Implementation and Performance of Automated Software for Computing Right-to-Left Ventricular Diameter Ratio From Computed Tomography Pulmonary Angiography Images

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Objective: The aim of this study was to prospectively test the performance and potential for clinical integration of software that automatically calculates the right-to-left ventricular (RV/LV) diameter ratio from computed tomography pulmonary angiography images.

Methods: Using 115 computed tomography pulmonary angiography images that were positive for acute pulmonary embolism, we prospectively evaluated RV/LV ratio measurements that were obtained as follows: (1) completely manual measurement (reference standard), (2) completely automated measurement using the software, and (3 and 4) using a customized software interface that allowed 2 independent radiologists to manually adjust the automatically positioned calipers.

Results: Automated measurements underestimated ($P < 0.001$) the reference standard (1.09 [0.25] vs1.03 [0.35]). With manual correction of the automatically positioned calipers, the mean ratio became closer to the reference standard (1.06 [0.29] by read 1 and 1.07 [0.30] by read 2), and the correlation improved ($r = 0.675$ to 0.872 and 0.887). The mean time required for manual adjustment (37 [20] seconds) was significantly less than the time required to perform measurements entirely manually (100 [23] seconds).

Conclusions: Automated CT RV/LV diameter ratio software shows promise for integration into the clinical workflow for patients with acute pulmonary embolism.

Key Words: pulmonary embolism, computer-aided detection, prognosis, right ventricular strain, diameter ratio

Acute pulmonary embolism (PE) is a common condition that has a high mortality rate if untreated.[1,2] As the main pathophysiology of morbidity and mortality is right ventricular (RV) dysfunction,[3] information regarding RV size and function can be critical when deciding on the subset of patients warranting aggressive management such as thrombolysis.

Computed tomography pulmonary angiography (CTPA) is the first-line diagnostic modality used to confirm a clinical suspicion of acute PE.[4–6] In addition, data from the CT images enable intensive assessment of RV dysfunction, thus providing prognostic as well as diagnostic information. The RV-to-left ventricular (RV/LV) diameter ratio has emerged as the major metric, and although there are some conflicting reports, several large studies have validated the use of RV size on CTPA to predict prognosis after acute PE.[7–10] However, obtaining these measurements can be time consuming because it is necessary to use several caliper positions.

We previously developed and validated a Picture Archiving and Communication System (PACS)–integrated computer-aided detection (CAD) system that conducts ventricular analysis using CTPA images and automatically outputs the axial RV/LV diameter ratio.[11] The purpose of this study is to prospectively test the hypothesis that this software can be integrated into a simulated clinical workflow and obtain performance comparable with that of reference-standard manual clinical measurements.

MATERIALS AND METHODS

Study Population

Our institutional human research committee approved this Health Insurance Portability and Accountability Act-compliant study; informed consent was waived as the risks were considered no more than minimal. During the period between September 28, 2013, and February 22, 2014, each official CTPA radiological report generated at a single urban teaching hospital was reviewed by 1 physician for the finding of acute PE. A CTPA examination was included to the study when the report confirmed a diagnosis of acute PE.

CT Acquisition

Computed tomography pulmonary angiography images were acquired in the craniocaudal direction using 16-, 64-, or 128-detector row scanners (Siemens Healthcare, Erlangen, Germany) and were reconstructed at slice thickness of 1.0 mm. The scanning parameters were 80 to 120 kVp and ~200 effective mAs. All patients received 75 mL of iodinated contrast medium (370 mg iodine/mL) by power injector at a rate of 3 mL/s. The acquisition was triggered with bolus tracking of the main pulmonary artery with a threshold of 80 HU.

Ventricular Diameter Ratio Measurements

The following 4 sets of measurements of the RV/LV diameter ratio were obtained from each CTPA study.

Completely Manual Measurement (Reference Standard)

The RV and LV were measured manually on the axial images using a dedicated postprocessing workstation (Vitrea fX 3.1; Vital Images, Minnetonka, Minn), and the calculated RV/LV diameter

ratio was used for clinical evaluation. The diameters were defined as the largest distance between the luminal surface of the interventricular septum and the endocardium, for each ventricle, as previously described.[12 14] The RV and LV maximum diameters were commonly at different craniocaudal levels. The radiologist then reported the RV/LV diameter ratio to the referring clinicians.

Completely Automated Measurement

Computer-aided detection software was implemented in Matlab (The Mathworks Inc, Natick, Mass) and integrated as a simulation in the clinical workflow by an Osirix (Pixmeo, Geneva, Switzerland) plug-in. The DICOM images were input to a second dedicated workstation. After the identification of positive CTPA case by a radiologist, the same radiologist then performed the measurements described later.

The RV/LV axial diameter ratio was calculated using CAD software that automatically detects the largest diameter of each of the right and left ventricles, without any assistance from the radiologist, using a previously described algorithm in a 5-step approach[11]: (1) detection of the ventricles via machine-learning techniques, (2) placement of seeds within the ventricles, (3) estimation of septum position using the location of the seeds and the image properties, (4) segmentation of the right and left ventricles using a level set technique with curvature constraints, and (5) measurement of the ventricular diameters by automatically placed calipers and calculation of the RV/LV ratio. The RV/LV diameter ratio is outputted when the software is launched with the DICOM images, and the fully automated RV/LV diameter measurements are recorded by the software.

Automated Measurement With Manual Adjustment by 2 Independent Readers

Three radiologists with 5, 8, and 13 years of experience and who were all blinded to the clinical interpretation of the images served as investigators to adjust the RV/LV diameter ratio that was outputted from the CAD software. Two radiologists were randomly assigned to each data set; that is, each radiologist read 66% of the 115 cases. The data output from the CAD software were presented on the workstation (Fig. 1) as the RV and LV diameters computed from the axial images by the software. The 2 radiologists independently reviewed these images and corrected the caliper positions as necessary. The corrected RV/LV diameter ratio was then calculated automatically by the software, shown on the same screen, and electronically stored. For each data set, the radiologists documented the reasons for any adjustments made to the automated positions. The time taken for each measurement was recorded.

Statistical Analysis

Continuous variables are presented as the mean and standard deviation and shown as boxplots. Paired t tests, Bland-Altman plots, and the linear fit with Pearson correlation coefficients were used to compare values among the different measurement methods. Pitman test was used to identify proportional bias.

RESULTS

Of 946 CTPA studies performed during the study period and assessed for acute PE, this finding was identified in 125 studies (13.2%) from 125 patients; this group formed the initial study cohort. The completely automated measurement of RV/LV diameter ratio failed in 5 patients, and the software did not allow manual adjustment in 1 patient. In 4additional patients, the radiologist's time was not recorded. All 10 of these patients were excluded from further analyses, and thus, the final cohort included 115 patients (mean [SD] age, 59.0 [14.9] years; male-female, 53:62).

Comparison of RV/LV Diameter Ratio Measurements Obtained by Manual and Automated Methods

Compared with the manual measurements used clinically as the reference standard, the CAD system underestimated the RV/LV diameter ratio. The difference in mean [SD] ratio between the 2 methods was 0.07 (1.09 [0.25] for manual vs 1.03 [0.35] for automated measurements, $P < 0.001$; Fig. 2). A linear fit

FIGURE 1. Interface used to display the axial RV/LV diameter. Figure 1 can be viewed online in color at www.jcat.org.

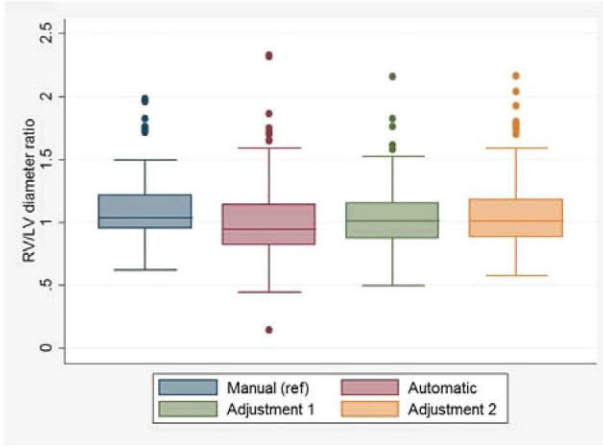


FIGURE 2. Boxplots of RV/LV diameter ratio obtained by the 4 different measurement methods. Figure 2 can be viewed online in color at www.jcat.org.

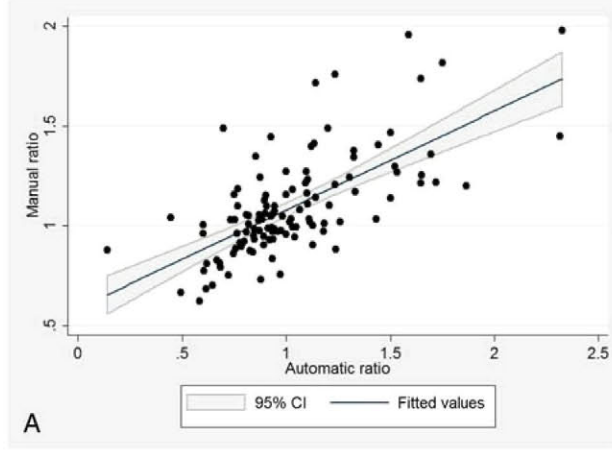
showed a moderate correlation (Pearson $r = 0.675$; Fig. 3A). The Bland-Altman plot showed a slight but significant negative proportional bias ($r = -0.39$, $P < 0.01$); that is, the larger the RV/LV diameter ratio, the more the software underestimated the reference standard value (Fig. 4A). The range of the limits of agreement was 1.0 (from −0.447 to 0.580).

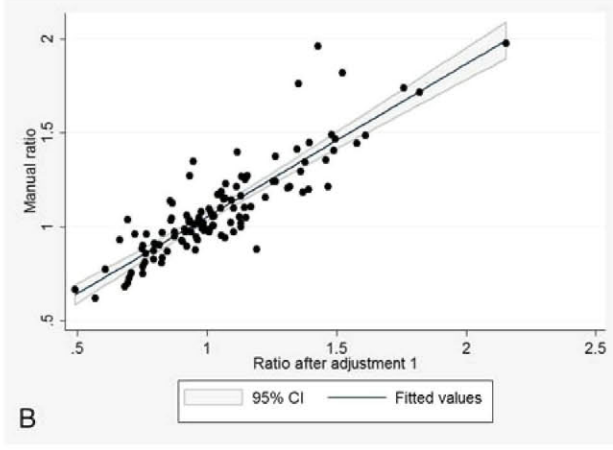
Comparison of RV/LV Diameter Ratio Measurements Obtained by Manual and Semiautomated Methods

The linear correlation of the radiologist-adjusted and manual measurements was higher than those obtained by the manual and automated methods (Pearson $r = 0.872$ and 0.887 after adjustment by reads 1 and 2, respectively) (Figs. 3B, C). The mean difference and the limits of agreements in RV/LV diameter ratio also decreased compared with those of the manual measurements (Figs. 4B, C). The proportional bias disappeared after adjustment by read 1 ($r = -0.139$, $P = 0.15$). The correlation coefficient between reads 1 and 2 was $r = 0.762$.

Reasons for Manual Adjustment

Table 1 summarizes the reasons documented independently by each radiologist for adjusting the data outputted by the software. For all 115 imaging studies, at least 1 of the 2 reads considered that manual adjustment of the automated RV and LV measurements was necessary. In 82.6% of the imaging studies, both reads thought that the defined ventricular edge required correction and that the automated method had not detected the largest possible diameter in 71.3% of the patients.





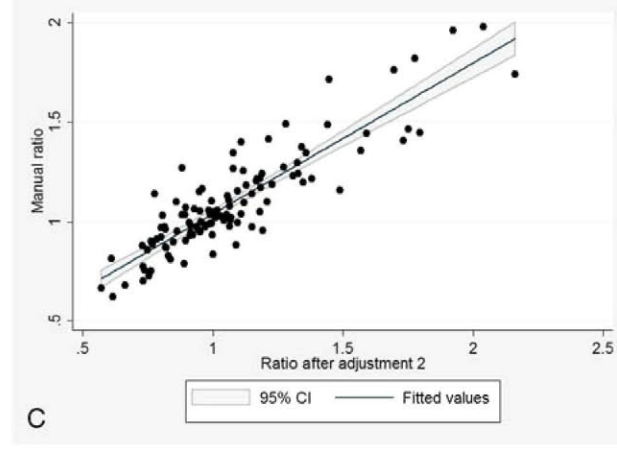


FIGURE 3. Linear fits between the manual measurement and (A) completely automated measurement, (B) automated measurement with adjustments by read 1, and (C) automated measurement with adjustments by read 2. The manual adjustments improved the fit. Figure 3 can be viewed online in color at www.jcat.org.

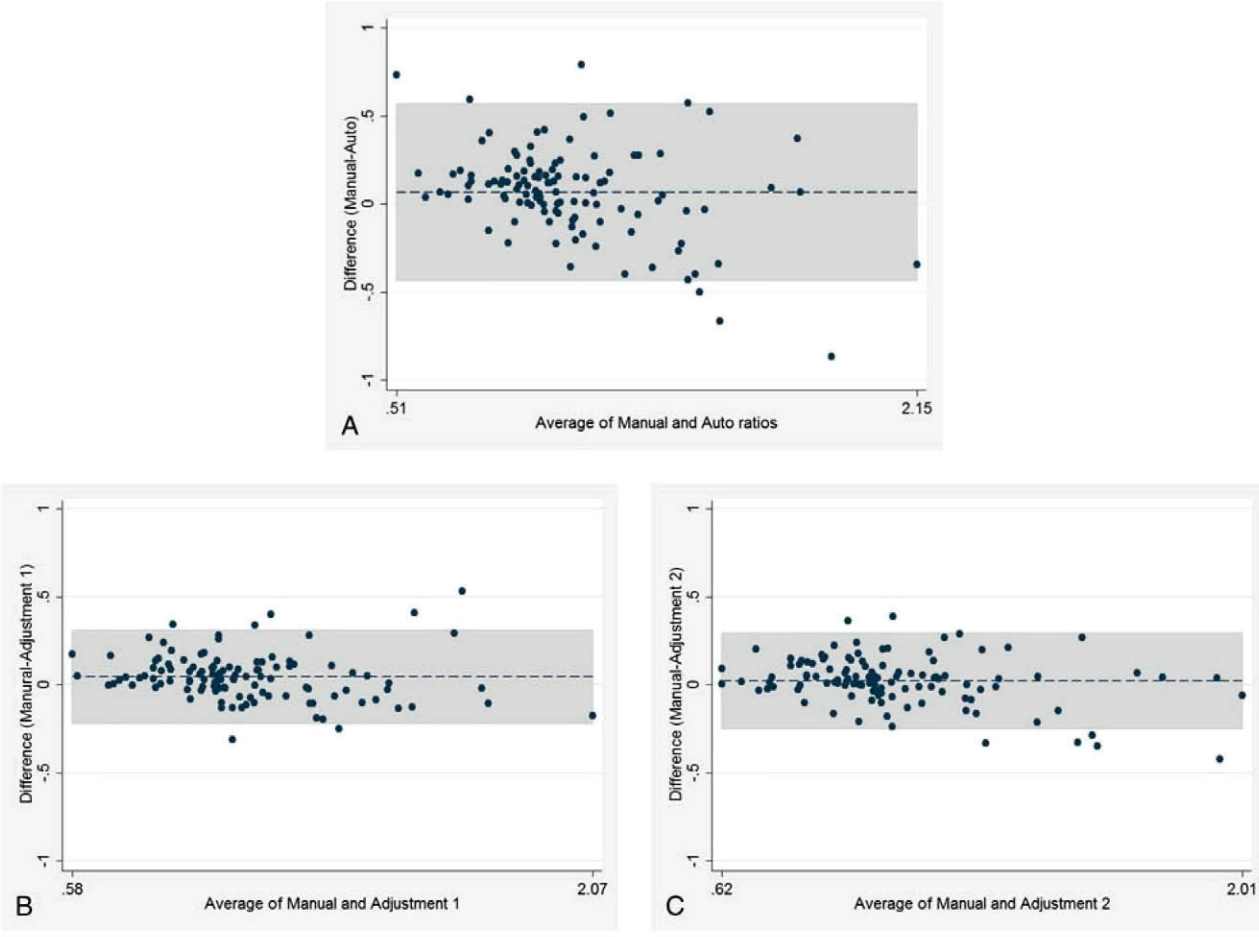


FIGURE 4. Bland-Altman plots comparing manual measurement and (A) completely automated measurement, (B) automated measurement with adjustment by read 1, and (C) automated measurement with adjustment by read 2. The mean difference and the limits of agreement decreased after manual adjustment. Figure 4 can be viewed online in color at www.jcat.org.

Time Required to Obtain the Measurements

The mean time required to manually adjust the automated data (37 [20] seconds) was significantly ($P < 0.001$) shorter than that required to perform fully manual measurements (100 [23] seconds).

DISCUSSION

Although guidelines support the routine use of CTPA images to confirm a diagnosis of acute PE,[15] it is likely that CT-derived prognostic information such as the RV/LV diameter ratio is not universally used. Factors that contribute to its underutilization include that the method is not standardized and that performing the measurements and calculations requires additional radiologist time. This prospective study was designed to first test the implementation of an automated RV/LV diameter ratio CAD software package and, second, to determine the accuracy of strategies for incorporating the software. The main findings are that (1) the RV/LV diameter ratio CAD package could be implemented into a clinical workflow pattern in 96% (120/125) of the present patients and, (2) although the fully automated diameter ratios underestimated the reference standard, the radiologist can complete manual corrections to the automated data and report in less than 1 minute.

TABLE 1. Reasons for Adjustment of Software Output Data and Prevalence

	n (%) of Cases For Which the Reason Was Given by			
	Read 1	**Read 2**	**Both Reads***	**At Least 1 of 2 Reads**
Wrong chamber was selected.	12 (10.4)	13 (11.3)	6 (5.2)	19 (16.5)
Ventricular edge was not detected correctly.	104 (90.4)	104 (90.4)	95 (82.6)	113 (98.3)
Largest diameter was not captured.	99 (86.1)	90 (78.3)	82 (71.3)	107 (93.0)
Orientation of the caliper was wrong.	61 (53.0)	53 (46.1)	28 (24.3)	85 (73.9)
Total (any reason)	111 (96.5)	112 (97.4)	106 (92.2)	115 (100)

*Prevalence of cases where both readers documented the same reasons for adjustment.

Although the software is designed to be fully integrated into a PACS environment, in this study, we simulated the clinical environment by adding a second workstation, as clinical PACS integration was beyond the scope of this project. Our results for generating a fully automated RV/LV diameter ratio failed to validate this feature of the software; that is, the positions of the RV and LV calipers required correction. However, the software is designed for DICOM upload and to output the RV and LV diameters while the radiologist reads the CTPA images. If the study is positive for acute PE, the RV and LV calipers can be corrected with minimal effort, and the RV/LV diameter ratio can be provided in less than 1 minute. These results are in keeping with the advantages of rapid reporting of the findings of acute PE to improve patient outcomes.[16] The differences between the corrected data and the manual measurements were minimal, which supports the use of a CAD-based approach for using the CT data to obtain prognostic information after a diagnosis of acute PE.

Although the CT RV/LV diameter ratio was reported to be well correlated with that on echocardiography,[17,18] which is the reference standard for RV assessment, the following CT metrics have also been used as markers of prognosis after acute PE[7,19–21]: pulmonary artery-to-aorta ratio, flattening and bowing of the interventricular septum, reflux of contrast medium into the inferior vena cava, and clot burden or clot volume. However, there are mixed results regarding an association with mortality. One study that evaluated all of the above metrics as well as clinical factors in 635 CTPAs from 635 patients concluded that only an increase in RV/LV ratio was associated with short-term mortality.[19] This finding further supports the use of ventricular size for assessing prognosis, whether reported alone or with other metrics.

The current results indicate that the software requires further improvement. The accuracy of measuring the calipers depends on the ventricular segmentation by the level set algorithm. It is challenging to find a parameter set that produces accurate segmentations in all patients and that takes into account anatomic variability and differences in contrast opacification of the ventricular cavities. For these reasons, we selected a conservative parameter for the level set algorithm, which led to the underestimations in the present results. Calibrating the level set parameters on the basis of estimated image contrast between the ventricles and the septum, or by using a shape-based segmentation algorithm, could theoretically yield better segmentation results, which would in turn improve the accuracy of caliper positioning and the RV/LV diameter ratio.

We acknowledge several study limitations. First, this is a single-center study that requires external validation. Second, the CAD measurements are based on axial images, and thus, the study does not include volumetric measurements or 4-chamber reformatted images. However, there is no evidence to suggest that the prognostic value of measurements derived from axial images alone is inferior to those calculated from 4-chamber reformatted images.[14] Third, as the results for manual adjustment combined the inputs from 3 readers, we did not calculate interobserver or intraobserver agreement. Fourth, knowledge of the presence of pulmonary hypertension in these critical patients would have given a stronger measure of the performance of the software in terms of its effectiveness and reliability for clinical use; however, these data were unavailable. Finally, although the prognostic value of CT-derived RV/LV diameter ratio has been confirmed in numerous studies, as yet no study has evaluated the changes to patient management or outcomes following the availability of any imaging (CT or echocardiography)-based metric in terms of prognosis after a diagnosis of acute PE.

In conclusion, it seems likely that an automated RV/LV diameter ratio software package will soon be integrated into the clinical workflow for reporting CT-derived prognostic information for patients with acute PE diagnosed by CTPA. Manual correction of the RV and LV diameter measurements can be completed in less than 1 minute, and the reported values are comparable with reference standard clinical measurements obtained manually.

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