Value of low-dose ECG cardiac gating for the assessment of right ventricular dysfunction in patients with suspected pulmonary embolism

Poster No.: B-0567
Congress: ECR 2017
Type: Scientific Paper
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Keywords: Cardiac, Emergency, Thorax, CT, CT-Angiography, Computer Applications-Detection, diagnosis, Diagnostic procedure, Technical aspects, Embolism / Thrombosis, Haemodynamics / Flow dynamics, Acute
DOI: 10.1594/ecr2017/B-0567

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Purpose

Right ventricular dysfunction (RVD) is the main predictor of short-term mortality in patients with acute pulmonary embolism (PE) [1]. Patients presenting with RVD require intensified monitoring and medical treatment [2]. To improve their prognosis, it is essential to assess right ventricular function as quickly as possible after PE diagnosis. Based on the current ESC guidelines, the degree of RVD can be quantified by echocardiography and right ventricular/left ventricular (RV/LV) ratios measured on computed tomography pulmonary angiography (CTPA) studies [3]. However, accurate assessment of right ventricular function using echocardiography is time-consuming, dependent on the examiner and might be complicated by patient-related factors such as obesity and dyspnea. While CTPA measurements are fast to perform and characterized by a small inter- and intraobserver variability [4], a possible disadvantage is the imaging of the heart in a random phase of the cardiac cycle, leading to possible over-/underestimation of the actual right ventricular function.

The aim of this prospective study was to investigate the differences between systolic and diastolic measurements using a novel dose-reduced electrocardiography (ECG)-gated CTPA protocol.
Methods and materials

Patient population

This study was part of a prospective clinical investigation evaluating a novel CT protocol with low-dose ECG cardiac gating for the assessment of right ventricular dysfunction in patients with suspected pulmonary embolism presenting in the Emergency Department of University Hospital Mannheim. After the approval by the ethics committees of the University Medical Center Mannheim, sixty-two patients (33 female, age 65.1 +/- 17.5 years) were prospectively included in this study between 07/31/2013 and 04/11/2014. All patients gave written informed consent before CT imaging. Inclusion criteria were suspected pulmonary embolism and age >18 y. Exclusion criteria were pregnancy, clinical instability and age <18 y.

CT protocol

All patients underwent a high pitch CTPA examination with 80 cc of iodinated contrast material followed directly by a functional cardiac examination with retrospective ECG-gating (4D cCT) using the same contrast material bolus. A contrast bolus was administered via an antecubital vein access followed by a saline flush of 30 ml with a flow rate of 4ml/s. 55 examinations were performed with a 2nd generation 64-slice Dual-Source CT (DSCT) scanner, 7 examinations were performed with a 3rd generation 96-slice DSCT scanner.

The dose-length product (DLP) was multiplied with a conversion coefficient (k) of 0.014 mSv/(mGy*cm) for calculation of the effective dose, as recommended by the European Guidelines of Multislice Computed Tomography [5].

CT pulmonary angiography

Scan parameters for the 64-slice DSCT scanner were 120 kV tube voltage, 80 mAs reference tube current using automated tube current modulation, pitch factor of 3.0, collimation of 128 x 0.6 mm, gantry rotation time of 0.28 s and reconstructed slice thickness of 1.0 mm. Scan parameters for the 96-slice DSCT scanner were 70 kV tube voltage, 140 mAs reference tube current using automated tube current modulation, pitch factor of 1.9, collimation of 192 x 0.6 mm, gantry rotation time of 0.25 s and reconstructed slice thickness of 1.5 mm.

The onset of scanning was determined by bolus tracking (>100 HU in the pulmonary trunk).
The functional cardiac examination was performed during inspiratory breath-hold.

Scan parameters for the 64-slice DSCT scanner were 120 kV tube voltage, 50 mAs reference tube current using automated tube current modulation, pitch factor of 0.23, collimation of 128 x 0.6 mm, gantry rotation time of 0.28 s and reconstructed slice thickness of 1.5 mm. Scan parameters for the 96-slice DSCT scanner were 70 kV tube voltage, 20 mAs reference tube current using automated tube current modulation, pitch factor of 0.38, collimation of 192 x 0.6 mm, gantry rotation time of 0.25 s and reconstructed slice thickness of 1.5 mm.

Scanning started with a delay of 5 s after the CTPA using an 80% reduced tube current over the whole cardiac cycle.

**Post processing**

The CT raw data was reconstructed using iterative reconstruction algorithms with 3 iterations (SAFIRE (Siemens Medical Solutions, Forchheim, Germany) for the 2nd generation DSCT scanner with a dedicated soft tissue kernel (I31f) and a lung kernel (I79f) for CTPA and an I26f kernel for 4D cCT, ADMIRE (Siemens Medical Solutions, Forchheim, Germany) for the 3rd generation DSCT scanner with a Bv36 and Bv40 kernel for CTPA and an Bv40 kernel for 4D cCT).

The 4D cCT data was reconstructed in 5% (2nd generation DSCT scanner)/10% (3rd generation DSCT scanner) steps of the R-R' interval.

CT examinations were evaluated by two radiologists (>5 years and <5 years experience in CT imaging) in consensus reading to rule out or confirm PE and to quantify RV function. For image analysis, Osirix Pro (Version 5.0.2; Aycan, Würzburg, Germany) was used.

**Measurements**

**CT pulmonary angiography**

Pulmonary embolism was diagnosed in case of the presence of at least one filling defect in the pulmonary artery tree.

The maximum diameter for both ventricles was measured in transverse sections and the reconstructed 4-chamber view of the heart and subsequently the axial RV/LV ratio and the 4-chamber view RV/LV ratio were calculated.

**4D cCT**
The reconstructed axial images were loaded into Syngo.Via VA30 (Siemens Healthcare, Forchheim, Germany) and adjusted to a 4-chamber view of the heart.

Endsystole (ES) and enddiastole (ED) were determined as the phases with the smallest or respectively the largest dimension of the ventricular cavity. Volumetric measurements were performed using automatically drawn ventricular contours with manual corrections if necessary. Papillary muscles were included in the ventricular cavity. The endsystolic and enddiastolic volume was used to calculate the ejection fraction (EF) of both ventricles.

To rule out the influence of body surface area, age and gender, the right ventricular to left ventricular EF ratio (RVEF/LVEF) was calculated.

Additionally, endsystolic (RV/LV 4ch sys) and enddiastolic 4-chamber view ratio (RV/LV 4ch diast) as well as endsystolic (RV/LV ESV) and enddiastolic volume ratio (RV/LV EDV) were assessed.

**Statistical analysis**

JMP 11.0 (SAS Institute, Cary, NC, USA) was used for statistical analysis. Continuous variables are expressed as mean +/- standard deviation (SD). To test continuous variables for normal distribution, the Shapiro-Wilk test was used and homogeneity of variances was verified using the F-test. Subsequently, for normally distributed variables a two-tailed Student’s t-test was applied to compare two groups and, if not normally distributed, the Mann-Whitney U-test was used. A p-value of <0.05 was considered statistically significant.
Results

Two patients had to be excluded from statistical analysis. Exclusion was due to non-diagnostic image quality in one case and the other patient did not fulfill the inclusion criteria retrospectively (with status post PE about one month ago). Acute PE was diagnosed in 9 of the remaining 60 cases.

For an example of RV/LV 4-chamber view ratios on 4D cCT compared to CTPA ratios see figure 1.

Systolic RV/LV ratios showed significantly higher values than the corresponding diastolic RV/LV ratios (RV/LV 4ch sys = 1.30 +/- 0.40 vs. RV/LV 4ch diast = 1.01 +/- 0.21 (p = <.0001), RV/LV ESV = 2.18 +/- 1.23 vs. RV/LV EDV = 1.33 +/- 0.40 (p = <.0001)) (table 1, figure 2+3).

After exclusion of patients with pre-existing congestive heart failure (CHF), there was a significant difference between patients with and without acute pulmonary embolism for RV/LV 4ch sys (p = 0.0048), RV/LV diast (p = 0.0127), RV/LV EDV (p = 0.0247) and RV/LV ESV (0.0070), but not for the RV/LV ratios measured in the CTPA (RV/LV axial: p = 0.5780, RV/LV 4ch: p = 0.5230). RVEF/LVEF also showed a statistically significant difference between the two groups (p = 0.0054). Mean values and SD of each RV/LV ratio are displayed in table 2.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Systole</th>
<th>Diastole</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean +/- SD</td>
<td>Mean +/- SD</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(95% CI)</td>
<td>(95% CI)</td>
<td></td>
</tr>
<tr>
<td>RV/LV 4ch view</td>
<td>1.30 +/- 0.40 (1.20 - 1.40)</td>
<td>1.01 +/- 0.21 (0.96 - 1.07)</td>
<td>&lt;.0001*</td>
</tr>
<tr>
<td>RV/LV vol</td>
<td>2.18 +/- 1.23 (1.86 - 2.50)</td>
<td>1.33 +/- 0.40 (1.22 - 1.43)</td>
<td>&lt;.0001*</td>
</tr>
</tbody>
</table>
Table 2:

Mean values of LV EF, RV EF, RV/LV 4ch sys, RV/LV 4ch diast, RV/LV ESV, RV/LV EDV, RV/LV 4ch thx, RV/LV axial thx and RVEF/LVEF for all patients, PE diagnosed patients and patients without PE to the exclusion of patients with pre-existing congestive heart failure. P-values for the statistical difference between PE and non-PE patients. LVEF = left ventricular ejection fraction, RVEF = right ventricular ejection fraction, RVEF/LVEF = ratio of right ventricular ejection fraction and left ventricular ejection fraction, RV = right ventricular, LV = left ventricular, RV/LV 4ch sys = endsystolic 4-chamber view ratio, RV/LV 4ch diast = diastolic 4-chamber view ratio, RV/LV ESV = endsystolic volume ratio, RV/LV EDV = enddiastolic volume ratio, RV/LV 4ch thx = 4-chamber view ratio CTPA, RV/LV 4ch axial = CTPA ratio measured in transverse sections, SD = standard deviation, PE = pulmonary embolism, CI = confidence interval.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean+/−SD all studies (95% CI)</th>
<th>Mean+/−SD PE (95% CI)</th>
<th>Mean+/−SD no PE (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEF (%)</td>
<td>65.68 +/- 9.94 (62.36 - 68.99)</td>
<td>72.50 +/- 6.12 (66.07 - 78.93)</td>
<td>64.35 +/- 10.07 (60.66 - 68.05)</td>
<td>0.0654</td>
</tr>
<tr>
<td>RVEF (%)</td>
<td>48.68 +/- 8.69 (45.78 - 51.57)</td>
<td>44.00 +/- 12.73 (30.64 - 57.36)</td>
<td>49.58 +/- 7.64 (46.78 - 52.38)</td>
<td>0.3410</td>
</tr>
<tr>
<td>RV/LV EDV</td>
<td>1.34 +/- 0.30 (1.24 - 1.44)</td>
<td>1.73 +/- 0.48 (1.23 - 2.23)</td>
<td>1.26 +/- 0.19 (1.19 - 1.33)</td>
<td>0.0247*</td>
</tr>
<tr>
<td>RV/LV ESV</td>
<td>2.25 +/- 1.16 (1.86 - 2.64)</td>
<td>3.80 +/- 1.61 (2.11 - 5.49)</td>
<td>1.95 +/- 0.78 (1.66 - 2.24)</td>
<td>0.0070*</td>
</tr>
<tr>
<td>RV/LV 4ch sys</td>
<td>1.35 +/- 0.38 (1.23 - 1.48)</td>
<td>1.88 +/- 0.55 (1.31 - 2.46)</td>
<td>1.25 +/- 0.24 (1.16 - 1.34)</td>
<td>0.0048*</td>
</tr>
<tr>
<td>RV/LV 4ch diast</td>
<td>1.01 +/- 1.19 (0.95 - 1.08)</td>
<td>1.25 +/- 0.27 (0.97 - 1.53)</td>
<td>0.97 +/- 0.13 (0.92 - 1.01)</td>
<td>0.0127*</td>
</tr>
<tr>
<td>RV/LV 4ch thx</td>
<td>1.13 +/- 0.24 (1.05 - 1.21)</td>
<td>1.21 +/- 0.32 (0.89 - 1.55)</td>
<td>1.12 +/- 0.22 (1.03 - 1.20)</td>
<td>0.5230</td>
</tr>
<tr>
<td></td>
<td>Mean ± SD</td>
<td>Lower Limit</td>
<td>Upper Limit</td>
<td>p-value</td>
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<td>---------------------</td>
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<tr>
<td>RV/LV axial</td>
<td>1.17 ± 0.27</td>
<td>(1.08 - 1.26)</td>
<td>(1.06 - 1.25)</td>
<td>0.5780</td>
</tr>
<tr>
<td>thx</td>
<td>1.24 ± 0.31</td>
<td>(0.91 - 1.57)</td>
<td>(0.91 - 1.57)</td>
<td></td>
</tr>
<tr>
<td>RVEF/LVEF</td>
<td>1.15 ± 0.26</td>
<td>(1.06 - 1.25)</td>
<td>(1.06 - 1.25)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.5780</td>
<td>(0.70 - 0.80)</td>
<td>(0.43 - 0.79)</td>
<td>0.0054*</td>
</tr>
<tr>
<td></td>
<td>(0.70 - 0.80)</td>
<td>(0.43 - 0.79)</td>
<td>(0.73 - 0.83)</td>
<td></td>
</tr>
</tbody>
</table>
Fig. 1: 72 year old female patient with acute central pulmonary embolism and acute cor pulmonale. She showed septum bowing, a LV EF of 73% and a RV EF of 27%. 3a: RV/LV ratio measured on transverse sections of CTPA. 3b: RV/LV ratio measured on reconstructed 4-chamber view of CTPA. 3c: RV/LV endsystolic ratio measured on reconstructed 4-chamber view of 4D cCT. 3d: RV/LV enddiastolic ratio measured on reconstructed 4-chamber view of 4D cCT. Abbreviations: LV = left ventricular, RV = right ventricular, CTPA = computed tomography pulmonary angiography, 4D cCT = functional cardiac examination with retrospective ECG-gating.

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**Fig. 2:** Comparison of endsystolic and enddiastolic 4-chamber view ratio. RV = right ventricular, LV = left ventricular, \(\text{view}_\text{Ratio}_\text{sys}_4\text{ch} = \) endsystolic 4-chamber view ratio, \(\text{view}_\text{Ratio}_\text{diast}_4\text{ch} = \) enddiastolic 4-chamber view ratio.

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**Fig. 3:** Comparison of endsystolic and enddiastolic volume ratio. RV = right ventricular, LV = left ventricular, \(\text{RV}_{\text{LV}}_{\text{EDV}} = \) enddiastolic volume ratio, \(\text{RV}_{\text{LV}}_{\text{ESV}} = \) endsystolic volume ratio.
Conclusion

This study was designed to assess the value of a single contrast bolus CTPA protocol with low dose ECG-gating for the assessment of right ventricular dysfunction in patients with suspected acute pulmonary embolism.

Previous studies also analyzed the additional value of CT ECG-gating in acute PE [6-8]. Common to all was the higher radiation dose compared to standard protocols and the use of two contrast boli. Van der Bijl et al. reported an effective radiation dose of 3.3 mSv, Dogan et al. had an effective radiation dose of 3.0 - 4.2 mSv for cardiac CT scanning alone. The total amount of contrast agent used for CTPA and ECG-gated scanning together reached from 95 mL up to 150 mL [7,8]. Unlike these studies, we only used one contrast bolus (80 mL) and documented considerably lower radiation doses (4.51 mSv overall effective dose, 2.18 mSv for cardiac scanning alone).

After exclusion of patients with pre-existing congestive heart failure, only the ECG-synchronized RV/LV ratios showed a significant difference between patients with and without PE, whereas the ratios on CTPA did not. These results indicate a potential benefit of additional cardiac function analysis in patients with acute PE, which might support early recognition of RVD.

It might not be irrelevant which ratio to use, given the statistically significant difference between systolic and corresponding diastolic RV/LV ratios shown in our study. As well, CTPA RV/LV ratios might not be adequate to diagnose RVD, considering that only a random phase of the cardiac cycle is pictured there, which might result in over-/underestimation of the actual right ventricular strain.

Like our results, Dogan et al., too, reported higher mean values for endsystolic than for enddiastolic volume ratio [8]. Endsystolic RV/LV ratios, additionally, showed lower p-values than enddiastolic RV/LV ratios, suggesting they might be more relevant in diagnosing RVD in PE patients.

Our study has several limitations: first, the sample size was relatively small - after exclusion of patients with pre-existing congestive heart failure, only 37 studies remained to be evaluated. Second, we did not correlate CT findings with transthoracic echocardiography. Third, we did no follow-up on the patients to correlate our findings with clinical outcome.

Further studies have to differentiate between endsystolic and enddiastolic measurements regarding their relevance for risk stratification and correlation with clinical outcome.
References


