available parameter in registries and populational studies is the antero-posterior (AP) diameter.<sup>[5]</sup> Current guidelines recommend AP diameter for LA size assessment, but volume is a more objective measurement to evaluate LA dilatation. In addition to echocardiography, other imaging techniques can be used, the most accurate being

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The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

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computed tomography (CT), an examination that is required for other purposes,<sup>[6]</sup> such as: calculation of the coronary calcium score or angio-tomography of the coronary arteries.<sup>[7]</sup>

There are different methods for estimating left atrial volume using one diameter of the LA: the prolate ellipsoid formula, the sphere formula, and the cube formula. The most accurate of these 3 in the study of Jiamsripong, was the cube formula.<sup>[8]</sup> Our study aimed to determine whether a simple measurement such as anteroposterior diameter on echocardiography can estimate the volume of the LA measured on CT, and find a simple formula that can approximate the LA volume.

## 2. Materials and method

### 2.1. Study population

We included 93 patients with atrial fibrillation who underwent catheter ablation between January 2018 and June 2019. The study was approved by the Ethics Committee of the Rehabilitation Clinical Hospital of Cluj-Napoca and all subjects signed informed consent.

Prior to the ablation procedure, a transesophageal echocardiography was performed to rule out a thrombus in the left atrium or LA appendage. A chest CT with contrast media was used to determine the atrial anatomy and the number of pulmonary veins.

#### 2.2. Size measurements

AP, longitudinal, and transverse diameters were measured in bidimensional echocardiography from the parasternal long-axis and apical views as recommended by the American Society of Cardiology and European Association of Echocardiography.<sup>[9]</sup> AP measurement was performed at the level of the aortic sinuses at the end of ventricular systole, during its maximal dimension.<sup>[10]</sup> Longitudinal and transverse diameters were measured from the apical 4-chamber and 2-chamber views using the innerto-inner edge method. Volume measurements were made after integrating CT images into the Carto Biosense Webster or NAVX Saint-Jude system, on the three-dimensional reconstructions of the LA and pulmonary veins. The atrial volume was measured outside the venous ostia, without including the pulmonary veins and left appendage,<sup>[11]</sup> in end-systole when the LA is at its maximum size. All echography and CT measurements were performed before the ablation procedure.

## 2.3. Statistical analysis

The distribution of continuous variables is presented as mean and standard deviation. Categorical variables are indicated in percentages. For the correlation between the diameters and the volume of the LA, the Spearman correlation was used. The relationship between LA diameter and volume was assessed using cubic regression and was plot against CT volume using Bland–Altman method. SPSS Statistics for Windows, Version 21.0. (Armonk, NY: IBM Corp.) was used for all the statistical analysis considering a significant value of *P* below .05.

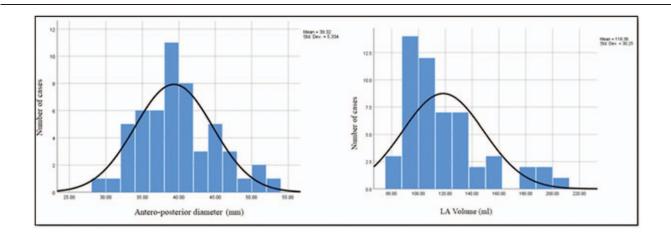
## 3. Results

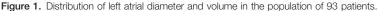
Of the 93 patients included in the study (mean age  $53\pm10.7$  years, 35.5% women) 68.8% had paroxysmal atrial fibrillation and the rest had persistent atrial fibrillation.

The LA in echocardiography had an AP diameter of  $45.0 \pm 6$  mm (median 45; Inter Quartile Range [IQR] 41–49, range 25–73 mm), longitudinal diameter of  $67.5 \pm 9.4$  (median 66; IQR 56–88, range 52–100 mm), and transversal diameter of  $42 \pm 9$  mm (IQR 30–59, range 23–64.5 mm) (Table 1). Most of the patients had an enlarged LA as they had atrial fibrillation and were addressed for catheter ablation. Only 21.5% (n=20) of patients had a normal LA, all of them being with paroxysmal AF. The measured volume in CT was  $123 \pm 29.4$  mL (median 118; IQR 103–160; range 86–194 mL). The distribution of both AP diameter and volume is shown in Fig. 1.

Using the Spearman analysis, there was no significant correlation between the longitudinal or transversal diameter and the LA volume but we observed a significant correlation (r= 0.702; P < .05) between the AP diameter and the LA volume. The correlation was stronger in women, in patients who had persistent atrial fibrillation and those without interatrial block on 12-lead ECG (Table 2).

The formula according to which the AP diameter of the LA can predict the volume was determined using cubic regression: LA volume = AP diam<sup>3</sup> + 45 mL (Fig. 2). Compared with our formula (vol = AP diam<sup>3</sup> + 45 mL), the cube formula (vol = diam<sup>3</sup>) yielded





	AP diameter	Long diameter	Trans diameter	LA volume in cmc	
Mean $\pm$ SD	$45.0 \pm 6$	$67.5 \pm 9.4$	42±8.9mm	123±29.4	
Range (min-max)	25–73	52-100	23-64.5	86–194	

Values fo	or left atrial	dimensions.

AP = antero-posterior, LA = left atrium.

Table 1

smaller values ([ $106.2 \pm 27.6 \text{ mL vs } 63.4 \pm 27.5 \text{ mL respectively}$ ], [P < .001]). Using Bland–Altman difference plot analysis of the agreement between 2 different formulas, we found that our formula was better than the old cube formula in estimating the measured volume of the LA.

The Bland–Altman graph<sup>[12]</sup> (Fig. 3) shows how the difference between our method and Cube method increases at smaller LA volumes. The difference between these 2 methods was constant across the entire range of LA volumes from 70 to 150 mL.

To determine which of the 2 formulas is more accurate in predicting left atrial volume, a simple linear regression was used between the measured volume determined by contrast-enhanced CT and the volume obtained with that specific formula. Thus, for

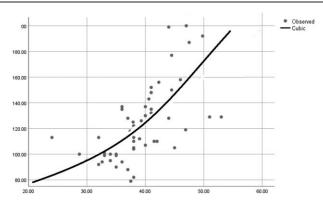


Figure 2. Cubic regression line estimates left atrial volume by the formula  $LAV = diam^3 + 45 mL.$ 

the cube formula, high beta coefficients and a statistically significant P < .05 were obtained, demonstrating measurement bias between the cubic formula and the measured (Table 3). On the other hand, using our method, the beta coefficients were close to 0 and the *P* statistically insignificant P > .05, proving that there is no bias between our method and the measured volume (Table 4).

## 4. Discussion

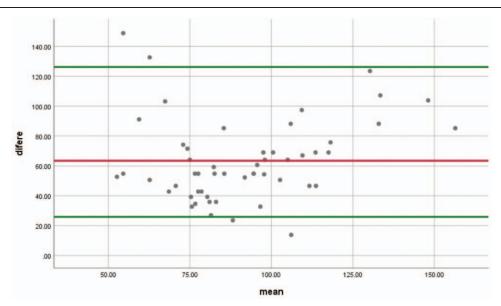
The exponential increase in the number of atrial fibrillation ablations in recent years, has stimulated the interest in the evaluation of left atrial volume,<sup>[13]</sup> because it is proved to be a crucial predictor of the short- and long-term results of ablation, as well as an indicator of structural remodeling.<sup>[14]</sup> Because the measurement of volume in CT imaging is time-consuming and labor-intensive, researchers explored simple methods to evaluate

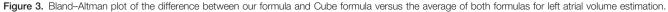
# Table 2

Pearson's	correlation	between	AP	diameter	and	LA	volume	in
specific ca	ategories.							

Category	<i>R</i> <sub>1</sub>	P value	
Male gender	0.574	.001	
Female gender	0.768	<.001	
Paroxysmal AF	0.540	<.01	
Persistent AF	0.726	<.01	
Interatrial block	0.61	<.0001	
Without interatrial block	0.810	<.0001	

AE = atrial fibrillation AP = antero-posterior IA = left atrium





# Table 3

Coofficiente

Simple linear regression between: Cubic Formula and LA volume determined by computed tomography shows high unstandardized beta coefficient and significant *P* values < .05 demonstrating proportional bias between the methods.

	Unstandardized coefficients		Standardized coefficients		
Model	В	Std. Error	Beta	t	Sig.
1 (Constant)	8.201	15.553		0.527	0.600
Mean	0.076	0.132	0.080	0.572	0.570

LA = left atrium.

# Table 4

Coofficients

Simple linear regression between: our Formula and LA volume determined by computed tomography shows unstandardized beta coefficient close to 0 and non-significant *P* values > .05 demonstrating lack of proportional bias between the 2 methods.

	Unstandardized coefficients		Standardized coefficients		
Model	В	Std. Error	Beta	t	Sig.
1 (Constant)	41.657	15.251		2.731	0.009
Mean	0.238	0.162	0.201	1.469	0.148

LA = left atrium.

LA volume using simple formulas, derived from simple measurements.

In this study we described our formula for estimating left atrial volume, based on AP diameter measured in echocardiography. Measurement of the AP LA diameter is simple and rapid and is part of the standard echocardiographic evaluation. It has been, for a long period of time, the only available method to determine LA size.<sup>[15]</sup> Although currently, recommendations strongly suggest use of LA volume as standard for LA size assessment, AP diameter is still used on a large scale for registries and cohorts such as the Framingham Heart Study.<sup>[16]</sup>

Our study demonstrates that LA volume can be predicted with good accuracy by using a simple measurement of the AP diameter. According to the American Society of Echocardiography, values <38 mm in women and <40 mm in men for AP diameter<sup>[17]</sup> are normal. In our study most of the patients (88.2%) had a dilated LA related to the fact that they were patients with paroxysmal or persistent atrial fibrillation.

LA volume is directly related to LA diameter, though it is biased to think that this relation between a linear and a threedimensional measure would be linear. Furthermore, the estimations of the left atrial volume according to the cube method (vol=diam<sup>3</sup>) or sphere method: (vol= $4\pi/3 \times \text{diam}^3$ ) are insufficient, because LA is a non-cuboid, non-spherical cavity. However, the cubic method is a reasonable assumption, as evidenced by studies that have compared the CT LA volume with the volume estimated by cube formula (vol=diam<sup>3</sup>).<sup>[18]</sup> In order to be more accurate, we used in our study non-linear cubic regression based on the measured values of LA volume in 93 patients undergoing catheter ablation of atrial fibrillation. Consequently, the formula that best estimates the left atrial volume is vol=APdiam<sup>3</sup>+45 mL.

The difference between our Formula and the old cube formula is that 45 mL is added to the volume of the cube. This is because the LA does not have a perfectly cubic shape, and parts that are situated anterior, posterior, superior, and inferior to the cube (Fig. 4) have been approximated to 45 mL by non-linear cubic regression. Cubic regression, is similar to the linear regression currently used in statistics, except that the formula includes a polynomial equation in which the diameter is raised to power 3.

In clinical practice, it is often necessary to compare our method with a standard of measurement. We compared our formula using Bland–Altman plot of difference between estimated and observed volumes. A very good overlap was obtained between our formula and the volume measured by CT.

In contrast to our study, Havranek et al<sup>[19]</sup> demonstrated that the AP diameter does not estimate LA volume as measured by LA direct catheter mapping. It is important to mention that in the

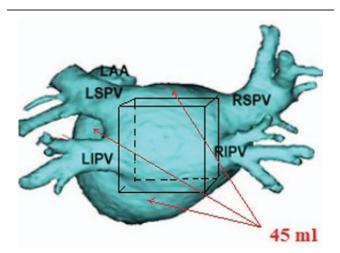


Figure 4. The cube formula is insufficient to approximate the volume of the left atrium because the left atrium does not have a cubic shape. If a cube is included inside the left atrium there are anterior, posterior, upper, and lower portions that are not taken into account as volume. Our Formula also includes these zones, approximating by regression the extra volume as counting 45 mL in addition to diameter raised to the 3rd power.

study of Havranek et al<sup>[19]</sup> the volume of the LA was based on mapping of the LA with the ablation catheter inserted inside the cavity, and "walking through" all areas of the atrium. However, in our study the volume of the LA was measured directly by CT, which we consider to be more accurate than the reconstruction of the LA with the catheter. For example, the junction between the LA and the pulmonary veins is difficult to determine and is based on the appearance of the intracardiac electrograms at the atrial and venous level as well as the measurement of local impedance, which can overestimate the atrial volume. In the study by Piorkovski et al who compared the CT image of the LA with the three-dimensional reconstruction performed with the catheter, the differences in size came from the fact that manipulation of the catheter through the transseptal puncture is difficult in the right upper and lower pulmonary veins. Therefore, the distance between right superior pulmonary vein and left superior pulmonary vein as well as between right superior pulmonary vein and the respective esophagus as well as the line around the ostium of the right veins, do not correspond to the real measurement made on the cardiac CT. The differences between the 2 techniques are 4 to 7 mm,<sup>[20]</sup> which can influence the total atrial volume.

In normal canine hearts, Fries et al<sup>[21]</sup> demonstrated that left ventricle, right ventricle, and right atrium volumes measured in cardiac magnetic resonance (CMR) correlated better with threedimensional echocardiography than CT. However, LA volume in CMR best correlated with CT. It has also been shown that compared to two-dimensional, three-dimensional echocardiography correlates better with computer tomography in dogs. Furthermore, two-dimensional evaluation of the volume by the area-length method or by the bidimensional disc method overestimates the left atrial volume compared with CT.<sup>[22]</sup>

Studies that compared the left atrial volume measured by the 2 methods: echocardiography and CT imaging in humans, showed significant differences between them, always the volume from CT being the largest: Agner et al<sup>[23]</sup> compared LA volume measured by echocardiography with CT imaging. In echo, volume was assessed using modified Simpson method from apical fur and 2chamber views and was underestimated compared with CT imaging (60 vs  $80 \text{ mL/m}^{2}$ ; P < .001). Also the study of Shin et al<sup>[24]</sup> showed the same results: echo based LA volume was underestimated compared with CT imaging (77.7 mL with arealength method vs 73.4 mL with Simpson method vs 126.8 mL with CT imaging; P < .001). Nedios et al<sup>[25]</sup> correlated different LA diameters from echocardiography and CT imaging with LA volume measured in CT imaging. He found better correlation for CT-imaging derived diameters:transverse diameter with LA volume r = 0.69; supero-inferior diameter with LA volume -r =0,58; AP with LA volume r = 0.60. Instead, the correlation with the AP diameter determined on echocardiography was moderate, but still significant r = 0.43; P < .001. The authors concluded that the best diameter for left atrial volume estimation is the transverse diameter. However, they had to perform CT imaging to obtain this measurement. The echocardiography measurement is much faster, and does not have the drawbacks of CT imaging. Christiaens study<sup>[26]</sup> also showed differences and underestimations of left atrial volume estimated on echocardiography compared with that measured on CT imaging: LA vol=32 mL/  $m^2$  with cubic formula,  $46 mL/m^2$  with ellipsoid formula,  $48 mL/m^2$ m<sup>2</sup> with Simpson formula, 52 mL/m<sup>2</sup> with diameter-length formula, 59 mL/m<sup>2</sup> with area-length formula and 74 mL/m<sup>2</sup> with CT imaging. We can easily observe from this study that the difference between the volume measured with CT imaging and the volume estimated by the cube formula using echocardiography is approximately 42 mL, a value close to that found in our study. Arsanjani et al<sup>[27]</sup> in a study of 64 patients also showed that the volume measured on CT imaging is higher than that measured on echocardiography using the biplane area-length method: 92 mL versus 68 mL, P < .01.

It is well known that atrial remodeling, especially in patients with atrial fibrillation and dilated LA occurs assimetrically, due to the limitations imposed by the sternum and the spine. Therefore the increase of the LA occurs less in the AP direction and more in the supero-inferior and medio-lateral direction.

The remodeling of the LA makes this structure impossible to fit in a sphere, cube, or an ellipsoid. Therefore, volume estimation formulas based on atrial diameter are insufficient. However, using a robust analysis such as cuboid regression, a formula can be developed to estimate the volume, taking into account the asymmetric atrial remodeling. This formula is: LA vol=diam<sup>3</sup>+45.

As for different atrial remodeling due to different etiologies, we would like to mention that most of our patients had lone atrial fibrillation or related to hypertension, diabetes, or obesity. There was no patient with valvular etiology or dilated cardiomyopathy (DCM). Only one patient had hypertrophic cardiomyopathy (HCM), so it is impossible to perform a subgroup analysis. In the study of Sabatino et al<sup>[28]</sup> left atrial volume indexed to body surface area was  $17 \,\mathrm{mL/m^2}$  in controls and  $59 \,\mathrm{mL/m^2}$  in patients with restrictive cardiomyopathy. Left atrial volume index was higher compared with control in patients with DCM, restrictive and hypertrophic cardiomyopathy. Differences in left atrial volume index were not significant between DCM and HCM groups.

The size of the LA is an important marker in stratifying the cardiovascular risk.<sup>[29,30]</sup> Although the diameter is not the ideal measurement, it is the fastest, easiest, and most used measurement in large population studies and clinical registries. It is reasonable that left atrial volume is a better predictor of outcomes than AP diameter. This has been demonstrated in patients with electrical cardioversion.<sup>[31]</sup> Abecasis et al<sup>[32]</sup> showed that a LAV >145 mL was associated with significantly higher AF recurrence after AF ablation. Helms et al<sup>[33]</sup> found a 135 mL LAV cut-off for AF recurrences. Similar results have been reported by other studies in different patient cohorts. Therefore, any information on the relationship between AP diameter in echo and LA volume in CT, may be of practical value.

#### 4.1. Limitations

This is a single-center study with the inherent limitations of the small number of patients.

We did not evaluate intra and inter-observer variability on different parameters, but this kind of work had already been performed by Ortiz De Murua et al,<sup>[34]</sup> Sievers et al,<sup>[35]</sup> and Nedios et al<sup>[25]</sup> showing a strong correlation between measurements.

Another limitation is that we did not compare LA volume measured in CT with the LA volume measured in Cardiac MRI, which the gold-standard for estimating LA dimensions.

We do not know if the formula applies to other categories than patients with dilated LA. We included selected patients with paroxysmal and persistent atrial fibrillation that underwent catheter ablation. For non-dilated LA, the formula for estimating the volume might be different.

CT imaging also has some drawbacks. First, there may be errors in the evaluation of the LA volume and second, a number of patients may have contraindications to this examination therefore another examination should be used. In terms of CT imaging measurement errors, the gold standard for measurements of chamber volumes<sup>[36]</sup> is considered CMR. CMR has been found reproducible<sup>[37]</sup> for measuring LA dimensions both in healthy and AF patients.<sup>[38]</sup> Agner et al<sup>[23]</sup> compared for the first time LA volume measured by CMR with volume measured by CT. They observed an overestimation of the left atrial volume measured by CT  $80 \pm 16 \text{ mL/m}^2$  versus CMR  $73 \pm 16$ mL/m<sup>2</sup>mL, the *P* value being statistically significant (<.01). Difference between the 2 techniques come from the fact that CT uses a single heart beat to acquire the whole heart image whether CMR uses an average of 12 heart beats per slice. Furthermore, usage of different software packages for quantification produces differences in spatial and temporal resolution between CMR and CT.

There is another problem in assessing left atrial volume on CT imaging. Namely, the exclusion of the left appendage and pulmonary veins. The connection between the pulmonary veins and the LA is made at the level of the antrum, which is not always symmetrical, and when the veins are excluded, a smaller or larger part of the antrum is also excluded. This is similar to the exclusion of left atrial appendage, where the ostium is not perfectly round or oval, so that a small volume might be lost from measurements. However, Christiaens et al<sup>[39]</sup> estimate these losses to be <10 mL and would be similar to those obtained on 3D echocardiography when excluding left atrial appendage and pulmonary veins.

Volume measurement by CT imaging requires three-dimensional reconstruction, exclusion of anatomical structures, and selection of the chamber of interest which is labor-intensive, time-consuming process. Furthermore, CT imaging requires exposure to ionizing radiation and the use of contrast agents. In our hospital, if creatinine is >1.3 mg% the examination is declined by the radiologist. However, new diagnostic tools, like 3D echo and CMR are available for patients with known allergy to intravenous contrast media, renal impairment with low glomerular filtration rate, and hyperthyroidism, that can be aggravated by iodinated agents.

#### 5. Conclusions

Left atrial AP diameter is a simple and quick ultrasound measurement that can predict LA volume in CT imaging. We propose a simple formula:  $vol = AP diam^3 + 45 mL$  to estimate LA volume using the diameter. This estimation might be convenient for a number of studies and registries in which determination of LA volume was not planned.

#### **Author contributions**

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- Investigation: Gabriel Cismaru, Muktapha Sangsriwong, Puiu Mihai, Lucian Muresan, Andrei Cismaru.
- Methodology: Gabriel Cismaru, Gelu Simu, Gabriel Gusetu.

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- Writing review & editing: Gabriel Cismaru, Dana Pop, Dumitru Zdrenghea, Radu Rosu, Andrei Cismaru.

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