Original Article

Clot ratio, new clot burden score with deep learning, correlates with the risk stratification of patients with acute pulmonary embolism

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Background: Risk stratification for patients with acute pulmonary embolism (APE) is significantly important for treatment and prognosis evaluation. We aimed to develop a novel clot burden score on computed tomography pulmonary angiography (CTPA) based on deep learning (DL) algorithm for risk stratification of APE.

Methods: The study retrospectively enrolled patients newly diagnosed with APE in China-Japan Friendship Hospital consecutively. We collected baseline data and CTPA parameters, and calculated four different clot burden scores, including Qanadli score, Mastora score, clot volume and clot ratio. The former two were calculated by two radiologists separately, while clot volume and clot ratio were based on the DL algorithm. The area under the curve (AUC) of four clot burden scores were analyzed.

Results: Seventy patients were enrolled, including 17 in high-/intermediate-high risk and 53 in low-/intermediate-low risk. Clot burden was related to the risk stratification of APE. Among four clot burden scores, clot ratio had the highest AUC (0.719, 95% CI: 0.569–0.868) to predict patients with higher risk. In the patients with hemodynamically stable APE, only clot ratio presented statistical difference (P=0.046).

Conclusions: Clot ratio is a new imaging marker of clot burden which correlates with the risk stratification of patients with APE. Higher clot ratio may indicate higher risk and acute right ventricular dysfunction in

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patients with hemodynamically stable status.

Keywords: Acute pulmonary embolism (APE); risk stratification; clot burden; deep learning (DL)

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Introduction

Acute pulmonary embolism (APE) is an acute cardiovascular syndrome with thrombi obstruction of pulmonary artery trunk or branches. Timely risk stratification of patients with APE is essential, which could not only assist in appropriate treatment decision, but also in predicting the adverse prognosis at an early stage (1). Current European guideline for the management and prevention stratifies the patients with APE into four groups, including high-risk, intermediate-high risk, intermediate-low risk, and low risk based on the hemodynamic status, clinical parameters, comorbidities, laboratory testing, and imaging indicators (1).

Computed tomography pulmonary angiography (CTPA) is not only used to initiate a diagnostic workup for APE but also to supply the clot burden. Several studies have demonstrated the association between clot burden and risk stratification of APE. Hemodynamic status is more likely to deteriorate with increased clot burden (2,3). In addition, clot burden is significantly associated with right ventricular function, which can serve as an independent risk factor and predictor for poor prognosis in high-risk APE patients (3-6). Patients with a clot burden >60% tend to have a poor clinical prognosis, which may help to identify those who require more aggressive treatment strategies (e.g., thrombolytic therapy) (7). The most widely recognised prognostic risk stratification scores include the Pulmonary Embolism Severity Index (PESI), the simplified PESI (sPESI) and Bova scores (1). A new decision tree based on CTPA, with the diameter ratio of right ventricle to left ventricle (RVd/LVd) and clot burden area as the main indicators, could predict poor prognosis better than current risk stratification scores like BOVA score (8) which focuses on hemodynamic-stable patients. However, some studies showed that clot burden was not associated with the clinical severity of APE and mortality within 30 days (9-12).

At present, Qanadli score (13) and Mastora score (14) are commonly utilized to assess clot burden of APE. However, these scoring systems bear notable shortcomings, including being time-consuming and having the potential for subjective interpretation, which collectively limit their broader application in clinical practice. Liu *et al.* (15) developed a fully deep learning convolutional neural network (DL-CNN) model based on CTPA to diagnose APE. Moreover, the model can automatically calculate clot volume of APE on CTPA (16). The clot volume assessed by DL-CNN model was highly correlated with Mastora score and Qanadli score (16). However, hemodynamics and prognosis of APE are not only influenced by clot volume but also by the loss of pulmonary vessel beds. Therefore, our study aimed to establish a novel clot burden marker, defined as clot ratio, which is the ratio of clot volume to pulmonary artery volume shown by CTPA. We hypothesized the novel marker could be a better indicator to reflect the risk stratification of APE. We aimed to compare clot ratio with Qanadli score (13), Mastora score (14) and clot volume to study the correlation of clot ratio with clinical severity and prognosis of APE patients. We present this article in accordance with the STARD reporting checklist (available at https://qims.amegroups.com/article/view/10.21037/qims-23-322/rc).

Methods

Study cohort and design

This was a single-center observational study and performed with approval from the Chinese Clinical Trials Registry Center (http://www.chictr.org/en/; Registration number ChiCTR-OCH-14004929) and was approved by our institutional review board (No. 2022-KY-240). Individual consent was waived for this retrospective study. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). We consecutively enrolled patients who underwent the baseline CTPA and was diagnosed as APE from 1 January 2019 to 31 December 2019 in our hospital and completed 30-day follow-up. The exclusion criteria were listed as: (I) patients with incomplete clinical data or laboratory data; (II) baseline CTPA performed after treatment including anticoagulation and reperfusion therapy; (III) diagnosis including other pulmonary vascular diseases such as arteritis, chronic thromboembolic pulmonary

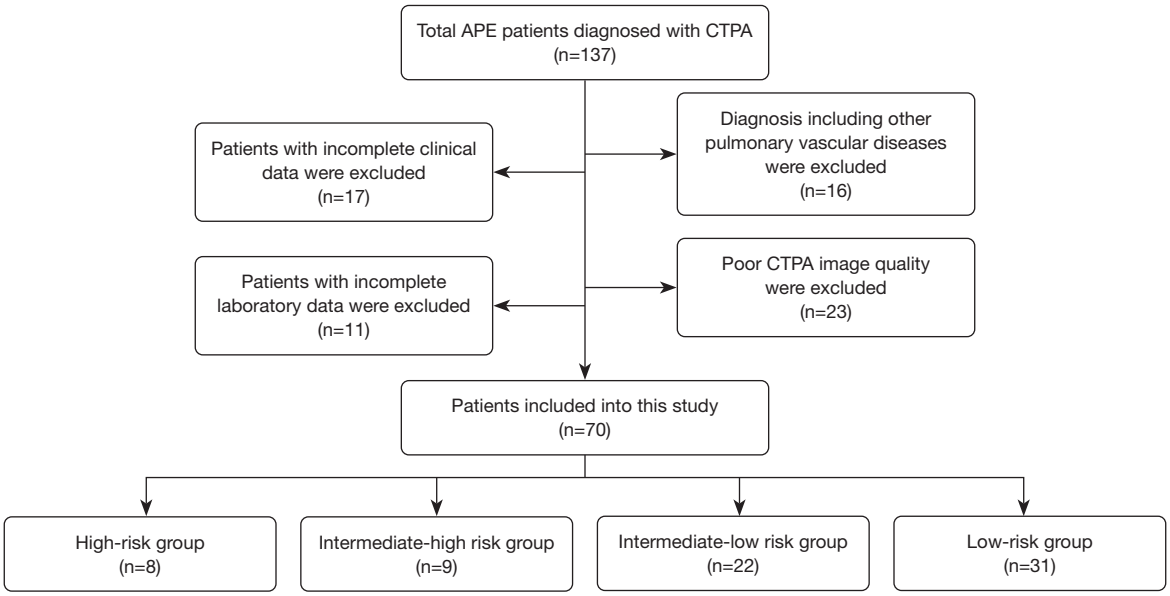

Figure 1 A flowchart detailing how participants were selected. APE, acute pulmonary embolism; CTPA, computed tomographic pulmonary angiography.

disease (CTEPD), chronic thromboembolic pulmonary hypertension (CTEPH), pulmonary artery sarcoma, fibrosing mediastinitis and pulmonary vascular malformation; (IV) non-diagnostic imaging quality of CTPA. The baseline clinical and laboratory information such as oxygenation index (PaO_2/FiO_2), sPESI, creatine kinase-MB (CK-MB), cardiac troponin T (cTnT), N-terminal pro-B-type natriuretic peptide (NT pro-BNP) and arterial oxygen saturation (SaO_2) were collected. According to 2019 European Guideline (1), patients were classified into high/intermediate-high risk group and intermediate-low/low risk group. *Figure 1* demonstrates the flowchart detailing how participants were selected.

CTPA protocol

CTPA was performed in the craniocaudal direction with multidetector computed tomography (CT) scanners (GE Revolution CT/256, GE Healthcare; Aquilion ONE/320, Canon Medical Systems, Otawara, Japan) by using a standard CTPA protocol. The CT scan parameters were as follows: the ball tube voltage of 100–120 kV, tube current 100–300 mAs, gantry rotation time 0.8 s, speed of CT table 39.37 mm/s, and the reconstructed section interval ranged from 1 to 1.25 mm. A mechanical injector was used for intravenous bolus injection of iopromide at a flow rate of 4.0 mL/s. For optimal intraluminal contrast enhancement, the automatic bolus-tracking technique with the region of interest positioned at the level of the main pulmonary artery with a threshold of 100 HU predefined threshold, and a fixed delay of 5 s was employed for data acquisition. The whole chest was craniocaudally scanned from lung apex to the lowest hemidiaphragm during a single breath-hold.

Measurements of clot ratio

Based on the previous method (15), clots and pulmonary arteries on CTPA were automatically segmented using U-Net and integration segmentation technique (InferRead CT Target Reconstruction version, T1.4; Infervision Medical Technology Co., Ltd., Beijing, China). The segmented lesions and pulmonary arteries were reviewed and corrected by two radiologists with 10- and 15-year experience. *Figure 2* illustrates the overall workflow: (I) clots and pulmonary artery segmentation and labeling; (II) clots and pulmonary artery reconstruction and volume calculation. Subsequently, the clot ratio was defined as the ratio of the total clot volume to the pulmonary artery volume. In this study, U-Net (15) was utilized to automatically perform the segmentation task and calculate the clot volume.

Both Qanadli score (13) and Mastora score (14) were independently evaluated by two radiologists with 5- and 7-year experience; they were blinded to the diagnosis and

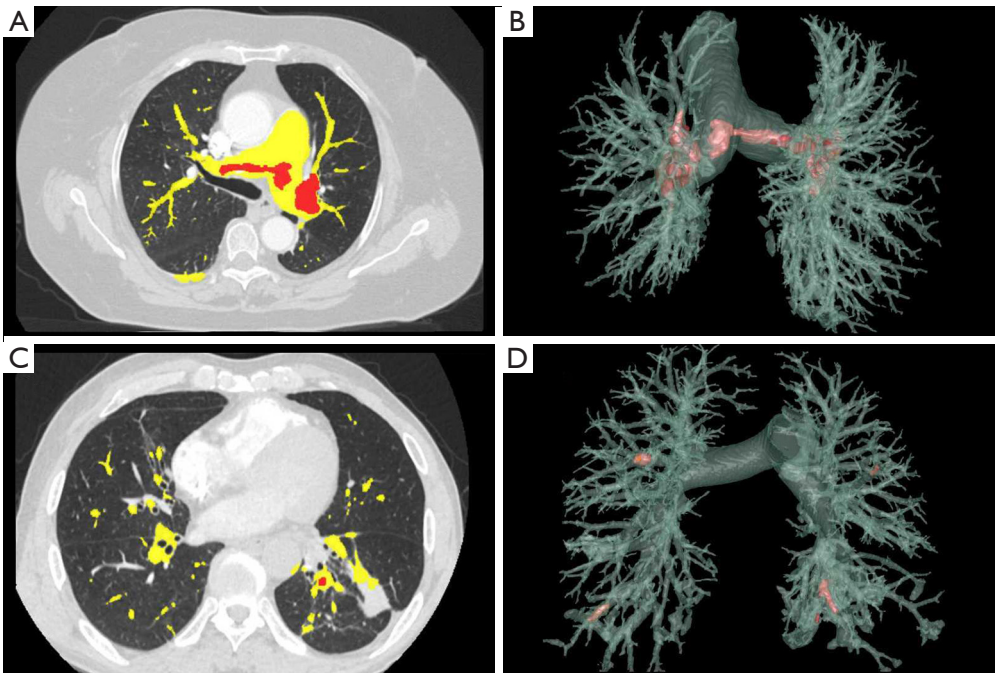

Figure 2 The identification, labeling, reconstruction of clot based on the DL-CNN model. (A) The identification and labeling of clot (red) in main pulmonary arteries (yellow); (C) the identification and labeling of clot (red) in segmental pulmonary arteries (yellow); (B,D) the reconstruction of clot (red) in the whole pulmonary arteries (green). The clot ratio was defined as the ratio of the total clot volume based on DL-CNN model to the pulmonary artery volume. (A) and (B) belong to the same patient with APE in the intermediate-high risk group; (C) and (D) belong to the same patient with APE in the low-risk group. DL-CNN, deep learning convolutional neural network; APE, acute pulmonary embolism.

clinical information. If the difference in scores between the two radiologists was within a certain range (≤5%), the average value was recorded. If the results diverged (>5%), the disagreement was resolved by consensus or the arbitration of a senior radiologist.

Other cardiovascular parameters on CTPA

In addition to Qanadli score and Mastora score, other cardiovascular parameters were also retrospectively collected. Diameters of right and left ventricle (RVd and LVd, seen in *Figure 3A*) were measured on axial CT images at the maximum short-axis between the inner surface of the free wall and the interventricular septum. Areas of right and left ventricle (RVa and LVa, seen in *Figure 3B*) were measured on axial CT images at the point of largest area. Subsequently, RVd/LVd and RVa/LVa were calculated. Besides, we measured the diameters of main pulmonary artery (MPAd) and the aortic artery (AAd). MPAd was measured as the maximum diameter on axial CT images, while the AAd was measured at the same level as MPAd (MPAd and AAd, seen in *Figure 3C*). Then the MPAd/AAd was calculated. Also, the spinal ventricular septal angle was measured (17), defined as an angle between the interventricular septum and the line joining the midpoint of the sternum to the thoracic vertebral spinous process (*Figure 3D*). Other qualitative indicators including pericardial effusion, pleural effusion, and pulmonary infarction on CT images were also collected.

Statistical analysis

All data were expressed as mean ± standard deviation (SD) or median (range) unless specified otherwise. Correlation analysis between clot burden scores and other parameters was evaluated by the Spearman's rank test. Correlation coefficient was defined as high when $0.5<|r|\leq 1$, medium when $0.3<|r|\leq 0.5$, and low when $|r|\leq 0.3$. Receiver operating characteristic (ROC) curves were used to analyze the best index for patients with higher risk APE. For statistical analyses, $P<0.05$ was considered significant. All statistical analyses were performed using SPSS 26.0 (SPSS

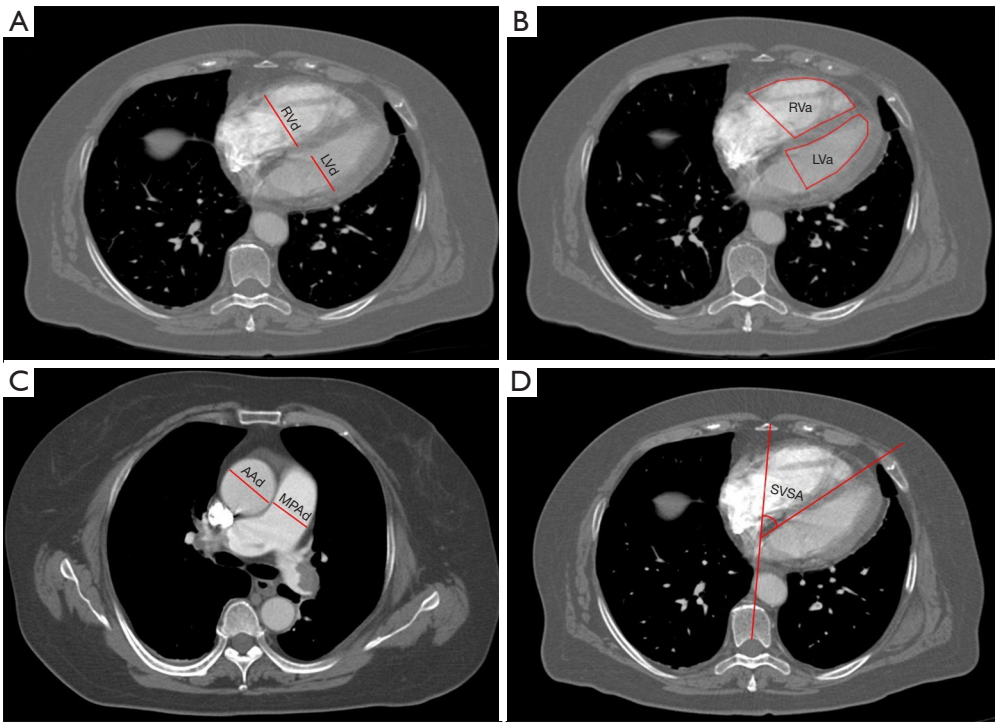

Figure 3 Right ventricular metrics measured on transversal CTPA. (A) RVd, LVd; (B) RVa, LVa; (C) AAd, MPAd; (D) SVSA. RVd, diameter of right ventricle; LVd, diameter of left ventricle; RVd/LVd, the diameter ratio of right ventricle to left ventricle; RVa, area of right ventricle; LVa, area of left ventricle; RVa/LVa, the area ratio of right ventricle to left ventricle; MPAd, diameter of main pulmonary artery; AAd, diameter of aorta; MPAd/AAd, the diameter ratio of main pulmonary artery diameter to aorta diameter; SVSA, spinal ventricular septal angle; CTPA, computed tomographic pulmonary angiography.

Inc., Chicago, IL, USA) and Medcalc (MedCalc Software Ltd for windows, v20.0.22).

Results

Baseline characteristics

Seventy patients diagnosed with APE [34 (48.5%) males, mean age, 65±15 years old] were enrolled, in whom 17 patients and 53 patients were respectively divided into high/intermediate-high risk group (24.3%) and intermediate-low/low risk group (75.7%). Baseline clinical information between two groups is shown in *Table 1*. APE patients in high/intermediate-high risk group were more often presented with hemodynamic instability (P<0.01) and worse clinical conditions (sPESI ≥1, P<0.01) compared with those in intermediate-low/low risk group, but without statistical difference in age and gender. As for laboratory indicators, patients with APE in the high/intermediate-high risk group had significantly higher CK-MB (P=0.005), cTnT (P=0.002), NT pro-BNP (P=0.001), and tended to have respiratory failure and a lower PaO_2/FiO_2 (P<0.01). D-dimer (P=0.732) and arterial oxygen saturation (P=0.39) were not associated with risk stratification.

Correlation analysis between clot ratio and other parameters

Clot ratio correlated with Qanadli score, Mastora score and clot volume (P<0.01, see Figure S1). *Table 2* indicates four clot burden scores correlated with PaO_2/FiO_2, RVd, RVd/LVd and RVa/LVa. There were medium correlations between clot ratio and RVd (r=0.319, P<0.01), RVa (r=0.323, P<0.01), RVa/LVa (r=0.378, P<0.01). Low correlations were found between clot ratio and RVd/LVd (r=0.272, P<0.05), AAd (r=0.249, P<0.05). Moderate correlations were noted between clot ratio and PaO_2/FiO_2 (r=–0.504, P<0.001), NT pro-BNP (r=0.406, P<0.01), which could indicate right ventricle dysfunction (RVD) and poor prognosis.

Clot burden and risk stratification

Table 3 shows that Qanadli score, clot volume and clot ratio

Table 1 Baseline data of the patients

Baseline data	Total (N=70)	High/intermediate-high risk (N=17)	Intermediate-low/low risk (N=53)	U/χ^2	P value
Baseline characteristics					
Age, years	65±15	71±15	63±15	NA	0.742
Gender (male)	34 (48.5)	5 (29.4)	29 (54.7)	3.300	0.069
Chronic heart failure	5 (7.1)	2 (11.7)	3 (5.6)	NA	0.589
Cancer	12 (17.1)	4 (23.5)	8 (15.0)	0.188	0.665
Hemodynamic instability	9 (12.8)	9 (52.9)	0	27.647	<0.05*
sPESI ≥1	38 (54.2)	16 (94.1)	22 (41.5)	14.355	<0.05*
Laboratory tests					
D-dimer (mg/L)	3.18 (1.61–11.16)	2.72 (2.30–7.88)	3.32 (1.53–11.11)	425.5	0.732
CK-MB (ng/mL)	1.55 (1.00–2.44)	2.50 (1.54–3.73)	1.37 (0.78–1.88)	247.5	<0.05*
cTnT (ng/mL)	0.02 (0.01–0.04)	0.04 (0.02–0.12)	0.01 (0.01–0.02)	143.5	<0.05*
NT pro-BNP (pg/mL)	210.0 (61.3–906.0)	1,313.5 (384.0–4,497.0)	151.0 (33.5–594.5)	143.0	<0.05*
SaO_2 (%)	95.4±2.6	95.8±2.6	95.2±2.6	NA	0.388
PaO_2/FiO_2	308±89	248±74	326±86	NA	<0.05*

Data are presented as mean ± standard deviation, median [interquartile range] or number (frequency). *, P<0.05 is statistically significant. sPESI, Simplified Pulmonary Embolism Severity Index; CK-MB, creatine kinase-MB; cTnT, cardiac troponin T; NT pro-BNP, N-terminal pro-B-type natriuretic peptide; SaO_2, arterial oxygen saturation; PaO_2/FiO_2, arterial oxygen tension/inspired oxygen fraction; NA, not applicable.

were significantly different between high/intermediate-high risk group and intermediate-low/low risk group (P<0.05), while other parameters were comparable (P≥0.05). ROC curves of the clot burden scores in predicting the risk stratification for patients with APE are shown in *Figure 4*. The clot ratio presented the highest efficacy [area under the curve (AUC) =0.719] for high/intermediate-high risk identification, followed by the clot volume (AUC =0.695), Qanadli score (AUC =0.688), and Mastora score (AUC =0.652). However, no statistically significant differences were found after a pairwise comparison of the AUCs among four clot burden scores (Table S1). Moreover, we did ROC curves to predict RVD, which was defined as the elevation of laboratory biomarkers (NT pro-BNP ≥600 pg/mL) or the signs of RVD on echocardiography or CTPA. We found clot ratio outperformed clot volume, Qanadli score and Mastora score in predicting RVD (AUC =0.755, *Table 4*).

Clot burden and 30-day prognosis

After 30 days of follow-up, a total of 6 patients experienced adverse events, including death, bleeding, and recurrence of APE. The causes of deaths included 3 APE cases, 1 cerebral hemorrhage case and 1 primary tumor case. In addition, one patient suffered from recurrent APE. *Table 5* indicates that there was a statistically significant difference in D-dimer between APE patients with and without adverse prognosis within 30 days. However, there was no statistically significant difference in clot burden between the two groups.

Subgroup analysis

Table 6 presents the subgroup analysis of four clot burden scores of hemodynamically stable patients in intermediate-high risk and intermediate-low/low risk. Among 70 patients, a total of 61 (87.1%) patients were hemodynamically stable. Compared to lower-risk APE patients, those in the intermediate-high risk group had higher clot ratios (P=0.046) but no significant difference in other clot burden scores. Moreover, the clot ratio was the most effective marker in predicting higher risk patients with stable APE (AUC =0.752, Table S2).

Discussion

In this study, we developed a novel imaging marker called

Table 2 Correlation analysis of clot burden with clinical and CTPA parameters

Clinical and CTPA parameters	Qanadli score	Mastora score	Clot volume	Clot ratio
Clinical data				
sPESI =0	−0.047	−0.050	0.013	0.074
Chronic heart failure	−0.220	−0.203	−0.103	−0.091
Active cancer	0.068	0.032	0.054	0.093
Laboratory test data				
D-dimer	0.310**	0.304*	0.120	0.157
CK-MB	0.126	0.105	0.048	0.033
cTnT	0.339**	0.322*	−0.065	−0.054
NT pro-BNP	0.436***	0.445***	0.249	0.406**
SaO_2	−0.119	−0.121	−0.118	−0.033
PaO_2/FiO_2	−0.328**	−0.300*	−0.432***	−0.504***
CTPA parameters				
RVd	0.291*	0.270*	0.297*	0.319**
LVd	−0.010	−0.087	−0.060*	−0.072
RVd/LVd	0.272*	0.288*	0.237*	0.272*
RVa	0.248*	0.235	0.306*	0.323**
LVa	0.010	−0.073	−0.041	−0.116
RVa/LVa	0.275*	0.326**	0.281*	0.378**
MPAd	0.093	0.119	0.123	0.220
AAd	0.043	0.113	0.243*	0.249*
MPAd/AAd	−0.011	−0.037	−0.096	−0.018
SVSA	0.154	0.149	0.118	0.128
Pulmonary infraction	0.222	0.247	0.142	0.194
Pericardial effusion	0.065	0.070	−0.059	0.029
Pleura effusion	−0.046	0.020	0.149	0.039

*, P<0.05; **, P<0.01; ***, P<0.001. CTPA, computed tomography pulmonary angiography; sPESI, Simplified Pulmonary Embolism Severity Index; CK-MB, creatine kinase-MB; cTnT, cardiac troponin T; NT pro-BNP, N-terminal pro-B-type natriuretic peptide; SaO_2, arterial oxygen saturation; PaO_2/FiO_2, arterial oxygen tension/inspired oxygen fraction; RVd, diameter of right ventricle; LVd, diameter of left ventricle; RVd/LVd, the diameter ratio of right ventricle to left ventricle; RVa, area of right ventricle; LVa, area of left ventricle; RVa/LVa, the area ratio of right ventricle to left ventricle; MPAd, diameter of main pulmonary artery; AAd, diameter of aorta; MPAd/AAd, the diameter ratio of main pulmonary artery diameter to aorta diameter; SVSA, spinal ventricular septal angle.

"clot ratio" for evaluating clot burden in APE patients. Among the four clot burden scores, clot ratio demonstrated the most reliable performance in predicting higher-risk patients and stratifying prognosis. Additionally, clot ratio was the only marker that exhibited a statistically significant difference among hemodynamically stable patients, making it valuable for identifying individuals with potential deterioration. This suggests that clot ratio has the potential as a risk stratification and prognosis assessment tool for APE. A DL model based on the U-Net framework can be employed to automatically segment clots and the pulmonary artery from CTPA images.

Table 3 CTPA parameters of the patients with APE between high/intermediate-high risk group and low/intermediate-low risk group

CTPA parameters	High/intermediate-high risk (N=17)	Intermediate-low/low risk (N=53)	$U/t/\chi^2$	P value
Clot burden scores				
Qanadli score (%)	42.5 (27.5–50.0)	27.5 (10.0–40.0)	281.0	0.020*
Mastora score (%)	34.2 (23.2–49.0)	18.7 (5.8–29.7)	313.5	0.061
Clot volume (mL)	6.5 (3.7–8.1)	2.0 (0.6–5.9)	275.0	0.016*
Clot ratio (%)	12.0 (8.0–23.0)	3.0 (1.0–10.0)	253.5	0.007*
RVd (mm)	33.8±8.0	32.7±7.16	0.503	0.616
LVd (mm)	34.6±7.8	33.6±7.7	0.470	0.642
RVd/LVd	1.0±0.3	1.0±0.3	0.066	0.948
RVa (mm^2)	16.2±6.5	15.8±4.8	0.296	0.768
LVa (mm^2)	17.9±5.6	17.5±4.9	0.308	0.759
RVa/LVa	0.8 (0.7–0.9)	0.8 (0.7–1.2)	379.0	0.33
MPAd (mm)	28.5±4.6	29.0±5.4	0.396	0.694
AAd (mm)	34.0±4.7	35.6±5.8	1.020	0.311
MPAd/AAd	0.8±0.1	0.8±0.2	0.239	0.812
Septal angle (°)	44.0±8.5	45.1±10.6	0.057	0.959
Pulmonary infraction, n (%)	5 (29.4)	11 (20.7)	0.166	0.683
Pericardial effusion, n (%)	2 (11.7)	5 (9.4)	<0.001	>0.99
Pleural effusion, n (%)	7 (41.1)	17 (32.0)	0.473	0.492

Data are presented as mean ± standard deviation, median (interquartile range) or number (frequency). *, P<0.05 is statistically significant. CTPA, computed tomography pulmonary angiography; RVd, diameter of right ventricle; LVd, diameter of left ventricle; RVd/LVd, the diameter ratio of right ventricle to left ventricle; RVa, area of right ventricle; LVa, area of left ventricle; RVa/LVa, the area ratio of right ventricle to left ventricle; MPAd, diameter of main pulmonary artery; AAd, diameter of aorta; MPAd/AAd, the diameter ratio of main pulmonary artery diameter to aorta diameter.

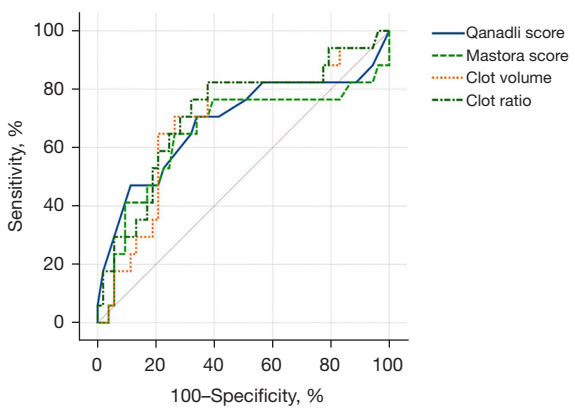

Figure 4 Performance of clot burden scores for discriminating high/intermediate-high patients from low/intermediate-low patients as indicated by ROC curves. ROC, receiver operating characteristic.

The clot ratio, calculated as the ratio of clot volume to pulmonary artery volume on CTPA, serves as a measure of clot severity. Compared with Qanadli and Mastora score, the evaluation of clot volume and clot ratio is independent of radiologists' experience. The concept of clot volume is limited in its perspective as it exclusively contemplates the absolute size of the embolus, neglecting the extent of impairment to the vascular bed volume it incurs. In contrast, the clot ratio, which is calculated by dividing the clot volume by the pulmonary arterial volume, offers a more comprehensive evaluation. It takes into account both the size of the embolus and its impact on the overall vascular bed, providing valuable insights into the severity of the clot. This measure inherently encapsulates both the occlusive properties of the clot and its consequential impact on perfusion, thus transcending mere quantification of clot volume.

Table 4 Comparison of four clot burden scores to predict RVD in patients with APE

Clot burden scores	AUC (95% CI)	Sensitivity	Specificity	Threshold
Qanadli score (%)	0.713 (0.592–0.815)	0.781	0.605	22.5
Mastora score (%)	0.715 (0.595–0.817)	0.781	0.605	16.1
Clot volume (mL)	0.742 (0.624–0.839)	0.625	0.842	5.5
Clot ratio (%)	0.755 (0.637–0.850)	0.500	0.947	0.1

RVD, right ventricular dysfunction; APE, acute pulmonary embolism; AUC, area under the curve; CI, confidence interval.

Table 5 Comparison of laboratory tests and CTPA metrics in APE patients with 30-day adverse prognosis

Laboratory tests and CTPA metrics	With 30-day adverse prognosis (N=6)	Without 30-day adverse prognosis (N=64)	U/χ^2	P value
Laboratory tests				
cTnT (ng/mL)	0.03 (0.01–0.96)	0.02 (0.01–0.03)	129.0	0.352
D-dimer (mg/L)	15.6 (7.0–20.0)	2.45 (1.39–6.34)	63.0	0.007*
CK-MB (ng/mL)	3.61 (1.06–9.06)	1.55 (1.01–2.04)	118.0	0.121
NT pro-BNP (pg/mL)	710.0 (138.8–6,071.8)	181.0 (33.5–811.0)	117.0	0.225
SaO_2 (%)	96.9 (95.9–98.8)	96.0 (93.0–97.0)	105.5	0.088
PaO_2/FiO_2 (mmHg)	313.1±54.8	307.7±11.0	–	0.890
CTPA metrics				
Qanadli score (%)	18.8 (8.1–33.9)	30.0 (10.6–45.0)	144.5	0.317
Mastora score (%)	12.3 (3.5–21.8)	23.2 (6.5–44.3)	119.5	0.128
Clot volume (mL)	1.3 (0.2–6.7)	3.2 (0.8–7.0)	142.5	0.294
Clot ratio (%)	3.0 (0–16.0)	5.0 (1.0–13.0)	165.0	0.571
RVd/LVd	0.8 (0.6–1.0)	0.9 (0.8–1.1)	113.0	0.097
RVa/LVa	0.8 (0.8–0.9)	0.8 (0.7–1.0)	181.0	0.817
MPAd (mm)	29.3 (27.4–30.8)	28.1 (24.9–31.5)	168.0	0.615
MPAd/AAd	0.8 (0.7–0.9)	0.8 (0.7–0.9)	179.0	0.785
SVSA (°)	44.7±12.9	44.1±9.9	NA	0.884
Pericardial effusion, n (%)	0	7 (10.9)	0.02	0.877
Pleural effusion, n (%)	2 (33.3)	22 (34.4)	–	1.000
Pulmonary infarction, n (%)	0	16 (25.0)	–	0.325

Data are presented as mean ± standard deviation, median (interquartile range) or number (frequency). *, P<0.05 is statistically significant. CTPA, computed tomography pulmonary angiography; APE, acute pulmonary embolism; cTnT, cardiac troponin T; CK-MB, creatine kinase-MB; NT pro-BNP, N-terminal pro-B-type natriuretic peptide; SaO_2, Arterial oxygen saturation; PaO_2/FiO_2, arterial oxygen tension/inspired oxygen fraction; RVd/LVd, the diameter ratio of right ventricle to left ventricle; RVa/LVa, the area ratio of right ventricle to left ventricle; MPAd, diameter of main pulmonary artery; MPAd/AAd, the diameter ratio of main pulmonary artery diameter to aorta diameter; SVSA, spinal ventricular septal angle; NA, not applicable.

Table 6 Clot burden scores in patients with hemodynamically stable APE

Clot burden scores	Total (N=61)	High/intermediate-high risk (N=8)	Intermediate-low/low risk (N=53)	P value
Qanadli score (%)	26.3±17.3	33.4±20.3	25.2±16.7	0.306
Mastora score (%)	22.1±18.4	28.9±20.1	21.0±18.1	0.332
Clot volume (mL)	4.6±5.6	6.8±4.0	4.3±5.8	0.146
Clot ratio (%)	7.0±8.4	13.0±7.6	7.0±8.3	0.046*

Data are presented as mean ± standard deviation. *, P<0.05 is statistically significant. APE, acute pulmonary embolism.

Although clot burden could not be used directly as an index to assess right heart failure or death, the current study reported that clot burden is highly correlated with right heart dysfunction and risk stratification of APE (18). Thrombi-induced mechanical blockage, combined with neurohumoral constituents and hypoxic consequences, has the potential to elevate pulmonary vascular resistance and instigate pulmonary hypertension through a reflexive constriction of the pulmonary artery. Further, right ventricular afterload could raise up rapidly with increased right ventricular wall tension to a certain degree, causing acute pulmonary heart disease and right ventricular enlargement. All these changes lead to RVD, reduced returned blood volume and stagnant venous system, contributing to systemic hypoxemia and type I respiratory failure in patients (19).

Van der meer *et al.* noted the value of clot burden and RVd/LVd in predicting mortality in patients with hemodynamically stable APE (20). Akhoundi *et al.* found that clot burden was strongly correlated with RVd/LVd (r=0.548, P<0.001), suggesting that clot burden could be used to predict the occurrence of RVD in patients with APE (21). Praveen Kumar *et al.* (22) concluded that clot burden was a strong independent predictor of RVD in APE patients, and it was strongly associated with increased morbidity and mortality, suggesting that patients in need of aggressive therapy could be selected by precise risk stratification using clot burden.

Our study was in accordance with previous studies. We found correlations between clot burden and PaO_2/FiO_2, RVd, RVa, and RVa/LVa in patients with APE, suggesting that higher clot burden may lead to higher possibility of respiratory failure or RVD by affecting respiratory or cardiac function. Given that clot burden demonstrated significant predictive accuracy for high/intermediate-high risk APE (AUC ranging from 0.652 to 0.719), it is expected to be included in the risk stratification of APE to assist in early recognition of illness exacerbation.

Klok *et al.* (23) found that APE patients with high concentrations of B-type natriuretic peptide (BNP) were at higher risk of complicated in-hospital course and death. Lankeit *et al.* (24) identified the prognostic value of NT pro-BNP and suggested NT pro-BNP should be used in combination with a clinical score and an imaging procedure for detecting RVD. In our study, clot ratio was closely correlated with PaO_2/FiO_2 and NT pro-BNP, indicating that it might serve as a more accurate and reliable metric for gauging illness severity and right heart function. Moreover, RVd/LVd, the well-recognized CTPA parameter for evaluating right heart function in APE patients, also displayed a correlation with clot ratio, which underscores the potential viability of clot ratio as an effective indicator of right heart function.

In total, clot ratio may have higher clinical application value than previous clot burden score. As a new score based on the DL model, clot ratio has the advantages of being automated, real-time and time-saving, as well as being more accurate and individualized in the assessment of each APE patient. Traditional manual scores such as the Mastora score and Qanadli score are highly reproducible yet complex and time-consuming, leading to less application in daily practice. In addition, a previous study found that 3D measurement of clot burden was not only more accurate, but also had better prediction of risk stratification and short-term adverse prognosis of APE patients, especially on the occurrence of RVD and shock (25).

In subgroup analysis, we found that clot ratio was significantly higher in hemodynamically stable APE patients, indicating a possible high proportion of patients with impaired right heart function who were at risk of faster deterioration. Therefore, it is necessary and valuable to further specify the risk stratification of current intermediate-high risk group, and clot ratio might be a promising tool.

Our study has some limitations. First, our study was a single-center retrospective cohort study with small sample size, which may have influence on the establishment of DL

model and collection of poor outcomes to some degree. Second, echocardiography data were not compared with CTPA parameters in our study. Third, our CT protocol did not incorporate the ECG-gated scanning technique, creating a limitation for the measurement of cardiac chambers. In the future, prospective studies with larger samples and more detailed baseline data are needed to refine the clot ratio and explore the significance of the novel index in the risk stratification and prognosis of APE patients. Meanwhile, trends of clot ratio in APE patients and incidence of residual thrombus should be explored to investigate the correlation between clot burden especially those with poor prognosis of APE in the long-term follow up.

Conclusions

With the DL model, the clot ratio demonstrated more accurate prediction of APE patients at higher risk, especially within the hemodynamically stable group. Furthermore, a significant correlation between clot ratio, PaO_2/FiO_2, and right ventricular load indicates its potential use as a predictive tool for acute RVD.

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Footnote

Reporting Checklist: The authors have completed the STARD reporting checklist. Available at https://qims.amegroups.com/article/view/10.21037/qims-23-322/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-23-322/coif). Author HK and RZ are employees of the Institute of Advanced Research, Infervision Medical Technology Co., Ltd. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study complied with the Declaration of Helsinki (as revised in 2013) and was approved by the Institutional Ethics Committee of China-Japan Friendship Hospital (No. 2022-KY-240). Informed consent was waived for this retrospective study.

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Supplementary

Appendix 1 Sample size calculation

In the phase of designing, we calculated the minimal sample size based on the reference to the preliminary study (15) and the sample size calculation formula. The formula is as follows.

$$n = \left(\frac{z_{1-\alpha/2} * \sqrt{p*(1-p)}}{\delta} \right)^2$$

In the formula, α=0.05, δ=0.1, sensitivity =0.9, specificity =0.8. Therefore, the final number of total sample size was 62. Our sample size (n=70) fit the minimal requirement.

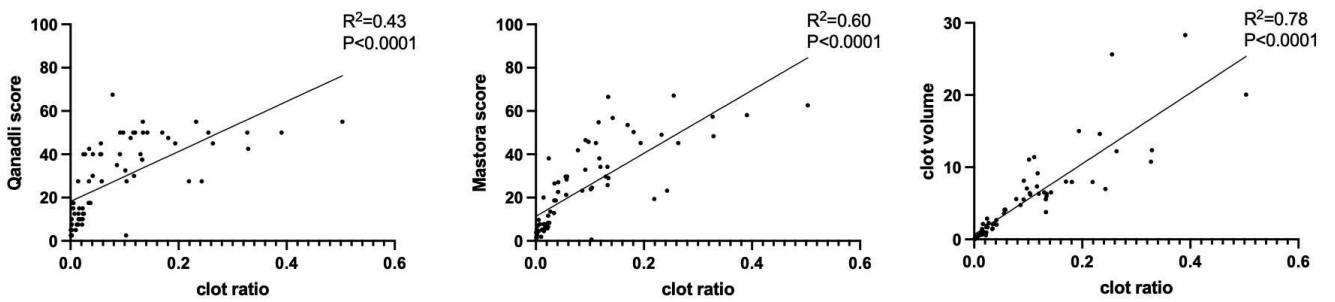

Figure S1 Correlation analysis of clot ratio with Qanadli score, Mastora score and clot volume.

Table S1 AUC of the clot burden in predicting the risk stratification of patients with APE

Clot burden scores	AUC (95% CI)	Sensitivity	Specificity	Threshold
Qanadli score	0.688 (0.520–0.857)	0.706	0.660	36.0
Mastora score	0.652 (0.529–0.762)	0.647	0.736	29.4
Clot volume	0.695 (0.545–0.844)	0.824	0.623	3.2
Clot ratio	0.719 (0.569–0.868)	0.824	0.623	5.0

AUC, area under the curve; CI, confidence interval; APE, acute pulmonary embolism.

Table S2 AUC of the clot burden scores to predict risk stratification in hemodynamically stable patients with APE

Clot burden scores	AUC (95% CI)	Sensitivity	Specificity	Threshold
Qanadli score	0.613 (0.480–0.735)	0.625	0.660	36.2
Mastora score	0.603 (0.469–0.726)	0.750	0.604	22.9
Clot volume	0.731 (0.602–0.837)	0.750	0.792	6.3
Clot ratio	0.752 (0.625–0.854)	0.875	0.717	0.1

AUC, area under the curve; APE, acute pulmonary embolism; CI, confidence interval.

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