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# Automatic assessment of cardiac load due to acute pulmonary embolism: Saddle vs. central and peripheral emboli distribution

Galit Aviram, MD [a,*], Eugene Soikher, MD [a], Achiude Bendet, MD [a], Tomer Ziv-Baran, PhD [d], Shlomo Berliner, MD, PhD [b], Hezzy Shmueli, MD [c], Limor Friedensohn, MD [b], Assi Milwidsky, MD [c], Ofer Sadovnik, MD [a], Yan Topilsky, MD [c]

[a] Department of Radiology, Tel Aviv Sourasky Medical Center, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel
[b] Department of Internal Medicine 'D' and 'E', Tel Aviv Sourasky Medical Center, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel
[c] Department of Cardiology, Tel Aviv Sourasky Medical Center, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel
[d] Department of Epidemiology and Preventive Medicine, School of Public Health, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

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ABSTRACT

*Background:* Changes in cardiac chambers' volumes in relations to different distributions of pulmonary embolism (PE) have not been investigated.
*Objectives:* To compare cardiac chambers' volumes of patients with saddle, central or peripheral PE.
*Methods:* Consecutive patients with PE on computed tomography pulmonary angiography (CTPA), 1/2007-12/2010, divided according to emboli distribution. Software automatically provided the volumes of each cardiac compartment. We measured the ability of each chamber's volume and ratios between the right and left ventricles (RV/LV) and right and left atria (RA/LA) to discriminate between emboli locations.
*Results:* Among the 636 patients, 325 (51%) had peripheral, 278 (44%) central and 33 (5%) had saddle emboli. The RV/LV and RA/LA volume ratios discriminated well between saddle and central PE (AUC ≥0.74) and saddle and peripheral PE (AUC ≥0.83), but not between central and peripheral PE (AUC ≤0.6).
*Conclusion:* Automatic volumetric analysis of diagnostic CTPAs provides rapid tool which can discriminate between cardiac responses in saddle, central or peripheral PE.


## Introduction

Computed tomography pulmonary angiography (CTPA) is currently the modality of choice for the diagnosis of acute pulmonary embolism (PE).[1,2] CTPA-based risk stratification of patients with acute PE is an attractive alternative to echocardiography by effectively using an already available diagnostic CTPA scan for rapid assessment without delay or additional cost. The presence of an increased ratio between the diameters of the right ventricle (RV) and left ventricle (LV) as measured on CTPA suggests RV failure, which is considered the primary cause of death in severe PE.[1,3,4] This measurement on CTPA, however, has been shown to have inconsistent results.[4–6] Recently an automatic 4-chamber volumetric analysis (4CVA) software was introduced, that enabled obtaining information about the volumes of the various heart chambers immediately following the performance of non-gated CTPA.[7] Since the 4CVA provides 3-dimensional (3D) data rather than diameter measurements, and enables the assessment of the left and right atria in addition to the ventricles, it might open up a new approach to the evaluation of the response of the various cardiac compartments to an acute PE. PE may appear within a large spectrum of emboli distributions. The most severe is the saddle location, defined as the most proximal pulmonary thromboembolus that straddles the bifurcation of the main pulmonary artery trunk, and one that may cause significant concern for impending hemodynamic collapse and poor prognosis.[8] On the other end of the spectrum are peripheral subsegmental emboli whose significance is uncertain, and the mandatory need for anticoagulation in some of the patients is open to question.[9,10] The various changes in the volumes of the four cardiac chambers that take place in response to the different severities of PEs (as reflected by the emboli distribution) have not been previously investigated. The aim of the present study was to quantitatively assess the cardiac chambers' volume load in patients with various distributions of PE using the 4CVA data derived from non-gated CTPA.

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* Corresponding author. Department of Radiology, Tel Aviv Sourasky Medical Center, Weitzman Street, Tel Aviv 64239, Israel.
*E-mail address:* aviramgalit@hotmail.com (G. Aviram).

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## Materials and methods

### Study design

This study was conducted in a large, university-affiliated tertiary care 1200-bed hospital. The institutional review board approved this retrospective analysis and waived the need for informed consent. The hospital's database was used to retrospectively identify the inpatients that underwent CTPA between January 1, 2007 and December 31, 2010.

### Study population

Patients were included if they were diagnosed on their CTPA as having an acute PE. The medical records of these patients were then reviewed by two clinicians (L.F. and H.S.) who used an integrated radiological–clinical information system database to retrieve clinical information that included gender, age, background, comorbid conditions, and recent (during the preceding three months) events of cardiovascular disease, infection, operation, trauma, or hospitalization. Patients were excluded if their CTPA was inadequate (due to incomplete coverage of the heart in the *Z*-axis or to inaccurate detection of the chambers' boundaries by the volumetric software), or if all the relevant clinical information was unavailable.

## Methods

In the event of multiple scans, the results of the first one were entered into the analysis. Referral for CTPA studies was based on clinical suspicion of acute PE in patients with no contraindications to undergo them (e.g., severe allergic reactions to iodine-containing contrast media or renal failure). The same cohort of patients had been described and analyzed in a previous report for a different purpose.[11]

### CT technique

All patients were scanned by a multi-detector CT scanner (Mx8000 IDT or Brilliance; Philips Medical Systems, Cleveland, OH, USA) with 16 or 64 detector rows. The reconstructed slice thickness was 1.0–2.0 mm with an increment of 0.5–1 mm. Scans were acquired according to our routine non-electrocardiographic-gated protocol with contrast injections of 70–100 mL of iodinated contrast material at a concentration of 300 mg iodine per mL (Ultravist, Schering, Berlin, Germany) and at rates of 3–4 mL/s. To optimize visualization of the pulmonary arteries, an automated bolus-tracking technique was used with a region of interest placed within the main pulmonary artery. Scanning began 5 s after reaching a threshold of 100 Hounsfield Units at the region of interest, covering the chest from the lung bases to the thoracic inlet. All scans were obtained in a caudal-cranial direction at end-of-inspiration during a single breath-hold.

### CT review

The CT scans were reviewed in consensus by two radiologists (E.S., G.A.), the former with six years of experience in CT imaging and the latter with 15 years of experience in cardiothoracic imaging, who were unaware of the clinical history, the results of other imaging techniques, and patient outcome. The radiologists reviewed the scans to assess the location of the most central emboli and classified them accordingly into three groups: Group A included patients who had a saddle embolus (i.e., located within the right and left pulmonary arteries and including the bifurcation of the main pulmonary trunk), Group B included patients who had central emboli (i.e., emboli in the main left and/or right pulmonary arteries or lobar arteries with no connection through the pulmonary trunk), and Group C included patients who had solely peripheral emboli (i.e., segmental and subsegmental). Each CTPA was also investigated with novel volumetric analysis software which automatically provides the volumes of the RV, right atrium (RA), LV and left atrium (LA). Automated volumetric measurements of the RV, RA, LV, and LA were obtained using a new fully automatic algorithm (Comprehensive Cardiac Analysis, Extended Brilliance Workspace, Research Version Philips Healthcare, Cleveland, OH) that adapts an anatomical model of the heart chambers to the CT image volume.[7,12–14] The output consists of a 3D graphic display of the heart segmented into its main structures. We analyzed the volumes of the RV, RA, LV (excluding the myocardium) and LA. The volume of each cardiac chamber was automatically calculated as the product of a single voxel volume and the sum of all voxels included in it. This approach requires only that the reconstructed images of the entire volume of the chest be uploaded at once at the workstation. Importantly, no other human interaction was needed or performed. Loading and processing by the automated system took 20–40 s per study. The software allows the relevant segmentation structure to be color-coded and viewed simultaneously in both 3D and 2D superimposed on the reference image in the axial, coronal, sagittal, or cardiac views (short axis, vertical long axis, horizontal long axis). Fig. 1 presents examples of the software's output. Each structure was inspected visually on the reference images for conformity to the imaged cardiac anatomy in order to validate the correctness of the segmentation by the two reviewing radiologists. In the event that the automatic segmentation was visually assessed as being incorrect, the patient's data were excluded from the study. A previous version of this software had been validated on cardiac-gated scans,[12] and the current study is based on a newer version using an algorithm which was designed to improve the analysis of non-gated CTPA studies.

### Statistical analysis

Categorical variables were reported as numbers (percentages), and continuous variables as means (standard deviations, SD) or medians (interquartile ranges, IQR). Continuous variables were tested for normal distribution using histograms, the Kolmogorov–Smirnov test and Q–Q plots. Differences of age and the various cardiac chambers' volumes and the ratios between the RA/LA and RV/LV volumes, according to PE distribution, were assessed using analysis of variance (ANOVA) with the Scheffe post hoc test or the Kruskal Wallis and Mann Whitney tests. Differences of gender and comorbidities were evaluated with the Chi-square or Fisher's exact tests. The area under the receiver operating characteristics curves (AUC) was used to evaluate the ability of each chamber's volume and the ratios between RA/LA and RV/LV volumes to discriminate between the different groups based on PE location. Comparison of the AUCs of these parameters was done using DeLong's test.[15] Classification tree methodology of chi-squared automatic interaction detection (CHAID)[16] was used to identify threshold values that classify patients into homogeneous groups according to each parameter. A two-tailed $p$ value $<0.05$ was considered statistically significant. Analyses were performed with SPSS version 22 and R version 3.1.3.