Reproducibility of CT signs of right heart strain in acute pulmonary embolism

Poster No.: B-397
Congress: ECR 2010
Type: Scientific Paper
Topic: Chest - Without Subtopic
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Keywords: Pulmonary embolism, Right heart strain, Computed tomography angiography
Keywords: Lung, Respiratory system, Thorax
DOI: 10.1594/ecr2010/B-397

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Purpose

Purpose: To determine the interobserver reproducibility of previously-described CTPA findings to indicate RV dysfunction, with the goal of identifying the most consistent, least observer-dependent method.

Introduction:

- Acute pulmonary embolism (PE) is a common but deadly event with a 3 month mortality rate of up to 17.4%.
- Even if PE is properly treated with anticoagulation, the mortality rate in hemodynamically stable patients varies from 8.1% to 15.1%.
- The most common cause of death in PE patients is acute right heart failure.
- Acute PE increases the pressure of the pulmonary arterial system and right ventricle (RV), resulting in RV dysfunction, which may progress to right heart failure and circulatory collapse.
- Patients with RV dysfunction have a higher mortality rate than those without, even if they are initially hemodynamically stable.
- The presence of RV dysfunction is a marker for adverse clinical outcome in patients with acute PE.
- Contrast medium enhanced Computed Tomography Pulmonary Angiography (CTPA) is increasingly used as the first-line imaging test in suspected PE, and is available 24 hours a day at most institutions.
- CTPA not only allows direct visualization of emboli, but also provides information regarding right-heart status.
- The literature shows variable results for the prognostic power of CTPA evidence of RV dysfunction as a predictor of adverse outcomes.
- This variability may, in part, be explained by the somewhat subjective nature of diagnosing RV dysfunction via CTPA, since formal criteria for establishing these signs of dysfunction are not available.
Methods and Materials

Patients:

We retrospectively identified 52 consecutive patients hospitalized at our institution between October 2008 and August 2009 with acute PE diagnosed on CTPA. Two patients were excluded from the study due to insufficient contrast enhancement of ventricular chambers for reliable delineation of the endocardial borders; thus a total of 50 patients were eligible for the study.

- The mean age of the subjects was 56 ± 15 years.
- Women: 58% (n=29)
- Men: 42% (n=21)

All patients included in this study had undergone a clinical assessment by an attending physician of the probability of pulmonary embolism, using the Wells scoring system.

- 33 patients with high probability according to Wells score
- 17 patients with abnormal D-Dimer test.

CTPA Acquisition:

Non-ECG gated CTPA using a 64-slice multi detector-row CT system (Somatom Sensation, Siemens, Forchheim, Germany)

Image acquisition parameters

- 0.33 msec gantry rotation time
- 32×0.6 mm collimation with z-flying focal spot technique
- 120 kV, 160 mAseff
- Pitch of 1.2
- A reconstructed section-thickness of 1 mm

Contrast-medium enhancement

- 100 mL of a non-ionic iodinated contrast medium (Ultravist 370, Bayer-Schering, Berlin, Germany) injected at 4 mL/sec
- Automated bolus-triggering with a threshold of 100 HU

CTPA Interpretation (Figure 1 on page 8):
All CTPA studies were independently reviewed by two observers with 6 and 3 years post-training experience, respectively, in cardiothoracic CT.

Observers were blinded to the patients’ clinical characteristics. Studies were reviewed electronically on a clinical workstation (Multi Modality Workplace, Siemens).

The window and level settings were individually adjusted for each patient-study for optimized display of pulmonary emboli and the cardiac chambers.

The initial clinical diagnosis of PE was confirmed in the presence of at least one filling defect in the pulmonary artery tree, including at the subsegmental level.

Deviation of the interventricular septum

- Normal (convex toward the RV)
- Flattened septum
- Septal bowing (convex toward the LV)

IVC Reflux

- 1 = no reflux into IVC
- 2 = trace of reflux into IVC only
- 3 = reflux into IVC but not hepatic veins
- 4 = reflux into IVC with opacification of proximal hepatic veins
- 5 = reflux into IVC with opacification of hepatic veins to the level of the mid-portion of the liver
- 6 = reflux into IVC with opacification of distal hepatic veins.

\[ RVD_{\text{axial}} / LVD_{\text{axial}} \] Ratio

- The two observers identified the axial sections through the RV and LV that showed the greatest distance, perpendicular to the long axis of the heart, between the endocardium and the interventricular septum.
- \( RVD_{\text{axial}} \) and \( LVD_{\text{axial}} \) distance were subsequently measured, and the \( RVD_{\text{axial}} / LVD_{\text{axial}} \) ratio was calculated.

\[ RVD_{4-\text{CH}} / LVD_{4-\text{CH}} \] Ratio

- Observers independently reconstructed four-chamber (4-CH) views on the workstation using the approach illustrated in Figure 2 on page 8.
- The two observers then identified the levels of reconstructed 4-CH views for RV and LV that showed the greatest distance between the ventricular endocardium and the interventricular septum. \( RVD_{4-\text{CH}} \) and \( LVD_{4-\text{CH}} \) were subsequently calculated.
RVV/LVV Ratio

- The volumetric analysis of both ventricles was performed using the workstation's volume-analysis application (Volume analysis, software version VE31A, Siemens).
- The endocardial contours were semi-automatically segmented from the valvular plane down to the apex of both ventricles.

This involved manually outlining the endocardial contours on the transverse sections comprising the minimal and maximal expanse of the ventricle; these were then automatically propagated to the neighboring sections.

- The RVV/LVV ratio was subsequently calculated.
- The time needed to perform workstation volumetric measurements was recorded.

Statistical Analysis:

Interobserver reproducibility for determining the grade of IVC reflux and the position of the interventricular septum

- Unweighted Kappa statistics.
- The k value for agreement

Poor: < 0.20
Fair: 0.21 - 0.40
Moderate: 0.41 - 0.60
Good: 0.61 - 0.80
Very Good: 0.81 - 1.00

For continuous variables

- Spearman's rank correlation
- Bland-Altman analysis

MedCalc (version 10.4.8, MedCalc Software, Mariakerke, Belgium) was used for all statistical analyses.

Limitations:
The various signs evaluated in the study were not correlated with outside reference standards, such as echocardiography.

The prognostic value of the findings were not studied for adverse patient outcomes.

- This study aimed solely at analyzing the observer-dependence of the CT signs of RV dysfunction

Participation was limited to two observers; additional observers would have increased the validity of the findings.

The cohort would be too small to meaningfully contribute to existing data.

Another potential limitation of the study is that image acquisition by CTPA was not ECG-gated.

- Non-ECG gated CTPA measurement of ventricular chamber size is invariably inaccurate, because the images are obtained in different phases of the cardiac cycle.
- Both overestimation and underestimation of the CTPA-derived RVD/LVD ratio may occur because of motion-artifact and insufficient contrast-medium attenuation.
- However, the use of ECG-gated CTPA protocols over routine non-ECG gated CTPA has been shown to result in only limited incremental diagnostic improvement.

Lastly, performance of heart chamber volumetry is somewhat, but not substantially more time consuming.

- Mean 6 minutes 14 sec for observer 1
- Mean 7 minutes 22 sec for observer 2
**Fig. 0:** CT signs of RV dysfunction in a 57 year old woman with acute PE. A. 4-CH view shows septal bowing (arrow), convex toward the LV. B. Grade 5 reflux of contrast medium into the IVC (short arrow) and proximal hepatic veins (long arrows). C and D. Measurements of maximal RV (C) and LV (D) diameters on transverse sections show RVDaxial/LVDaxial ratio of 1.3. E and F. Measurements of maximal RV (E) and LV (F) diameters on 4-CH views show RVD4-CH/LVD4-CH ratio of 1.4. G and H. Semi-automated volumetry of the RV (pink) and LV (orange) displayed on transverse sections (G) and as coronal reformat (H) shows RVV/LVV ratio of 2.57.

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**Fig. 0:** Reconstruction of 4-CH views: (A) the vertical long-axis plane is aligned on axial sections through the center of the mitral valve and the LV apex, (B) the horizontal long-axis plane is aligned on the vertical long-axis plane through the center of the mitral valve and the LV apex, (C) the short-axis plane is aligned on the vertical and horizontal long-axis planes, perpendicular to both, (D) the 4-CH plane is aligned on the short-axis plane through the anterior mitral valve papillary muscle and the apex of the RV.
Results

The initial clinical diagnosis of acute PE, which had served as an inclusion criterion, was confirmed by both observers in all 50 patients.

The most central level of involvement with PE:

- Main pulmonary arteries: 12 patients (24%)
- Segmental pulmonary artery: 24 patients (48%)
- Subsegmental pulmonary artery: 14 patients (28%)

Within 30 days of follow-up

- Death: one patient
- Adverse clinical event: 10 patients

6 requiring endotracheal intubation

5 requiring thrombolysis

One requiring vasopressors

One requiring cardiopulmonary resuscitation

During nine-month follow up

- Death: 4 patients (8%)

Septal Bowing

Observer 1

- Normal in 48% (n=24)
- Flattened in 34% (n=17)
- Septal bowing in 18% (n=9)

Observer 2

- Normal in 60% (n=30)
- Flattened septum in 32% (n=16)
- Septal bowing in 8% (n=4)

Overall interobserver reproducibility for describing the position of the ventricular septum:
• Fair (k=0.32, 95% CI 0.090 - 0.551)

Reproducibility for differentiating normal versus abnormal (i.e. flattening or bowing) position of the septum:
  • Moderate (k=0.44, 95% CI 0.2204 - 0.685)

**IVC Reflux**

Observer 1

  • Grade 1 in 30% (n=15)
  • Grade 2 in 30% (n=15)
  • Grade 3 in 18% (n=9)
  • Grade 4 in 10% (n=5)
  • Grade 5 in 4% (n=2)
  • Grade 6 in 8% (n=4)

Observer 2

  • Grade 1 in 22% (n=11)
  • Grade 2 in 42% (n=21)
  • Grade 3 in 20% (n=10)
  • Grade 4 in 8% (n=4)
  • Grade 5 in 8% (n=4)

No reflux (grade 1) vs. minimal (grade 2-3) vs. substantial (grade 4-6):
  • Moderate agreement (k=0.57, 95% CI 0.365 - 0.770)

Substantial (grade 4-6) vs. non-substantial reflux (grade 1-3):
  • Good agreement (k=0.68, 95% CI 0.408 - 0.946)

**Inter-Observer Correlation of CT Measures of Right Heart Dysfunction**

<table>
<thead>
<tr>
<th></th>
<th>Observer 1</th>
<th>Observer 2</th>
<th>Correlation coefficient*</th>
</tr>
</thead>
<tbody>
<tr>
<td>RVD$_{axial}$</td>
<td>4.5 ± 0.9 cm</td>
<td>4.5 ± 0.7 cm</td>
<td>0.88 (p&lt;0.0001)</td>
</tr>
<tr>
<td>LVD$_{axial}$</td>
<td>4.1 ± 0.9 cm</td>
<td>4.0 ± 0.8 cm</td>
<td>0.87 (p&lt;0.0001)</td>
</tr>
<tr>
<td>RVD$<em>{axial}$/LVD$</em>{axial}$ ratio</td>
<td>1.16 ± 0.45</td>
<td>1.18 ± 0.4</td>
<td>0.88 (p&lt;0.0001)</td>
</tr>
<tr>
<td></td>
<td>RVD&lt;sub&gt;4-CH&lt;/sub&gt;</td>
<td>LVD&lt;sub&gt;4-CH&lt;/sub&gt;</td>
<td>Ratio</td>
</tr>
<tr>
<td>----------------</td>
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<td>------------</td>
</tr>
<tr>
<td>Diameter</td>
<td>4.4 ± 0.7 cm</td>
<td>4.5 ± 0.6 cm</td>
<td>0.83 (p&lt;0.0001)</td>
</tr>
<tr>
<td>Diameter</td>
<td>3.9 ± 0.8 cm</td>
<td>3.9 ± 0.8 cm</td>
<td>0.82 (p&lt;0.0001)</td>
</tr>
<tr>
<td>Ratio</td>
<td>1.21 ± 0.46</td>
<td>1.21 ± 0.38</td>
<td>0.85 (p&lt;0.0001)</td>
</tr>
<tr>
<td>RVV</td>
<td>130.5 ± 48.9 ml</td>
<td>130.1 ± 47.9 ml</td>
<td>0.95 (p&lt;0.0001)</td>
</tr>
<tr>
<td>LVV</td>
<td>92.6 ± 42.2 ml</td>
<td>90.4 ± 39.9 ml</td>
<td>0.97 (p&lt;0.0001)</td>
</tr>
<tr>
<td>RVV/LVV ratio</td>
<td>1.68 ± 1.06</td>
<td>1.71 ± 1.14</td>
<td>0.93 (p&lt;0.0001)</td>
</tr>
</tbody>
</table>

RVD<sub>axial</sub> = RV diameter on axial sections, LVD<sub>axial</sub> = LV diameter on axial sections
RVD<sub>4-CH</sub> = RV volume on 4-CH views, LVD<sub>4-CH</sub> = LV volume on 4-CH views
RVV = RV volume, LVV = LV volume, * Spearman' rank correlation coefficient

**RVD/LVD Ratio**

On Bland-Altman analysis

- RVD<sub>axial</sub>/LVD<sub>axial</sub> ratio measurements (Figure 1 on page 14):
  
The means = 0.014
  
  Standard deviations = 0.195

- RVD<sub>4-CH</sub>/LVD<sub>4-CH</sub> ratio (Figure 2 on page 14):
  
The means = 0.001
  
  Standard deviations = 0.242

- RVV/LVV ratio (Figure 3 on page 15):
  
The means = 0.033
  
  Standard deviations = 0.229
Fig. 0: Bland-Altman analysis of RVDaxial/LVDaxial ratio measured by the two observers

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**Fig. 0:** Bland-Altman analysis of RVD4-CH/LVD4-CH ratio measured by the two observers.

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**Fig. 0:** Bland-Altman analysis of RVV/LVV ratio measured by the two observers

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Conclusion

This study shows that considerable differences exist in the interobserver reproducibility of CT findings of RV dysfunction on CTPA in patients with acute PE.

Cardiac chamber measurements are more reproducible than septal bowing and IVC reflux, which have more limited interobserver correlation for establishing their presence and severity.

According to the data, volumetric determination of the RVV/LVV ratio is the least user-dependent and most reproducible.

We propose the use of volumetric measurements of cardiac chambers to study RV dysfunction in patients with acute PE.
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