European Journal of Radiology 82 (2013) 1236–1239

Contents lists available at SciVerse ScienceDirect

European Journal of Radiology

journal homepage: www.elsevier.com/locate/ejrad

Logistic regression model for identification of right ventricular dysfunction in patients with acute pulmonary embolism by means of computed tomography

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ARTICLE INFO

Article history:
Received 29 August 2011
Received in revised form 3 January 2013
Accepted 4 February 2013

Keywords:
Pulmonary embolism
Computed tomography
Right ventricular dysfunction

ABSTRACT

Purpose: Diagnosis of right ventricular dysfunction in patients with acute pulmonary embolism (PE) is known to be associated with increased risk of mortality. The aim of the study was to calculate a logistic regression model for reliable identification of right ventricular dysfunction (RVD) in patients diagnosed with computed tomography pulmonary angiography.

Material and methods: Ninety-seven consecutive patients with acute pulmonary embolism were divided into groups with and without RVD basing upon echocardiographic measurement of pulmonary artery systolic pressure (PASP). PE severity was graded with the pulmonary obstruction score. CT measurements of heart chambers and mediastinal vessels were performed; position of interventricular septum and presence of contrast reflux into the inferior vena cava were also recorded. The logistic regression model was prepared by means of stepwise logistic regression.

Results: Among the used parameters, the final model consisted of pulmonary obstruction score, short axis diameter of right ventricle and diameter of inferior vena cava. The calculated model is characterized by 79% sensitivity and 81% specificity, and its performance was significantly better than single CT-based measurements.

Conclusion: Logistic regression model identifies RVD significantly better, than single CT-based measurements.

1. Introduction

Pulmonary embolism (PE) is the third most common of the "great cardiovascular killers" after myocardial infarction and stroke [1]. As opposed to the two others, the clinical symptoms and signs in patients with PE may mimic multiple other conditions, cardiovascular or pulmonary. Imaging methods have become one of the cornerstones in the diagnostic process for this group of patients.

Wide accessibility of multidetector computed tomography (MDCT), full chest submilimiter coverage with one breathhold, concurrent assessment of pulmonary parenchyma and mediastinum, and, last but not least, chance of providing alternative diagnosis, have lead to MDCT being the gold standard in the imaging of suspected PE.

Visualization of the heart chambers and the mediastinal vessels allowed signs of right ventricular dysfunction (RVD) to be assessed during the same computed tomography pulmonary angiography (CTPA) performed to confirm presence of PE.

Even in patients with hemodynamically stable PE, RVD is associated with an increased risk of mortality. However, in normotensive patient, identification of RVD requires additional testing, including echocardiography or biomarkers [2].

Multiple CT signs of RVD were evaluated and reported in recent years, with different cutoff values, sensitivities and specificities reported. Therefore, the aim of the study was to generate a highly accurate predictive model composed of multiple measurements for the identification of RVD in the course of acute PE by computed tomography pulmonary angiography (CTPA).

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http://dx.doi.org/10.1016/j.ejrad.2013.02.004

2. Material and methods

The institutional ethical review board approved the protocol of the study with a waiver of informed consent (Decision No.: KE-0254/41/2011). For the purpose of this retrospective study, we identified 97 patients, in whom echocardiographic examination with pulmonary artery systolic pressure (PASP) assessment was performed within the 12 h of the CT scan. The CTPA studies were performed with 64-row VCT scanner (GE Medical Systems), with a standard protocol used at our institution, which includes craniocaudal scanning of the chest, 64×0.625 mm collimation, slice thickness 0.625 mm, continous reconstruction. SmartPrep protocol was used for adjustment of the injection time of average 70 mL (1 mL/kg) of iodinated contrast medium (Ultravist 370, Bayer Healthcare, Germany), which was administered at a flow rate of 4–5 mL/sec by automatic injector, followed by 40 mL NaCl bolus.

Raw tomographic data was imported into the OsiriX software. The exams were reviewed by two readers in consensus. The readers were blinded to PASP values.

Obstruction of pulmonary arteries was scored according to Qanadli et al. [3]. Maximum short axis of the right (RV) and left ventricle (LV) were measured at a four chamber view, according to Quiroz et al. [4]. The diameter of the pulmonary artery (PA) was measured proximal to its bifurcation; diameter of superior vena cava (SVC) was measured at the level of arch of azygos vein; and diameter of inferior vena cava (IVC) in its thoracic part. Dimensions of each mediastinal vessel were measured in a plane perpendicular to a long axis of the vessel, with respect to the largest observed diameter. RV/LV ratio was calculated. Diameter of coronary sinus (CS) was measured in the axial plane, proximal to its opening, as described elsewhere [5]. Position of the interventricular septum was evaluated and classified as normal or convex toward left ventricle. Contrast medium reflux into the IVC was also recorded.

RVD was defined as echocardiographically measured PASP value > 30 mmHg, as described elsewhere [6]; based on this value, patients were divided into RVD(−) and RVD(+) groups (PASP ≤ 30 mmHg and >30 mmHg, respectively).

Statistical analysis was performed with SPSS 16.0, SPSS Inc., Chicago, IL. Quantitative parameters are presented as minimal, maximal and median values. Qualitative parameters are presented as numbers and percentages.

χ^2 test was used to compare qualitative data, and the Mann–Whitney test for quantitative data. Values of $p \leq 0.05$ were considered to be significant. The area under ROC curve (AUC) and 95% confidence limits were used to assess predictive power for RVD of all parameters that differed significantly between the study groups. Cutoff values with best sensitivity to specificity ratio were calculated.

In order to find the best combination of CT-based indicators of RVD, a multivariate model was built by means of logistic regression analysis. A backward conditional stepwise method was used to select the parameters which were included in the final model. In this process, the weakest predictors of RVD are deleted starting with the least significant ones. The parameters which remain in the final model are independently associated with the risk of RVD. Values predicted by the model belong to $\langle 0, 1 \rangle$ interval, and represent probability of RVD. The model is as follows [7]:

$$p = \frac{1}{1 + e^{-z}},$$

where e is a base of natural logarithm, =2.71828..., and z is a linear combination of x_i variables and their estimators b_i included in the model:

$$z = b_0 + b_1 x_1 + b_2 x_2 + \ldots + b_n x_n.$$

Table 1
Characteristics of the study population in patients with and without right ventricular dysfunction: RVD(+) and RVD(−), respectively. Numbers represent median, minimal and maximal values, and (*) absolute value and percentage for qualitative values.

	RVD(−) PASP ≤ 30 mmHg; n = 46	RVD(+) PASP > 30 mmHg; n = 51	p
Age [years]	71.5 (27–91)	67 (22–92)	NS
BMI	26.79 (23.23–38.51)	26.57 (19.15–34.29)	NS
Systolic BP [mmHg]	119 (85–168)	124 (70–163)	NS
Heart rate [bpm]	94 (60–125)	96 (48–144)	NS
PASP [mmHg]	25 (18–30)	45 (32–95)	<0.001
Length of hospitalization [days]	9 (1–31)	12 (1–44)	0.03
ICU admission (*)	21 (46%)	34 (67%)	0.04
Mortality (*)	4 (8.7%)	7 (13.7%)	NS

The model-based probability of >0.5 classified the patient as RVD(+). The Hosmer–Lemeshow goodness-of-fit test was used to evaluate the overall fit of the final model. To compare the accuracy of the proposed model with single CT-based parameters and calculate specificity, sensitivity and accuracy of the used parameters, ROC curves were constructed, and areas under the curve (AUC) were compared with Aabel 3 package (Gigawiz Ltd., Tulsa, OK).

3. Results

The study group consisted of 97 patients, median age 69 years (range: 22–92). 46 patients were included in group RVD(−) and 51 patients in RVD(+) group. Patients characteristics are presented in Table 1. No significant differences of frequency of DVT, immobilization, surgery, or history of malignancy were observed between the groups. RVD(+) group was characterized by a significantly longer hospitalizations, as well as more frequent ICU admissions.

Results of comparative analysis of the CT-based parameters and the probabilities calculated by the logistic regression model are presented in Table 2.

Details of logistic regression analysis are presented in Table 3, and the obtained model for identification of RVD is as follows:

$$z = -8.361 + 0.132 \times \text{Obstruction score} + 0.078 \times \text{RV} + 0.094 \times \text{IV}$$

The highest sensitivity and specificity at assumed risk of RVD of 50% for the obtained predictive model were 0.79 and 0.81, respectively. Analysis of the areas under the ROC curves (AUC) showed, that the largest AUC, sensitivity and specificity were observed for the model-calculated probability, as the area was significantly larger (p = 0.02) than for any of the single CT-based parameters (AUC = 0.860, 95% CI: 0.802–0.917).

Measurements used for the final model are presented in Fig. 1, and the ROC curve of RVD probability calculated by the model is shown in Fig. 2. Hosmer–Lemeshow test showed value of 3.065 (p = 0.930), which shows a good fit of the model.

4. Discussion

Short-term prognosis of PE depends on the hemodynamic status of the patient as well as comorbidities [8]. Therefore, identification of RVD in PE patients is crucial for the prognosis and treatment [2]. However, the number of suggested CT-based signs of RVD is large, and different cutoffs, sensitivities and specificities are reported.

Pulmonary obstruction index according to Qanadli et al. has been linked to RVD since its introduction [3], and its feasibility has been confirmed in more recent papers by Collomb et al. [9] and van der Meer et al. [10]. Furthermore, the Qanadli index has been linked to mortality in PE patients, including a significantly higher 2-weeks mortality rate in those with an obstruction score >60%

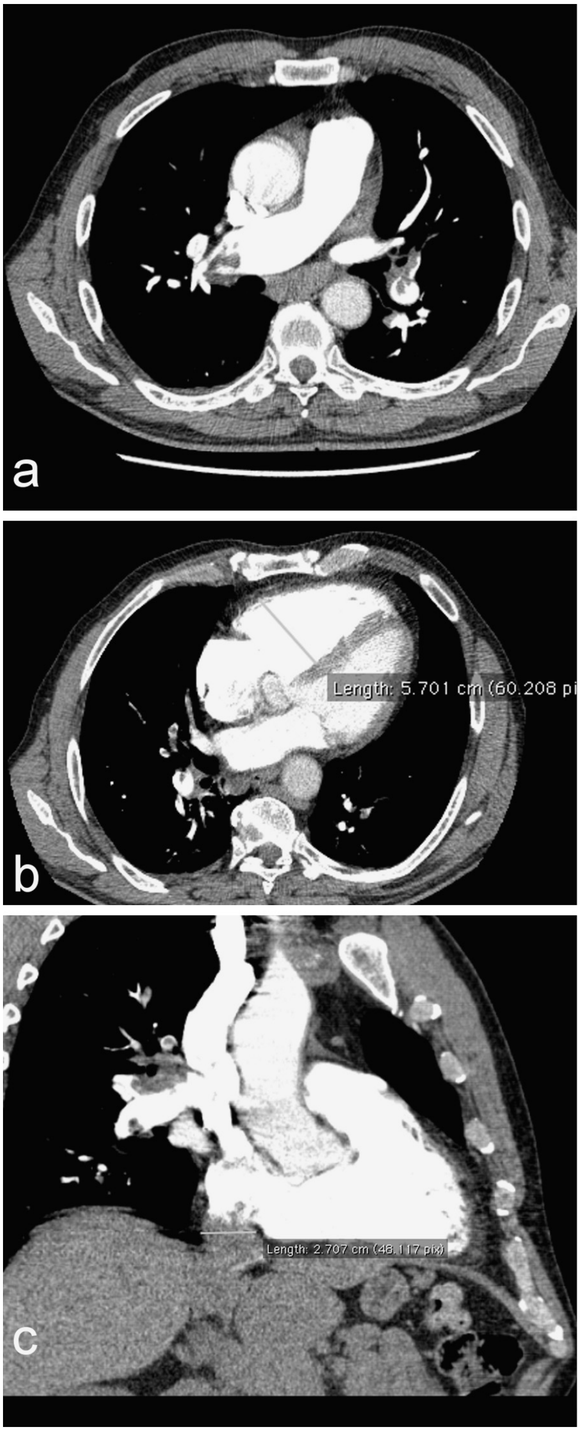

Fig. 1. Measurements used in the final model. Patient with PASP = 46 mmHg, Pulmonary obstruction score = 20 (a), Short axis diameter of right ventricle – RV = 57 mm (b), diameter of Inferior Vena Cava – IVC = 27 mm (c). Calculated probability of right ventricular dysfunction – RVD = 0.78.

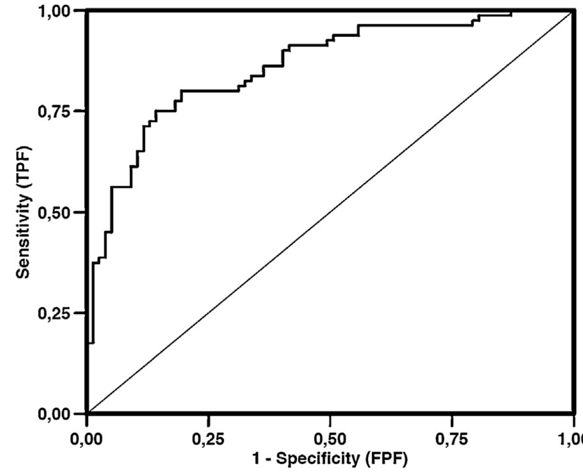

Fig. 2. ROC curve for the obtained model. Area under the curve = 0.860, 95% CI: 0.802 – 0.917.

(Wu et al. [11]), while according to van der Meer et al. [10], score <40% is a significant prognostic factor of 3-month survival. Ghaye et al. [12] calculate a 3-month mortality of 20% in patients with obstruction score of about 60%, and 40% mortality for 80–90% obstruction score. Nevertheless, other authors do not confirm this impact of obstruction score [13], and recently Moroni et al. [14] reported, that increased mortality in PE was observed, when high obstruction score (<40%) is accompanied by increased RV/LV ratio. In our study, we found a significantly lower obstruction scores in RVD(−) patients, with median value of 7 points (17.5%), vs. 22 points (55%) in RVD(+) patients. ROC analysis shows 40% of pulmonary obstruction as a cutoff value with both specificity and sensitivity of about 0.75. Nural et al. [15] reported a 48% obstruction score to reach 95% sensitivity and 76% specificity, however, their definition of hemodynamically unstable PE is different than the RVD(+) definition in our study.

RV diameter and RV/LV ratio are among the most widely recognized CT-based signs of RVD. Recently, Nural et al. [15] reported significantly larger RV diameter in hemodynamically unstable PE patients (median 55 mm vs. 42 mm in hemodynamically stable group) and RV/LV ratio (1.4 vs. 1.0 in respective groups). Araoz et al. [16] reported, that RV/LV ratio of >1 is associated with over 3-times increased risk of admission to intensive care unit.

Recognized signs of RVD include widening of tributaries of the right atrium, including widening of SVC, azygos vein, IVC and coronary sinus, as well as reflux of contrast medium into IVC. SVC widening has been reported in patients with severe PE by Collomb et al. [9], as well by Ghaye et al. [12] in non-survivors. IVC widening has been reported as an ultrasonographic sign of RVD [17], while the frequency of reflux of contrast medium into IVC is variously reported [9]. In our group, contrast reflux into IVC was not significantly more frequent in RVD(+) group. IVC diameter was significantly larger in the RVD(+) group in our study. Park et al. [18] reported no significant difference of this diameter, however, they used a different method of measurement.

CS diameter was significantly larger in the RVD(+) group, similar to the previous report [5], however, the AUC was smaller than in the cited study. This may be explained by the study group composition, as in the other study patient selection was more restricted regarding pre-existing cardiac conditions, including history of arrhythmias, and the CS diameter is known to be larger in patients with some forms of arrhythmia [19].

Widening of PA is another measurement, which may serve as an increased pulmonary pressure indicator [20], which is confirmed by other authors to occur in severe PE [9]; however, recently Nural et al. [15] did not find a significant difference of PA diameter between hemodynamically stable and unstable PE patients.

In our study, we used logistic regression analysis to construct a mathematical algorithm that would enable us to calculate individual probability of RVD in patients with acute PE. Accuracy of such probability evaluation, measured by AUC, was significantly higher than the accuracy of individual CT-based parameters.

Using an individual opportunity quotient, we calculated, that the risk of RVD increases almost twice when the obstruction score

Table 2
Characteristics of the assessed parameters in study groups. The cut-off value, sensitivity and specificity were calculated for linear parameters with significant differences between groups. ns – not significant.

	RVD (−) PASP ≤ 30mmHg	RVD (+) PASP > 30mmHg	p	AUC [95% CI]	best cutoff	sensitivity	specificity
Regression model probability	0.22 (0.44–0.94)	0.79 (0.12–0.99)	<0.001	0.860 [0.802–0.917]	0.5	0.79	0.81
Obstruction score [points]	7 (2–31)	22 (2–38)	<0.001	0.765 [0.727–0.876]	16	0.72	0.73
RV [mm]	41 (22–68)	48.63 (30.07–69.13)	<0.001	0.725 [0.647–0.809]	46.3	0.65	0.76
RV/LV	0,95 (0,56–2,38)	1.25 (0.49–3.02)	<0.001	0.709 [0.624–0.794]	1.03	0.71	0.60
PA [mm]	29 (20–47)	32 (21–48)	0.007	0.657 [0.566–0.747]	29.9	0.68	0.62
SVC [mm]	23 (12–31)	25 (17–36)	0.002	0.653 [0.562–0.744]	24.1	0.58	0.63
IVC [mm]	30 (19–44)	32 (22–45)	0.003	0.676 [0.587–0.764]	30.7	0.67	0.60
CS[mm]	13 (5,15–29)	15 (5.77–28)	0.008	0.609 [0.513–0.705]	13.1	0.71	0.49
Lung infarction	22 (47.8%)	33 (64.7%)	ns	–	–	–	–
IVS bowing (%)	4 (9%)	17 (33%)	<0.01	–	–	–	–
IVC reflux (%)	17 (37%)	26 (51%)	ns	–	–	–	–

Table 3
Results of logistic regression analysis.

		Estimate	SE	T test	P level	OR	95.0% C.I.	
							Lower	Upper
b_0	Intercept log. reg.	−8.361	1.92	18.85	<0.001	0.001	–	–
b_1	Obstruction score	0.132	0.02	29.75	<0.001	1.141	1.088	1.196
b_2	RV	0.078	0.03	8.48	0.004	1.082	1.025	1.140
b_3	IVC	0.094	0.05	3.61	0.012	1.098	0.997	1.211

difference is 5 points ($(e^{0.132})^5 = (1.1412)^5 \approx 1.94$), similarly to a 9 mm increase of RV diameter ($\approx$2.00) or a 7 mm increase of IVC diameter ($\approx$1.93).

In conclusion, the suggested prognostic model constructed with the use of logistic regression analysis of CT-based measurements is characterized by higher sensitivity and specificity than individually applied parameters. Intended prospective evaluation of the predictive model in a larger group of patients with PE should enable precise evaluation of its feasibility.

Our study was limited by its retrospective character. A prospective study on a large group of patients should allow further evaluation of applicability of the calculated model.

5. Conclusion

The presented study shows, that combination of CT-derived measurements allows for a reliable assessment of RVD in the course of the acute PE with application of binary logistic regression, and the suggested model seems to be a promising indicator of RVD in this group of patients.

Acknowledgements

This research was supported by Iuventus Plus Grant of Ministry of Science and Higher Education, Poland, Grant Number: 0389/P01/2010/70. The authors declare no conflict of interest.

The authors would like to acknowledge Kaushal N. Bhatt for his assistance with preparing the final version of the manuscript.

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