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Assessment of Acute Pulmonary Embolism by Computer-Aided Technique: A Reliability Study

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Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
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Background:

Acute pulmonary embolism is one of the most common cardiovascular diseases. Computer-aided technique is widely used in chest imaging, especially for assessing pulmonary embolism. The reliability and quantitative analyses of computer-aided technique are necessary. This study aimed to evaluate the reliability of geometry-based computer-aided detection and quantification for emboli morphology and severity of acute pulmonary embolism.

Material/Methods:

Thirty patients suspected of acute pulmonary embolism were analyzed by both manual and computer-aided interpretation of vascular obstruction index and computer-aided measurements of emboli quantitative parameters. The reliability of Qanadli and Mastora scores was analyzed using computer-aided and manual interpretation.

Results:

The time costs of manual and computer-aided interpretation were statistically different (374.90 ± 150.16 versus 121.07 ± 51.76 , $P < 0.001$). The difference between the computer-aided and manual interpretation of Qanadli score was 1.83 ± 2.19 , and 96.7% (29 out of 30) of the measurements were within 95% confidence interval (intra-class correlation coefficient, $ICC = 0.998$). The difference between the computer-aided and manual interpretation of Mastora score was 1.46 ± 1.62 , and 96.7% (29 out of 30) of the measurements were within 95% confidence interval ($ICC = 0.997$). The emboli quantitative parameters were moderately correlated with the Qanadli and Mastora scores (all $P < 0.001$).

Conclusions:

Computer-aided technique could reduce the time costs, improve the and reliability of vascular obstruction index and provided additional quantitative parameters for disease assessment.

MeSH Keywords:


Angiography • Pulmonary Embolism • Tomography, X-Ray Computed

Abbreviations:

CAT – computer-aided technique; **CTPA** – computed tomography pulmonary angiography; **ICC** – intra-class correlation coefficient; **mLVa** – maximal left ventricular area; **mLVd** – maximal left ventricular diameter; **mRVa** – the maximal right ventricular area; **mRVd** – maximal right ventricular diameter; **PE** – pulmonary embolism; **ROI** – region of interest; **VOI** – vascular obstruction index

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Background

Acute pulmonary embolism (PE) is one of the most common cardiovascular diseases in China, especially in developed areas [1]. The incidence of acute PE is 0.1%, and the mortality is up to 15% within 3 months [2,3]. A clinical study including on 796 patients showed that a delay of more than 1.5 hours in diagnosis delayed the initial treatment, thus significantly increasing the mortality risk within 30 days [4]. The causes of death in patients with acute PE are associated with pulmonary hypertension and the increased overload of right ventricle after PE [5]. Therefore, rapid and accurate diagnosis and assessment of acute PE are very important for the rational treatment and prognosis evaluation.

In recent years, with the development and innovation of multi-slice spiral computed tomography (CT) technique, CT pulmonary angiography (CTPA) has become a routine tool for the diagnosis and assessment of acute PE [6]. However, amounts of images and complex anatomical structures of pulmonary vessels led to visual fatigue and thus increase the influence of subjectivity among clinicians, which would result in reduction in reliability and repeatability and finally increase the misdiagnosis rate [7–9]. In addition, manual data analysis was time-consuming. Therefore, a simple, rapid, and reliable diagnostic and evaluation method, such as computer-aided technique (CAT), was needed to improve manual interpretation.

At present, CAT is widely used in chest imaging, especially for detecting pulmonary nodules/early lung cancer, asthma/chronic obstructive pulmonary disease, and thrombi [10]. A number of studies demonstrated the potential value of CAT in assessing PE [10]. CAT could identify emboli which were previously missed by observers, help the inexperienced observers to detect emboli [11], and improve the confidence and reproducibility in the diagnosis [12]. However, radiologists mainly focused on the ability of CAT to detect emboli [10,13,14] and optimized the image quality [15]. The reliability and quantitative analyses of emboli morphology and severity of embolism were ignored, though it was very necessary and important for diagnosis and therapy decision.

This study aimed to evaluate the reliability of geometry-based computer-aided detection and quantification method for analyzing the emboli morphology and severity of acute PE.

Material and Methods

Study population

This retrospective study was approved by the Ethics and Academic Committee of our hospital. All patients were

exempted from informed consent. Patients suspected of acute PE and underwent CTPA examination, were registered in this study from January 2017 to June 2017. The inclusion criteria were as follows: patients diagnosed with acute PE based on the 2014 European Society of Cardiology guideline [16], but without treatment. The exclusion criteria were as follows: 1) severe cardiopulmonary diseases, including myocardial infarction, heart valve disease, pulmonary heart disease, chronic obstructive pulmonary disease, and lung tumors; 2) pleural effusion with atelectasis; 3) incomplete clinical data; and 4) unsatisfactory image quality.

CT scan protocol

The elbow vein was catheterized with an 18-gauge catheter (BD Intima II 18G, BD, Jiangsu, China), and the indwelling needle was tested with 20 mL of physiological saline before contrast agent injection. All CTPA examinations were performed using a 64-slice CT scanner (Light Speed VCT-XT, GE Healthcare, WI, USA). Acquisition parameters were as follows: detector collimation of 64×0.625 mm, gantry rotation time of 500 ms, tube voltage of 120 kV, and tube current of 400 mA. The reconstruction thickness and the interval of the axial image were 0.625 mm. The standard algorithm was used for reconstruction. The matrix was 512×512. A region of interest was placed into the right atrium, and image acquisition started 2 seconds after intense enhancement of the right atrium (triggered threshold >100 HU). The injection volume and rate of administering contrast agent (iodixanol injection 370 mgI/mL, Bayer Schering Pharma AG Guangzhou Branch, Guangdong, China) were 50 mL and 5.0 mL/second, respectively.

At the end of the scan, the images were uploaded to the computer-aided diagnostic system (FACT-Lung version 1.0, Dexin-lung CAD workstation, Shaanxi Shenzhou Dexin Medical Imaging Technology Co., Ltd., Shaanxi, China) for automatic detection and quantification.

Imaging interpretation

Manual interpretation

Two observers with 8 and 10 years of chest imaging diagnostic experience independently interpreted the data without other information and calculated the Qanadli and Mastora scores [17,18]. When the results were inconsistent, the agreements were reached with negotiation. The working time of the 2 observers in interpreting the Qanadli and Mastora scores of each patient were recorded, and the mean working time was referenced as the manual time.

Computer-aided interpretation

After 8 hours of relevant software training, the observers re-interpreted the Qanadli and Mastora scores using computer-aided detection 30 days later. The consistency of the results was determined by consensus. The working time of the Qanadli and Mastora scores using CAT was recorded, and the mean working time was regarded as the computer-aided time cost.

In addition, quantitative morphological parameters of pulmonary thrombo-emboli were obtained and recorded by computer-aided quantification method.

Evaluation of vascular obstruction index

Qanadli scoring system

Bilateral pulmonary arteries were divided into 3 branches in the upper lobe, 2 branches in the middle or lingual lobe, and 5 branches in the lower lobe. Thus, 10 pulmonary segmental arteries were present on each side, totaling 20 branches. The embolism severity was calculated using a 2-point scale: 1 point for partial embolism and 2 points for total embolism. In addition, the embolus of each segmental artery was recorded as 1 point, and the total score of the pulmonary emboli above the segmental level was the sum of the segmental artery scores under it. The maximum embolism score of each patient was $2 \times 20 = 40$. The following expression was used for the calculation:

Qanadli embolism index = $\frac{\sum(\text{embolism number} \times \text{embolism degree})}{40} \times 100\%$.

Mastora scoring system

The pulmonary arteries were divided into 5 mediastinal arteries (1 branch for the pulmonary trunk, 2 branches for right and left pulmonary arteries, and 2 branches for right and left interlobar arteries), 6 branches for lobar arteries, and 20 branches for segmental arteries, totaling 31 branches. Based on the percentage of embolic cross-sectional area on the pulmonary artery, the embolism severity was calculated using the 5-grade score (grade 1: 0–25%; grade 2: 25–49%; grade 3: 50–74%; grade 4: 75–99%; and grade 5: 100%). The maximum embolism score of each patient was $31 \times 5 = 155$. The following expression was used for the calculation:

Mastora embolism index = $\frac{\sum(\text{embolism number} \times \text{embolism degree})}{155} \times 100\%$.

Measurements of right ventricular function parameters

Maximum short-axis diameter and ratio of the bilateral ventricle

The maximal right ventricular diameter (mRVd) and the maximal left ventricular diameter (mLVd) were measured perpendicular to the long axis of the left ventricle. The mRVd/mLVd ratio was calculated.

Maximum short-axis area and ratio of the bilateral ventricle

After observing and selecting the maximum four-chamber section, the maximal right ventricular area (mRVa) and the maximal left ventricular area (mLVa) were delineated manually along the wall of the ventricle. The values of the area were calculated automatically using CAT. The mRVa/mLVa ratio was calculated. When drawing the inner wall of the ventricle, attention should be paid to continuity and smoothness to avoid computer extraction failure.

Statistical analysis

SPSS software (version 13, SPSS Inc., IL, USA) was used for statistical analysis. Quantitative variables were expressed as mean \pm standard deviation (SD), and categorical variables were expressed as frequencies or percentages. The paired sample *t*-test or Mann-Whitney U test were employed to compare paired quantitative variables. Categorical variables were compared with the chi-square test. Pearson or Spearman correlation was used for correlation analysis. The intraclass correlation coefficient (ICC) was used for reliability analysis. The Bland-Altman plot displayed the average difference ± 1.96 SD as the consistency of the limits. *P* values less than 0.05 were considered statistically significant.

Results

Study participants

According to the inclusion and exclusion criteria, 30 patients (18 males and 12 females; mean age, 58.8 ± 14.4 years; range, 27–78 years) with acute PE were included in this study, 22 patients had multiple embolism on double pulmonary arteries, 2 had multiple embolism on double upper lobe arteries, 2 had multiple embolism on left upper lobe arteries, 1 had multiple embolism on the left pulmonary artery, 2 had multiple embolism on right pulmonary arteries and 1 had multiple embolism on the right lower lobe artery. The mean scan time of 30 patients was 5.47 seconds, and the mean effective dose was 5.46 ± 0.62 mSv.

Table 1. Comparison of manual and computer-aided time costs (Qanadli and Mastora scores).

Parameter	Manual interpretation	Computer-aided interpretation	Statistic	P value
Time costs (sec)	374.90±150.16	121.07±51.76	12.510*	<0.001

* *t* value.

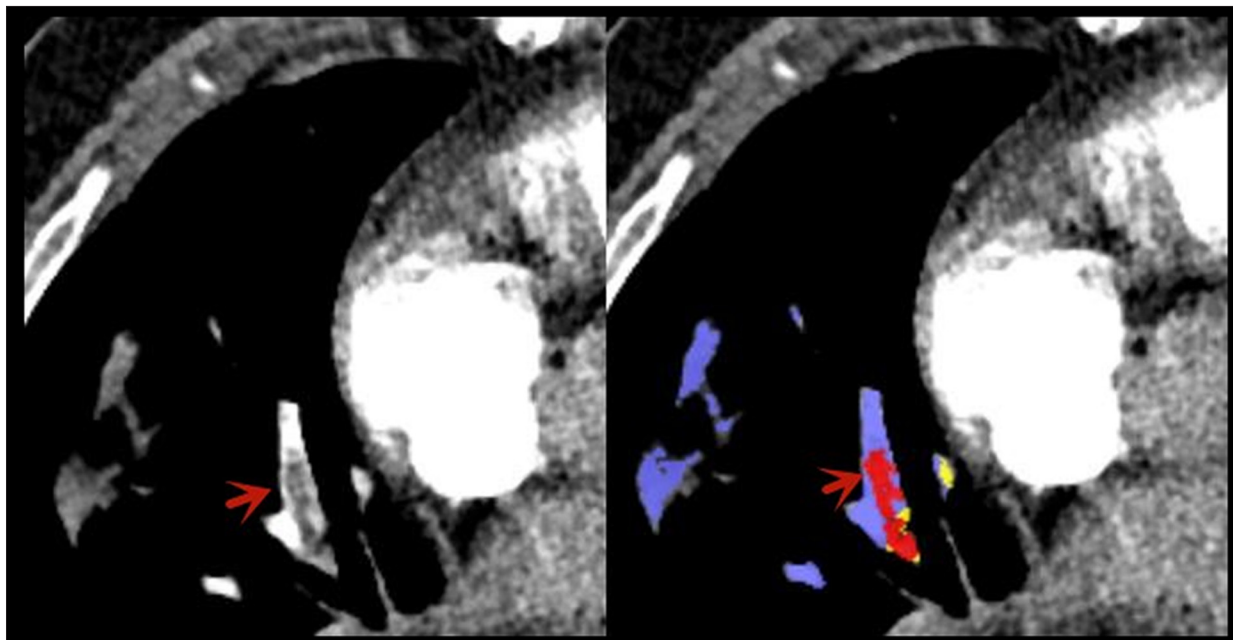


Figure 1. A 69-years-old female patient presented with chest pain and dyspnea for 4 hours. The Qanadli score was 75%, and the Mastora score was 41.93%. The red arrows showed the low-density filling defect of the right middle lobe medial segment artery. The pulmonary embolus was correctly identified by computer-aided detection (CAD).

Computer-aided detection

Comparison of manual and computer-aided time costs

The mean working time costs for Qanadli and Mastora scores obtained by manual and computer-aided interpretation was 374.90±150.16 s (range 168–630 seconds) and 121.07±51.76 seconds (range 49–248 s), respectively. The difference was statistically significant ($t=12.510$, $P<0.001$). The working time cost of computer-aided interpretation was less than that of manual interpretation (Table 1).

Repeatability of vascular obstruction index by manual and computer-aided interpretation

A total of 318 emboli were identified by computer-aided interpretation, of which 26 were false positive and 17 were false negative by manual interpretation (Figures 1–3). The true positive detection rate of acute PE by CAT was 87.2%. The difference between computer-aided and manual interpretation of the Qanadli score was 1.83±2.19; 96.7% (29 out of 30) of the measurements was within the 95% confidence interval (ICC=0.998).

The difference between computer-aided and manual interpretation of the Mastora score was 1.46±1.62; 96.7% (29 out of 30) of the measurements was within the 95% confidence interval (ICC=0.997). The differences between computer-aided and manual interpretation of Qanadli and Mastora scores are shown as Figure 4.

Computer-aided quantification analysis

Correlations of manual and computer-aided parameters

The statistical description of each parameter was summarized in Table 2. Moderately correlations were found between embolic volume and vascular obstruction index (VOI) ($r=0.635$ for Qanadli score, and 0.619 for Mastora score, all $P<0.001$), and between embolic mural length and VOI, Mildly correlations were found between embolism area/lumen area and VOI, and between number of emboli and VOI (Figure 5, Table 3).

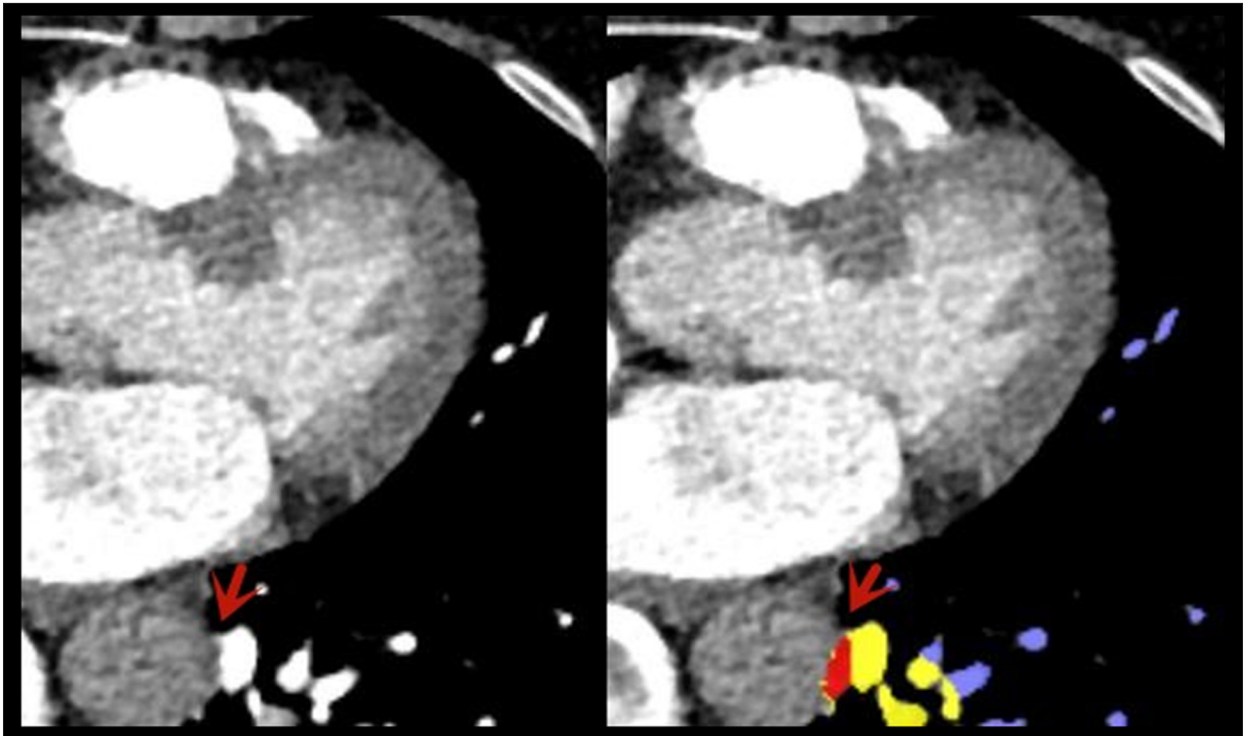


Figure 2. A 48-years-old male patient presented with dyspnea for 1 hour. In the left lower lobe of the lung, an error recognition occurred due to computer-aided detection (CAD) (red arrow). The vascular space is a common type of error made by CAD.

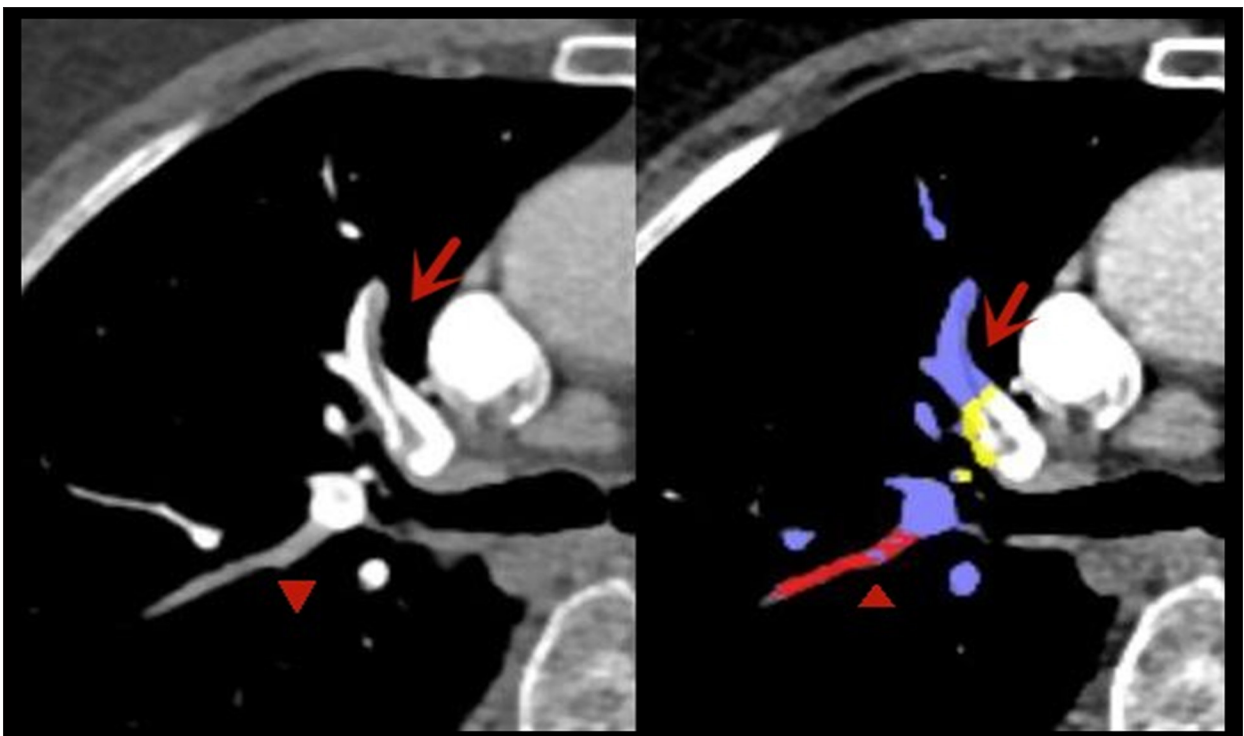


Figure 3. A 59-year-old female patient presented with chest pain for 6 hours. A low-density filling defect was seen in the right superior lobar artery, but this sign was ignored by computer-aided detection (CAD) (red arrow), resulting in a false-negative outcome. In a branch of the right superior lobar vein, an error recognition occurred due to the insufficient mixing of the contrast agent (red triangle), resulting in a false-positive outcome. A poorly filled vein is another common type of error made by CAD.

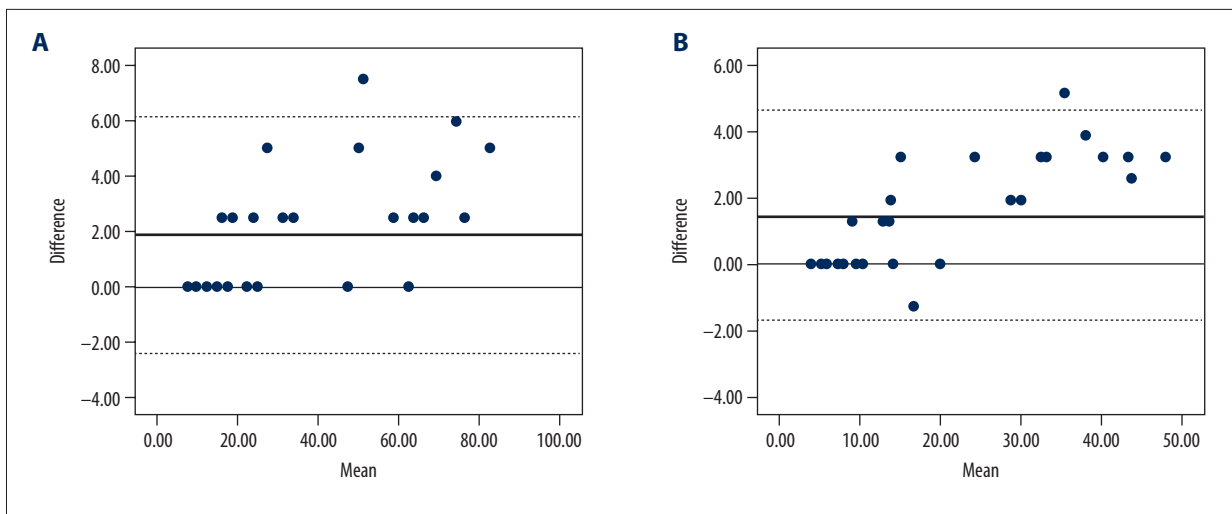


Figure 4. Bland-Altman plots of vascular obstruction index (VOI) for manual and computer-aided interpretation. For the Qanadli score (A), 96.7% of the measuring targets were inside the 95% agreement limits. For the Mastora score (B), 96.7% of the measuring targets were inside the 95% agreement limits.

Table 2. Manual and computer-aided indicators.

Parameters	Data
Qanadli score (%)	36.22±24.60
Mastora score (%)	20.45±14.56
Embolitic volume (mL)	9.10±6.62
Embolitic mural length (cm)	16.90±11.25
Embolism area/lumen area (%)	9.57±5.96
Number of emboli	10.70±4.74

Correlations of right ventricular function and computer-aided parameters

The mRVd/mLVD and mRVA/mLVA ratios were 1.23±0.38 and 1.22±0.56, respectively. Moderately positive correlations were found between right ventricular function and computer-aided parameters (Table 4).

Discussion

In this study, PE was identified automatically based on the “digital lung” detection system [19,20], by which the emboli could be automatically segmented, extracted, and quantitatively analyzed. Our results indicated that the computer-aided interpretation was better than manual interpretation in reducing time-costs, which was consistent with other previous studies [12,21]. In addition, the consistency between computer-aided and manual interpretation was satisfying. The computer-aided quantitative parameters were moderately correlated with routine VOI, suggested that the CAT had the advantages in rapid and

accurate diagnosis and assessment of acute PE and simplifying the work process. Several shortcomings of manual interpretation, such as strong subjectivity, diagnostic fatigue, inadequate observation, could be partly overcome by computer-aided technique. The CAT was a reliable method for assessing acute PE. In clinical practice, CAT helped radiologists reduce perceptual errors and workload in PE detection and quantitative analysis. Hence, the diagnostic results rarely depended on radiologists’ technical ability [21], and the disease severity could be quickly judged, and more time could be saved for clinical rational treatment [22].

Computer-aided detection and diagnosis system is more suitable for medical imaging than postprocessing technique and helps in qualitative and quantitative assessments to assist physicians in diagnosing and analyzing lesions [23]. CAT can identify abnormal signs in the scanning range and remind doctors to interpret these signs and provide an assessment of the disease type, severity, stage, and progression [23]. For PE, the computer-aided method could detect the emboli in the minimum branch of pulmonary vessels within the tolerance of CT spatial resolution, which greatly exceeded the limit of manual interpretation, so that the positive rate of PE is much higher [24,25]. Computer-aided quantitative method could not only obtain the location and embolism severity information but also quantify the volume and length of emboli accurately. The quantitative outcomes using CAT are perceptible and measurable units, which are more reliable and repeatable than those using manual interpretation [19,20].

The results showed that embolic volume and embolic mural length had a close relationship with Qanadli and Mastora scores. The severity of acute PE depended on the degree of

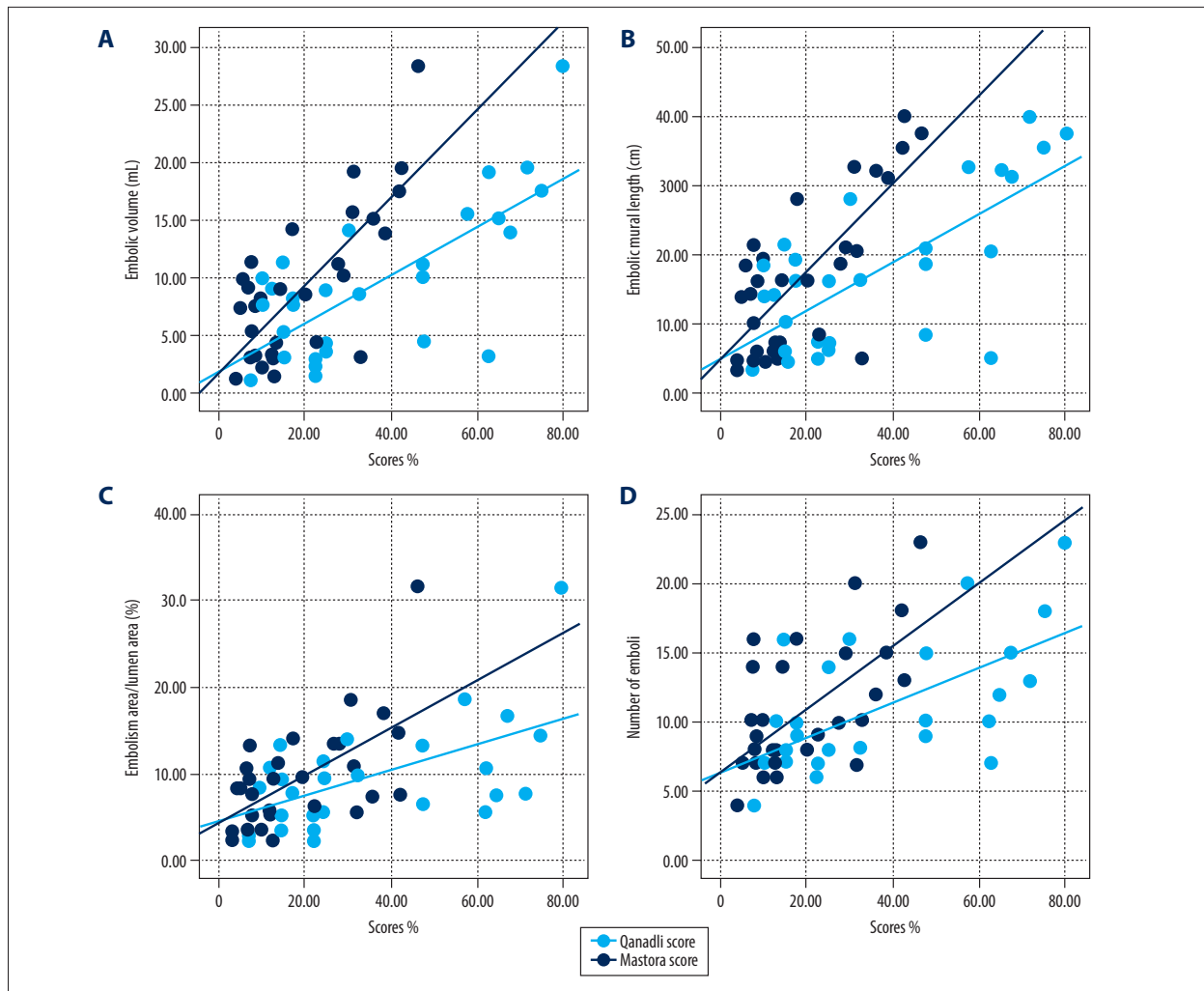


Figure 5. Scatter plots of the correlations for vascular obstruction index and computer-aided indicators, including embolic volume (A), embolic mural length (B), embolism area/lumen area (C), and number of emboli (D), which revealed moderate correlations (range of r values, 0.487–0.635), $P < 0.05$ (Spearman correlation). Qanadli score: light blue; Mastora score: deep blue.

Table 3. Correlations of manual and computer-aided indicators.

Parameters	Embolic volume	Embolic mural length	Embolism area/lumen area	Number of emboli
Qanadli score	0.635*	0.630*	0.505*	0.576*
Mastora score	0.619*	0.616*	0.487*	0.560*

Spearman correlation, * $P < 0.001$.

Table 4. Correlations of manual right ventricular function and computer-aided indicators.

Parameters	Embolic volume	Embolic mural length	Embolism area/lumen area	Number of emboli
mRVd/mLVD	0.520*	0.554*	0.233**	0.303**
mRVa/mLVA	0.645*	0.608*	0.512*	0.507*

Pearson correlation, * $P < 0.001$, ** $P > 0.05$.

embolism, hemodynamic changes, embolus morphology, and potential cardiopulmonary disease [26]. The volume of embolus was not affected by weight, which was considered as a stable indicator in reflecting the severity of embolism [27]. The increased volume of embolus might seriously affect hemodynamics [18]. The emboli attached to the pulmonary arterial wall directly blocked the blood–air exchange, resulting in the redistribution of pulmonary blood flow and imbalance in ventilation and blood flow [26]. With the increase of the embolic mural length, the blocked blood–air exchange area became larger, aggravating the embolism. However, the embolic volume and embolic mural length could not explain the impact of embolism on blood vessels completely. According to the equation $R=\Delta P/CO=8L\eta/\omega^4$, the vascular resistance was extremely sensitive to the change in the vascular diameter. Here, a new quantitative indicator was introduced in this study: embolism area/lumen area ratio. After acute PE, the changes in the pulmonary systolic pressure were closely related to the degree of pulmonary vascular obstruction [28]. With the increase in the severity of pulmonary vascular obstruction, pulmonary arterial pressure gradually increased, and a series of clinical symptoms appeared. The degree of embolism exceeding 85% would greatly increase the risk of sudden death [29]. Computer-aided quantification can quickly estimate the embolism area/lumen area ratio, providing reliable and repeatable evidence for clinical treatment.

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This study had some limitations. Firstly, the sample size was small, affecting the overall inference. Therefore, more cases were needed to improve statistical reliability. Secondly, CAT was determined by the image quality to a great extent. Therefore, image quality should be strictly controlled, and software recognition ability should be improved. Finally, the outcomes of computer-aided interpretation might be influenced by different levels of technology.

Conclusions

In conclusion, the quantitative analysis of PE via computer-aided technique was successfully performed, providing a satisfactory new indicator for the evaluation of disease severity. The quantification was helpful in improving the timeliness and reliability of VOI, thus providing a reliable basis for the assessment of disease severity.

Conflict of interest

None.

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