

where the other categories all relate to myocyte necrosis due to vascular obstruction, whether spontaneous or iatrogenic. Indeed, we are trying to pound a square peg into a round hole.

The Oxford English Dictionary defines “infarction” as “the action of stuffing up” (from the Latin root meaning “to stuff up or obstruct”), with the word now defined as “morbid conditions of the tissues resulting from obstruction of the circulation.” We feel by keeping with the original sense of the word and limiting the use of the term “myocardial infarction” to situations where there is clearly an obstructed coronary artery, we would harmonize the term with unequivocal physiology, guide our choice of diagnostic and therapeutic pathways, and avoid inappropriate clinical diagnoses which create epidemiologic as well as coding and billing confusion. We propose the collection of conditions and situations which result in troponin release without an obstructed coronary artery be labeled Troponin Release Without Vascular Obstruction. Type 1, 4a, 4b, 4c, and 5 myocardial infarctions would be managed with the usual panoply of diagnostic imaging, evidence-based therapies, and interventions, while given the multitude of possible causes of Troponin Release Without Vascular Obstruction ranging from renal insufficiency to Takotsubo syndrome, interventions (if any) which may improve the worsened outcome in these settings will likely vary greatly and usually have little to do with lipids or platelet-fibrin thrombi. By not classifying these causes of troponin release as myocardial infarctions, patients may not be mislabeled as having coronary disease, and we will improve coding, avoid inappropriate therapies, and redirect investigation into improved outcomes.

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3 April 2019  
15 April 2019  
25 April 2019

1. Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA, White HD. Fourth Universal Definition of Myocardial Infarction (2018). *J Am Coll Cardiol* 2018;72:2231–2264.
2. Korff S, Katus HA, Giannitsis E. Differential diagnosis of elevated troponins. *Heart* 2006;92:987–993.

3. Mendis S, Thygesen K, Kuulasmaa K, Giampaoli S. World Health Organization definition of myocardial infarction: 2008-09 revision. *Int J Epidemiol* 2011;40:139–146.

<https://doi.org/10.1016/j.amjcard.2019.04.040>

### Reply to “Comparison of Accuracy of Left Atrial Area and Volume by Two-Dimensional Transthoracic Echocardiography Versus Computed Tomography”



In their interesting study, Arsanjani et al<sup>1</sup> reported that left atrial (LA) volume, estimated by 2-dimensional echocardiography (2D-E) using the biplane area-length method, showed larger discrepancies than 4-chamber LA area when compared to the corresponding multi-detector computed tomography (MDCT) measurements. They conclude that LA volume determination is less reliable than direct LA area tracing for the estimation of LA size by 2D-E, suggesting a revisit of current ASE guidelines.<sup>2</sup>

We believe that these conclusions should be considered with caution. Firstly, the agreement between 2D-E and other imaging techniques for the assessment of LA size has been extensively studied, with evidence showing that the magnitude of the discrepancies increases passing from comparisons of linear measurements (e.g., antero-posterior LA diameter)<sup>3,4</sup> to those of areas and volumes.<sup>5–7</sup> Interpreting this expected increase as poor reliability of volumetric measurements is questionable, as it simply reflects the effect of error propagation, a rule by which linear measurement errors are amplified when areas and particularly volumes are estimated.<sup>8</sup> This effect is evident when the area-length formula is used, as this method directly combines LA areas and length to estimate LA volume.<sup>2</sup> In this view, performing comparisons among discrepancies in cm<sup>2</sup> and ml, even if expressed as per cent differences, may be misleading.

Secondly, it must be pointed out that a different agreement between 2D-E and MDCT for the estimation of LA volume and LA area does not necessarily translate into differences in the clinical utility between the 2 LA

measures. The concordance with a gold standard technique bears little relation with feasibility, reproducibility, diagnostic value, and prognostic performance, which mostly determine the clinical value of echocardiographic indexes. Accordingly, LA volume measurement by 2D-E was shown to be highly feasible and reproducible in many different populations,<sup>9–11</sup> and even in the study by Arsanjani et al<sup>1</sup> showed a good interobserver variability (7.1%). From a diagnostic point of view, the simple observation of good agreement between the values of 4-chamber LA area measured by 2D-E and MDCT has doubtful clinical utility, since 4-chamber LA area – irrespective of the technique used – has intrinsic limitations as a measure of LA size, resulting from the difficulty to account for the asymmetric LA shape using a single-plane measure.<sup>12</sup> Consistently with these limitations, 2D-E LA volume is superior to LA area as a predictor of LV diastolic dysfunction<sup>13</sup> and for the estimation of LA enlargement as identified by three-dimensional echocardiography.<sup>14</sup> In this context, the use of LA area for the categorical assessment of LA size yields a high risk of underestimation, with misclassification rates up to 70%.<sup>15</sup>

Thirdly, similar considerations can be made for the use of LA size as a prognostic marker. The clinical utility of LA volume for the prediction of cardiovascular outcome was established by a number of studies, both in general and referral populations,<sup>16–19</sup> with robust evidence of more accurate stratification of thromboembolic risk and better prognostic value when compared to LA area.<sup>20–22</sup> Among these studies, the authors cite an important Mayo Clinic paper where LA volume index outperformed LA area for the prediction of outcome in a group of 317 patients in sinus rhythm followed for a median of 3.5 years.<sup>20</sup> They argue that the difference in prognostic performance between LA area and LA volume in that analysis was modest (area under the curve 0.64 vs 0.71). Even assuming that such difference can be arbitrarily considered small, these values only refer to a single component of prognostic performance, i.e., discrimination. In that study, LA volume showed the strongest independent prognostic value for the prediction of the clinical endpoint, with a 6.6-fold

increased risk among patients with severely enlarged LA volume as compared to those with normal LA volume, and with higher significance than LA area. Moreover, a graded relationship between the degree of LA enlargement and risk of events was only evident for LA volume and not for LA area. This finding was also successively confirmed by our group in a study on patients aged >50 years, in sinus rhythm and referred for a general consultation, where only LA volume and particularly peak atrial longitudinal strain showed a graded association with the risk of cardiovascular events.<sup>21</sup> In this regard, it should also be pointed out that the assessment of LA function using 2-dimensional strain imaging provides important prognostic information, independent of LA size.<sup>23</sup>

Lastly, a major issue for the practical applicability of LA size measurements is the need of adequate normality ranges. To date, evidence provides robust normative data for LA volume, both as an absolute measure and after indexation to body surface area.<sup>9,24,25</sup> Moreover, the currently recommended upper normal value of 34 mL/m<sup>2</sup> is consistent with the American Society of Echocardiography/European Association of Cardiovascular Imaging guidelines for the evaluation of diastolic function<sup>26</sup> and has been prognostically validated in several prospective studies.<sup>27–29</sup> On the other hand, normality data for 2D-E LA area are relatively scarce. Only one study reported reference ranges for 4-chamber and 2-chamber LA areas, obtained in a population of relatively young (mean age 45.8 years) healthy volunteers.<sup>9</sup> This paucity of data represents a relevant problem to identify and grade LA enlargement by measurement of LA area.

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- Arsanjani R, Flint N, Beigel R, Khachatryan T, Shalev A, Shturman A, Lee C, Rader F, Berman DS, Heo R, Siegel RJ. Comparison of accuracy of left atrial area and volume by two-dimensional trans-thoracic echocardiography versus computed tomography. *Am J Cardiol* 2019;123:1180–1184.
- Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, Flachskampf FA, Foster E, Goldstein SA, Kuznetsova T, Lancellotti P, Muraru D, Picard MH, Rietzschel ER, Rudski L, Spencer KT, Tsang W, Voigt JU. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr* 2015;28:1–39.
- Taina M, Rissanen V, Hedman M, Jäkälä P, Järvinen V, Vanninen R, Sipola P. Diagnostic performance of left atrial diameter measurement in computed tomography to detect increased left atrial volume. *In Vivo* 2015; 29:487–491.
- Nedios S, Kosiuk J, Koutalas E, Kornej J, Sommer P, Arya A, Richter S, Rolf S, Husser D, Hindricks G, Bollmann A. Comparison of left atrial dimensions in CT and echocardiography as predictors of long-term success after catheter ablation of atrial fibrillation. *J Interv Card Electrophysiol* 2015;43:237–244.
- Kühl JT, Lønborg J, Fuchs A, Andersen MJ, Vejstrup N, Kelbæk H, Engstrøm T, Møller JE, Kofoed KF. Assessment of left atrial volume and function: a comparative study between echocardiography, magnetic resonance imaging and multi slice computed tomography. *Int J Cardiovasc Imaging* 2012; 28:1061–1071.
- Agner BF, Kühl JT, Linde JJ, Kofoed KF, Åkeson P, Rasmussen BV, Jensen GB, Dixon U. Assessment of left atrial volume and function in patients with permanent atrial fibrillation: comparison of cardiac magnetic resonance imaging, 320-slice multi-detector computed tomography, and transthoracic echocardiography. *Eur Heart J Cardiovasc Imaging* 2014;15:532–540.
- Rabbat MG, Wilber D, Thomas K, Malick O, Bashir A, Agrawal A, Biswas S, Sanagala T, Syed MA. Left atrial volume assessment in atrial fibrillation using multimodality imaging: a comparison of echocardiography, invasive three-dimensional CARTO and cardiac magnetic resonance imaging. *Int J Cardiovasc Imaging* 2015;31:1011–1018.
- Farrance I, Frenkel R. Uncertainty of measurement: a review of the rules for calculating uncertainty components through functional relationships. *Clin Biochem Rev* 2012;33:49–75.
- Kou S, Caballero L, Dulgheru R, et al. Echocardiographic reference ranges for normal cardiac chamber size: results from the NORRE study. *Eur Heart J Cardiovasc Imaging* 2014;15:680–690.
- Jiamsripong P, Honda T, Reuss CS, Hurst RT, Chaliki HP, Grill DE, Schneck SL, Tyler R, Khandheria BK, Lester SJ. Three methods for evaluation of left atrial volume. *Eur J Echocardiogr* 2008;9:351–355.
- Henriksen E, Selmerud J, Leppert J, Hedberg P. Echocardiographic assessment of maximum and minimum left atrial volumes: a population-based study of middle-aged and older subjects without apparent cardiovascular disease. *Int J Cardiovasc Imaging* 2014;31:57–64.
- Ballo P, Nistri S, Galderisi M, Mele D, Rossi A, Dini FL, Olivetto I, Losi MA, D'Andrea A, Zuppiroli A, Santoro GM, Mondillo S, Gentile F, Working Group on Echocardiography of the Italian Society of Cardiology. Determinants of discrepancies between two-dimensional echocardiographic methods for assessment of maximal left atrial volume. *Eur Heart J Cardiovasc Imaging* 2017;18:584–602.
- Stefano GT, Zhao H, Schluchter M, Hoit BD. Assessment of echocardiographic left atrial size: accuracy of M-mode and two-dimensional methods and prediction of diastolic dysfunction. *Echocardiography* 2012;29:379–384.
- Maddukuri PV, Vieira ML, DeCastro S, Maron MS, Kuvin JT, Patel AR, Pandian NG. What is the best approach for the assessment of left atrial size? Comparison of various unidimensional and two-dimensional parameters with three-dimensional echocardiographically determined left atrial volume. *J Am Soc Echocardiogr* 2006;19:1026–1032.
- Badano LP, Pezzutto N, Marinigh R, Cinello M, Nucifora G, Pavoni D, Gianfagna P, Fioretti PM. How many patients would be misclassified using M-mode and two-dimensional estimates of left atrial size instead of left atrial volume? A three-dimensional echocardiographic study. *J Cardiovasc Med* 2008;9:476–484.
- Pritchett AM, Jacobsen SJ, Mahoney DW, Rodeheffer RJ, Bailey KR, Redfield MM. Left atrial volume as an index of left atrial size: a population-based study. *J Am Coll Cardiol* 2003 Mar 19;41:1036–1043.
- Tsang TS, Barnes ME, Bailey KR, Leibson CL, Montgomery SC, Takemoto Y, Diamond PM, Marra MA, Gersh BJ, Wiebers DO, Petty GW, Seward JB. Left atrial volume: important risk marker of incident atrial fibrillation in 1655 older men and women. *Mayo Clin Proc* 2001;76:467–475.
- Leung DY, Chi C, Allman C, Boyd A, Ng AC, Kadappu KK, Leung M, Thomas L. Prognostic implications of left atrial volume index in patients in sinus rhythm. *Am J Cardiol* 2010;105:1635–1639.
- Bergamini C, Benfari G, Dolci G, Torelli F, Ghiselli L, Trevisani L, Truong S, Vinco G, La Russa F, Golia G, Molino A, Rossi A, Ribichini FL. Usefulness of left atrial remodeling in predicting cardiac toxicity during trastuzumab therapy for breast cancer. *Am J Cardiol* 2018;122:885–889.
- Tsang TS, Abhayaratna WP, Barnes ME, Miyasaka Y, Gersh BJ, Bailey KR, Cha SS, Seward JB. Prediction of cardiovascular outcomes with left atrial size: is volume superior to area or diameter? *J Am Coll Cardiol* 2006;47:1018–1023.
- Cameli M, Lisi M, Focardi M, Reccia R, Natali BM, Sparla S, Mondillo S. Left atrial deformation analysis by speckle tracking echocardiography for prediction of cardiovascular outcomes. *Am J Cardiol* 2012;110:264–269.
- Radwan HI. Relation between left atrial measurements and thromboembolic risk markers assessed by echocardiography in patients with nonvalvular atrial fibrillation: a cross-sectional study. *Egypt Heart J* 2017;69: 1–11.

23. Carluccio E, Biagioli P, Mengoni A, Francesca Cerasa M, Lauciello R, Zuchi C, Bardelli G, Alunni G, Coiro S, Gronda EG, Ambrosio G. Left atrial reservoir function and outcome in heart failure with reduced ejection fraction. *Circ Cardiovasc Imaging* 2018;11:e007696.
24. Nistri S, Galderisi M, Ballo P, Olivotto I, D'Andrea A, Pagliani L, et al. Determinants of echocardiographic left atrial volume: implications for normalcy. *Eur J Echocardiogr* 2011;12:826–833.
25. D'Ascenzi F, Piu P, Capone V, Sciacaluga C, Solari M, Mondillo S, Henein M. Reference values of left atrial size and function according to age: should we redefine the normal upper limits? *Int J Cardiovasc Imaging* 2019;35:41–48.
26. Nagueh SF, Appleton CP, Gillebert TC, Marino PN, Oh JK, Smiseth OA, et al. Recommendations for the evaluation of left ventricular diastolic function by echocardiography. *J Am Soc Echocardiogr* 2009;22:107–133.
27. Hsiao SH, Chiou KR, Porter TR, Huang WC, Lin SK, Kuo FY, Cheng CC, Lin KL, Lin SL. Left atrial parameters in the estimation of left ventricular filling pressure and prognosis in patients with acute coronary syndrome. *Am J Cardiol* 2011;107:1117–1124.
28. Hiemstra YL, Debonnaire P, Bootsma M, van Zwet EW, Delgado V, Schalij MJ, Atsma DE, Bax JJ, Marsan NA. Global longitudinal strain and left atrial volume index provide incremental prognostic value in patients with hypertrophic cardiomyopathy. *Circ Cardiovasc Imaging* 2017;10:e005706.
29. Christensen NL, Dahl JS, Carter-Storch R, Bakkestrøm R, Pecini R, Steffensen FH, Søndergaard EV, Videbæk LM, Møller JE. Relation of left atrial size, cardiac morphology, and clinical outcome in asymptomatic aortic stenosis. *Am J Cardiol* 2017;120:1877–1883.  
<https://doi.org/10.1016/j.amjcard.2019.05.003>