McGinn-White Sign or S1Q3T3-Pattern in Pulmonary Embolism; Significance and Differential Diagnosis; Narrative Updating Review

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ABSTRACT

Pulmonary embolism is a serious clinical cardiopulmonary event. The blockage of pulmonary vasculature by a substance that has moved from elsewhere in the body via the bloodstream is considered the prescriptive hallmark for pulmonary embolism. An acceleration in its early diagnosis and treatment is an essential step to prevent both morbidity and mortality. Pulmonary embolism has a high fatality rate with an outspread incidence. The annual incidence of pulmonary embolism in Europe is 430,000 cases and the rate is between 500,000 and 600,000 cases in the United States, and results in between 200,000 and 300,000 deaths. An electrocardiograph is an important tool for the diagnosis of pulmonary embolism. McGinn-White sign or S1Q3T3-pattern is a famous ancient electrocardiographic sign that carries wide significant prognostic value regards pulmonary embolism. But, the classic S1Q3T3-pattern is neither pathognomonic, sensitive, nor specific finding. The clinical data is the most important factor for the physician in the directory of the outcome for S1Q3T3-pattern. This is a pivotal step in the narrative updating review of the current sign.

Keywords: McGinn-White sign, S1Q3T3-pattern, Pulmonary embolism, Significance and differential diagnosis

ABBREVIATIONS

ACP: Acute cor-pulmonale
AF: Atrial fibrillation
ECG: Electrocardiograph
ED: Emergency department
LV: Left ventricle
PE: Pulmonary embolism
PHT: Pulmonary hypertension
RA: Right atrial
RAD: Right axis deviation
RBBB: Right bundle branch block
RV: Right ventricular
TR: Tricuspid regurgitation

HISTORICAL BIT

Historically, the initial elucidatory character of electrocardiographic (ECG) abnormalities in pulmonary embolism (PE) was described by both scientists; Sylvester McGinn and Paul White in 1935.1 They revealed that a remarkable number of cases shared the recognizable analogous constellation of findings of an S-wave (amplitudes of ≥1.5 mm) in lead I, Q-wave (amplitudes of ≥1.5 mm) in lead III, and an inverted T-wave in lead III.1,2 Indeed, the traditional McGinn-White sign (S1Q3T3) was detected in only one-tenth to one-half of cases of PE.3,4,5 McGinn and White first described the S1Q3T3-pattern with these subsequent voltage criteria in acute cor-pulmonale (ACP) due to PE: (A). S-wave in lead I. (B). Q-wave in lead III with an amplitude of more than 0.15 mV. (C). The inversion of the T-wave in lead III.1,5

INTRODUCTION

Pulmonary embolism is one of the most fatal cardiopulmonary presentations in the emergency department (ED).3 The blockage of pulmonary vasculature by a substance that has moved from elsewhere in the body via the bloodstream is considered the prescriptive hallmark for pulmonary embolism.2 An acceleration in its early diagnosis and treatment is an essential step to prevent both morbidity and mortality.6,7 The annual incidence of pulmonary embolism in Europe is 430,000 cases and the rate is between 500,000 and 600,000 cases in the United States, and results in between 200,000 and 300,000 deaths.8 Nearly, yearly 200,000 new cases of
venous thromboembolism (VTE) are diagnosed with an approximately six percent 30-day fatality rate from PE. \(^2\) Pulmonary embolism is a highly prevalent clinical disorder that is mostly carrying under-recognizing, under-diagnosing, and potentially fatal direction. \(^3\) Clinical findings of PE is usually having poor diagnostic value in the PE per se. \(^3\) The symptoms of PE are undependable in the diagnosis of PE. \(^3\) Nearly, most cases of PE do so within the first few hours of the presentation. \(^9\) About, 10% of PE is ending to sudden death in the first hour. Anyhow, PE presents with a wide-clinical spectrum, starting from asymptomatic embolism to fatal shocked massive PE. \(^9\) However, identifying these ECG signs could help clinicians to earlier diagnosis of the PE. \(^6\) According to an international registry study (IRS), massive PE was existing in less than 5% of adult PE but with a 50% mortality. \(^10,11\)

**THE DESCRIPTION OF SIGN**

McGinn and White had innovated the S1Q3T3-pattern in 1935 with these subsequent voltage criteria in ACP due to APE: S wave in lead I, Q-wave in lead III, and amplitude of more than 0.15 mV with the T-wave in lead III, and amplitude of more than 0.15 mV with the T-wave in lead III. \(^5\) The sign is defined as the presence of a Q-wave in lead III, late inversion of the T-wave in lead III, and S-wave in lead I with right QRS axis deviation. \(^4,12\) Indeed, the classic right ventricular (RV) strain, S1Q3T3-pattern is commonly debated but occasionally visible. \(^13\) McGinn and White\(^4\) revealed there are certain aberrations of a constellation of ECG S1Q3T3 signs that include: (A). Prominent S-wave with the low origin of the T-wave in lead I. (B). Gradual staircase ascent of the ST-interval from the S-wave to the T-wave in lead II. (C). Q-wave and definite late inversion of the T-wave in lead III. Both McGinn and White described ECG-patterns of deep S-wave in lead I, Q-wave in lead III, and inverted T-wave in lead III in patients with RV change due to pulmonary vascular disorders like in RV dilatation, pulmonary hypertension (PHT), and pneumothorax. \(^14-16\)

**INCIDENCE, CLINICAL IMPORTANCE, AND PROGNOSTIC VALUE**

Unfortunately, S1Q3T3-pattern is not detected in all cases of PE.\(^17\) The incidence of McGinn-White sign or S1Q3T3-pattern in classic PE is ranged between 10% to 50% of cases.\(^2,4,18-23\) There are wide variations according to the incidence in different studies (Table 1). A minority of patients (12%) post-angiographically documented acute PE, initially, had the ECG S1Q3T3.\(^31\)

<table>
<thead>
<tr>
<th>No</th>
<th>Study</th>
<th>Year</th>
<th>No of patients</th>
<th>Percent of S1Q3T3 Pattern in PE (%)</th>
<th>Notes</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Cutforth RH al.</td>
<td>1958</td>
<td>50</td>
<td>8.33</td>
<td></td>
<td>73</td>
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<tr>
<td>2.</td>
<td>Marchick MR et al.</td>
<td>2010</td>
<td>6049</td>
<td>8.5</td>
<td></td>
<td>70</td>
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<tr>
<td>4.</td>
<td>Chua JC et al.</td>
<td>2013</td>
<td>100</td>
<td>11</td>
<td></td>
<td>75</td>
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<tr>
<td>5.</td>
<td>Stein PD et al.</td>
<td>1975</td>
<td>90</td>
<td>12</td>
<td></td>
<td>55</td>
</tr>
<tr>
<td>6.</td>
<td>Rodrigues B et al.</td>
<td>2012</td>
<td>39</td>
<td>15.2 if QS(^&lt;)18</td>
<td>Subgroups according to QS(^*)</td>
<td>37</td>
</tr>
<tr>
<td>7.</td>
<td>Rodrigues B et al.</td>
<td>2012</td>
<td>63</td>
<td>35.1 if QS(^&gt;)18</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8.</td>
<td>Petruzzelli S et al.</td>
<td>1986</td>
<td>245</td>
<td>16</td>
<td></td>
<td>27</td>
</tr>
<tr>
<td>9.</td>
<td>Shopp JD et al.</td>
<td>2015</td>
<td>382</td>
<td>24</td>
<td></td>
<td>36</td>
</tr>
<tr>
<td>12.</td>
<td>Ferrari E et al.</td>
<td>1997</td>
<td>80</td>
<td>50</td>
<td></td>
<td>57</td>
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<tr>
<td>13.</td>
<td>Lenègre J et al.</td>
<td>1970</td>
<td>50</td>
<td>52</td>
<td></td>
<td>76</td>
</tr>
</tbody>
</table>

\(^*QS=Qanadli score\)  \(^**NR=not reported\)

S1Q3T3-pattern is ECG abnormalities harmonious with acute PE.\(^12\) Although, the S1Q3T3-pattern carries a lack of specificity in the diagnosis of PE. But the pattern is still used diagnostic tool. An identify the S1Q3T3 pattern is very important for clinical practice.\(^24,25\) It is an acceptable well-known signal for acute PE.\(^17\) Also, the pattern not sensitive, but it will raise the suspicion of APE.\(^6\) Thus the presence of this pattern associated with ECG along with clinical findings is highly suspicious of PTE.\(^26\) McGinn-White sign are remarkably more frequent in patients with confirmed PE.\(^5,27\) Despite it is not the commonest ECG finding in PE but the pattern is often taught in ECG classes.\(^28\) Recognizing the ECG McGinn-White sign could prompt clinicians to consider PE for the earlier right diagnosis.\(^6\) S1Q3T3 pattern is considered
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to be more common with massive embolism than with smaller emboli.29 Nevertheless, S1Q3T3-pattern has been shown to link with poorer short-term prognosis in acute PE.10 S1Q3T3 sign is more frequently seen in patients with complications post APE.30 This rare S1Q3T3-pattern have been correlating with poorer outcome in PE.11 The presence of the S1Q3T3 is an indicator of RV strain with ACP.4,22,31-34 It has been extrapolated that S1Q3T3 is a sign of RV change due to occlusion of the pulmonary vasculature.2 S1Q3T3 is also associated with the early affection of RV dysfunction.35 Presence of the S1Q3T3-pattern is suggestive of RV strain from acute PHT in the cases with acute PE.36 So, this pattern could be used as a predictor of RV dysfunction and as indirect markers for risk stratification in the cases of APE.35 However, S1Q3T3 is an independent predictor of PE.37,38 S1Q3T3 pattern is suggesting RV overload.39 Daniel et al. proposed a 21-point ECG scale to evaluate the relationship between the severity of PHT and ECG in patients with APE.30,40 The presence of classic McGinn-White sign in the case of PTE signifies associated severity rather than a higher mortality rate.26,41,42 Shopp et al reported that the S1Q3T3 sign in 16.6% of ECG findings that predicted hemodynamic collapse and death within 30 days of acute PE.36 The presence of the RV strain pattern on the ECG is linked to an increased risk of all-cause death and clinical deterioration.43 Systematic review and meta-analysis demonstrate that following 6 findings in ECG will be suggesting RV strain due to acute PHT: (A) Sinus tachycardia. (B). The S1Q3T3-pattern, (C). Right bundle branch block (RBBB). (D). T-wave inversions in V2 and V3. (E). ST-elevation in the aVR lead. (F). Atrial fibrillation (AF). All the above signs are significantly associated with the probability of circulatory shock and death from APE.36 The combination of patient’s symptoms with the ECG S1Q3T3 pattern is the way for suspected APE and therefore to request a ventilation and perfusion scan, which showed the low probability for PE.5 Calvo-Romero1 et al. reported that the S1Q3T3-pattern is one of the main determinants of severity between the ECG abnormalities at the time of diagnosis of acute PE.12 Numerous clinical benefits of S1Q3T3-pattern regards pulmonary embolism are listed (Table 2).

Table 2. List of clinical significance of S1Q3T3-pattern regards pulmonary embolism.

<table>
<thead>
<tr>
<th>No</th>
<th>Clinical Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>• It is a consistent with APE.14</td>
</tr>
<tr>
<td>2.</td>
<td>• It is a fairly well known as an indication of APE.17</td>
</tr>
<tr>
<td>3.</td>
<td>• Highly suspicious for APE.4,26</td>
</tr>
<tr>
<td>4.</td>
<td>• More common with massive PE than with smaller PE.29</td>
</tr>
<tr>
<td>5.</td>
<td>• Prompt clinicians to consider PE and lead to earlier diagnosis.6</td>
</tr>
<tr>
<td>6.</td>
<td>• An indicator for right heart strain and ACP.4,22,31-34</td>
</tr>
<tr>
<td>7.</td>
<td>• It is a suggestive of RV strain from acute PHT.36</td>
</tr>
<tr>
<td>8.</td>
<td>• An indirect marker for risk stratification in a cases of APE.35</td>
</tr>
<tr>
<td>9.</td>
<td>• Evaluate the usefulness of ECG in predicting RV dysfunction and outcome with confirmed APE using the 21-point ECG scale.30,40</td>
</tr>
<tr>
<td>10.</td>
<td>• It signifies severity and higher mortality.26,41,42</td>
</tr>
<tr>
<td>11.</td>
<td>• It is a predicted hemodynamic collapse and death within 30 days of APE.36</td>
</tr>
<tr>
<td>12.</td>
<td>• Request a ventilation and perfusion scan, which showed low probability for APE.5</td>
</tr>
<tr>
<td>13.</td>
<td>• Principal determinants of severity between the ECG abnormalities at time of diagnosis in acute PE.11</td>
</tr>
<tr>
<td>14.</td>
<td>• Significantly associated with an increased probability of circulatory shock and death from APE.36</td>
</tr>
</tbody>
</table>

ACP; Acute cor-pulmonale, APE; Acute pulmonary embolism, ECG; Electrocardiograph, PHT; Pulmonary hypertension, RV; Right ventricular.

CHILDREN

Almost 15% of patients in cohort studies presented with shock or cardiac arrest had previous echoing reports of APE.44,45 About 33.3% of patients described as having either massive or submassive PE.44,46 Evidence of the classic S1Q3T3 finding is only reported in 12% of acute thromboembolic PE in children.45

ECG AND PULMONARY EMBOLISM

The ECG may be helpful as a diagnostic tool for PE, but it has limited value due to its lack of both sensitivity and specificity. ECG is an initial choice workup because the results are normal in only about 18-29% of all cases of PE (6% massive and 23% submassive).3,47 In fact, a large number of patients with PE will have no ECG abnormalities at all!17 The animals and
humans studies have shown that approximately 50% of the occluded pulmonary arterial bed will be producing changes in the ECG.\textsuperscript{48} Electrocardiographic abnormalities are seen in 70%–80% of patients presented with APE. The common features including sinus tachycardia, RBBB, S1Q3T3 pattern, precordial non-specific ST-segment depression, and T-wave changes will authorize the physician for further diagnostic testing and treating the suspected PE.\textsuperscript{47} Although some ECG changes are more common in PE, the ECG alone is inadequate to accept or reject the diagnosis.\textsuperscript{3} Despite this sign has a low ECG sensitivity and specificity for diagnosing PE, but it can still direct clinicians.\textsuperscript{3,9} No characteristic ECG abnormality is definitively associated with PE.\textsuperscript{9} Sinha and associates\textsuperscript{51} revealed that even though standard ECG findings have relatively low clinical use, they could indicating the pretest probability of PE before performing computed tomography pulmonary angiography (CTPA). The physician should be considered the probability of pulmonary embolism (76%) if there is the presence of ≥3 of the following abnormalities:\textsuperscript{1,2,3,4,7,8}

1. Incomplete or complete RBBB which was associated with ST-segment elevation and positive T-wave in lead V1; 2) S-waves in leads I and aVL of > 1.5 mm; (3) a shift in the transition zone in the precordial leads to V5; (4) Q-waves in leads III and aVF, but not in lead II; (5) Right-axis deviation (RAD), with a frontal QRS-axis of > 90 degrees, or an indeterminate axis; (6) A low-voltage QRS-complex of < 5 mm in the limb leads; and (7) T-wave inversion in leads III and aVF or leads V1 to V4, which occurred more often in patients with symptoms for > 7 days. Sinus tachycardia was the most common followed by ST-T changes in V1–V3 and S1Q3T3 in cases of PE.\textsuperscript{9} The combination of S1Q3T3 with a new RBBB seen in this case presentation is indicative of ACP, but in this particular clinical setting was highly suspicious for PE with RV strain.\textsuperscript{3} The other ECG abnormalities are suggestive for RV overload and evaluated concerning their impact on in-hospital mortality\textsuperscript{52}.

1. Sinus tachycardia or bradycardia. (2) Atrial arrhythmias. (3) Heart block; (4) Abnormal axis deviation; (5) Shifting in the transition zone (R=S) to V5 or further leftward; (6) Complete or incomplete RBBB; (7) Peripheral low voltage (in the limb leads); (8) Pseudo-infarction pattern (deep Q waves) in leads III and aVF; (9) ST-segment elevation ≥ 0.1 mV over the right (V2–V3) or the left (V4–V6) precordial leads; (10) ST-segment depression ≥ 0.05 mV over the right or the left precordial leads; and (11) T-wave inversion over the right or the left precordial leads. Chou\textsuperscript{48} suggests that the following findings are typical: (1) an S1Q3 or S1Q3T3 pattern; (2) A RAD; (3) Transient complete or incomplete RBBB; (4) T-wave inversion in the right precordial leads; and (5) sinus tachycardia. Other more rare findings are (a) left displacement of the transitional zone; (b) left axis; (c) QR in V1; (d) R. S in V1; (e) ST elevation in lead III.

**Pathogenesis of McGinn-White Sign**

S1Q3T3-pattern is a consequence of volume and pressure overload in the RV. It may appear in other ACP-causing disorders. The S-wave in lead I indicate the presence of RBBB. The Q-wave with the T-wave inversion in lead III points to RV strain.\textsuperscript{3} It was extrapolated that the S1Q3T3-pattern was a sign of RV change due to occlusion of the pulmonary vasculature.\textsuperscript{2} Moreover, ECG features with RV strain have been found to correlate with the degree of pulmonary artery obstruction due to PE, increased pressure, and wall tension on the RV.\textsuperscript{43} The presence of the RV strain pattern on the ECG is correlating with an increased risk of all-cause death and clinical deterioration.\textsuperscript{43} In patients of RV dysfunction, T-wave inversion in leads V1–V3 has greater sensitivity and diagnostic accuracy if compared with the S1Q3T3 and RBBB features which have good specificity and moderate accuracy.\textsuperscript{43} The S1Q3T3-pattern is the direct result of right heart strain due to increased RV pressures (e.g., ACP). This will be parallel to meeting an increasing the resistance in the RV which it must pump against the strain will result.\textsuperscript{24,25} It was noted that with significant occlusion of the pulmonary artery, the RV and RA quickly dilate leading to ACP. When the right side of the heart dilates, it causes a rotation in the transverse level causing the RV to move anteriorly and the LV to move posteriorly. When this occurs changes in ECG occur, including the S1Q3T3-pattern.\textsuperscript{1,53}

**Sensitivity and Specificity of S1Q3T3 Sign**

The S1Q3T3-pattern is a frequently faced pattern that makes its diagnostic value will debatable.\textsuperscript{54,55} Unfortunately, the S1Q3T3 sign was mistakenly by numerous clinicians as the pathognomonic ECG-pattern for APE over decades.\textsuperscript{18,21} This classic sign is neither pathognomonic, sensitive, nor specific.\textsuperscript{56} It is not a certain pathognomonic of APE.\textsuperscript{18} While the
S1Q3T3-pattern is frequently taught in medical sessions worldwide as the pathognomonic ECG pattern for APE. However, The reported incidence in APE is quite highly variable with studies from10-50% and in some studies is equally likely in patients without APE. Regrettably, the McGinn-White sign is insensitive and non-specific for the diagnosis of APE. S1Q3T3-pattern had a sensitivity of 54% and a specificity of 62% in pulmonary embolism. This is a very non-specific pattern seen in patients with right heart strain. Thus, the S1Q3T3-pattern supports a diagnosis of pulmonary embolism but does not confirm it. The S1Q3T3-pattern in the ECG is highly non-specific for PE. However, it is equally likely to be found in patients without PE who were initially suspected to have PE.

**Potentiation of S1Q3T3-Pattern**

The presence of sinus tachycardia along with S-wave in the lead I, Q-wave, and inverted T-wave in the lead III are commonly associated with acute massive PE causing ACP. The combination of S1Q3T3 with a new RBBB seen in this case presentation is indicative of ACP. These are highly suspicious of PE with RV strain. If the V1 and V2 leads are an inverted in conjunction with S1Q3T3 pattern, this is a very specific finding in APE. PR displacement, late R in aVR, slurred S in V1 or V2, the S1Q3T3 pattern and T-wave inversion in V1 or V2 are remarkably common in patients with confirmed PE. Nazeeryrollas et al. found that the S-wave in I and Q-wave in III is significantly more common among those with confirmed PE.

**Transient S1Q3T3 and Reversibility of Sign**

Reported cases of reversible S1Q3T3-pattern were described with pulmonary embolism, pneumothorax, and in the pregnant asthmatic exacerbations. Spontaneous resolving is meaning that the S1Q3T3 pattern in subsequent electrocardiogram findings of a patient with PE is not a permanent sign. It is frequently transient, short-lived, and resolving within 14 days after onset of the disease. The S1Q3T3-pattern is commonly reversed into a normal state after the treatment for PE.

**Differential Diagnosis of S1Q3T3 Pattern**

However, this pattern is likely to be seen more often in pulmonary and non-pulmonary embolism patients. The ECG changes of S1Q3T3 were present in 10% of those with non-embolic pulmonary embolism. All causes of ACP, including PE, can result in the S1Q3T3 finding on the ECG left posterior fascicular block (LPFB), aortic intramural hematoma with extension to pulmonary artery, previous inferior myocardial infarction (IMI), acute bronchospasm (BA), in pregnant women, right side pneumothorax, lobar pneumonia, exacerbation of obstructive airway disease, atelectasis, recent pneumonectomy, or upper airway obstruction, pulmonary hypertension, obstructive sleep apnea (OSA), acute respiratory distress syndrome (ARDS), pulmonary hemorrhage, neoplastic disease, and other acute pulmonary diseases. S1Q3T3 pattern may present in Cor-Triatriatum.

Although the S1Q3T3 sign can be a helpful clue in the diagnosis of PE, this sign is rarely present in patients with ventilation-perfusion (VQ) mismatch like-pneumonia. This pattern reflects a RAD state so, the RV appears projected more anteriorly and to the right of the LV. This sign is poorly specific because it sometimes is seen in a normal state, in a slim patient, or in the various diseases associated with RV overload (PH, COPD and emphysema) or RBBB. Its diagnostic value increases with the presence of characteristic clinical signs or other evocative electrical signs and when it appears or accentuates suddenly and disappears on subsequent tracings. This sign is most often short-lived, appears early, and disappears within a few days. The S1Q3T3 sign may be acutely present in 12% with; tricuspid regurgitation (area >m/sec), septal flattening, and RV dilation. There is broad-spectrum etiological differentiation for the S1Q3T3-pattern (Table 3).

**Table 3. Etiological summary of S1Q3T3-pattern**

<table>
<thead>
<tr>
<th>Respiratory</th>
<th>Cardiovascular</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumothorax, Pneumonia</td>
<td>Pulmonary embolism</td>
<td>Normal variant (15%)</td>
</tr>
<tr>
<td>Acute bronchospasm or bronchial asthma</td>
<td>LPFB, Old IMI</td>
<td>Neoplasms</td>
</tr>
<tr>
<td>Exacerbation of obstructive airway disease</td>
<td>Cor-Triatriatum</td>
<td>Slim patient</td>
</tr>
<tr>
<td>Severe pneumonia</td>
<td>RBBB</td>
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International Journal of Research Studies in Medical and Health Sciences V5 ● 111 ● 2020 19
### S1Q3T3 PATTERN ALARMS

There are serious alarms for acute pulmonary embolism. Massive pulmonary embolism\(^5,6,8,9\), acute cor-pulmonale\(^1,5,6,8,9\), cardiogenic shock\(^8,9\), cardiogenic pulmonary edema\(^8\), and sudden death\(^8,9\) are common associations and serious sequels for S1Q3T3-pattern. (Figure 1)

#### CONCLUSIONS

The author had concluded that the McGinn-White sign or S1Q3T3-pattern not a pathognomonic sign for acute pulmonary embolism. But it is a guide for pulmonary embolism. S1Q3T3 sign can be found in other states like acute cor-pulmonale and right heart strain. The clinical data is the most important factor for the physician in the directory of the outcome for S1Q3T3-pattern.

#### ACKNOWLEDGMENT

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#### REFERENCES


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<tr>
<th>ARDS (^4,5)</th>
<th>RV dilation(^4,4)</th>
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<tbody>
<tr>
<td>Pulmonary hemorrhage(^4,5)</td>
<td>Septal flattening(^4,4)</td>
</tr>
<tr>
<td>Atelectasis</td>
<td>Aortic intramural hematoma with extension to pulmonary artery(^5,6,4)</td>
</tr>
<tr>
<td>Upper airway obstruction(^4,5)</td>
<td></td>
</tr>
<tr>
<td>OSA(^4,5)</td>
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<td>Recent pneumonectomy(^6)</td>
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