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# Risk Stratification of Patients with Acute Pulmonary Embolism

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## 1. Introduction

Acute pulmonary embolism (PE) is an under-diagnosed but potentially fatal condition. This condition presents with a wide clinical spectrum, from asymptomatic small PE to life-threatening one causing cardiogenic shock.

Depending on the estimated risk of an adverse outcome, treatment with thrombolysis or embolectomy may be indicated in high-risk individuals. Conversely, early hospital discharge or even home treatment with anti-coagulation may be considered in low risk PE.

Thus, a systematic approach to risk stratification is essential in guiding the management of patients diagnosed with acute PE. Evidence-based prognostic tools such as clinical scores, echocardiography, computed tomography scans, and cardiac biomarkers will be discussed.

## 2. Hemodynamic consequences of acute pulmonary embolism

Anatomically massive PE has been defined as having more than 50% obstruction of the pulmonary vasculature or the occlusion of two or more lobar arteries (Urokinase Pulmonary Embolism Study Group, 1970). In a unique situation, a large embolus may lodge at the bifurcation of the main pulmonary artery, i.e. saddle embolus. Although it was once regarded as a severe form of PE, a saddle PE shares a similar clinical course with a non-saddle PE, and low in-hospital mortality (Pruszczyk et al., 2003; Kaczyńska et al., 2005; Ryu et al., 2007).

An anatomically massive PE in a patient with adequate cardiopulmonary reserve and a submassive PE in a patient with poor reserve may manifest similar hemodynamic outcomes. The hemodynamic response to an acute PE depends not only the size of the embolus and the degree of pulmonary vasculature obstruction, but also on the physiologic reaction to the neurohumoral factors released and the underlying cardiopulmonary status of the patient.

Normally, the RV faces low resistance as it empties into a low-pressure system of the pulmonary vasculature. In acute PE, both mechanical obstruction and hypoxic vasoconstriction increase pulmonary vascular resistance, and this initiates a series of hemodynamic derangements leading to RV dysfunction (Figure 1). The release of humoral factors, such as serotonin from platelets, thrombin from plasma and histamine from tissue also contribute to pulmonary artery vasoconstriction. As a consequence of the elevated pulmonary resistance, the highly compliant RV dilates acutely.

Initially, compensatory maintenance of cardiac output is achieved by catecholamine-driven tachycardia and vasoconstriction. The left atrial contraction also contributes more than usual to

left ventricular filling. Eventually, with persistent pressure overload and wall stress, RV systolic function begins to fall. Cardiac output is decreased further by impaired distensibility of the left ventricle (LV) from the leftward shift and flattening of the interventricular septum during systole/early diastole, and impaired LV filling during diastole.

Myocardial ischemia also worsens RV function by increased oxygen demands due to elevated wall stress and decreased oxygen supply from elevated right-sided pressures (Goldhaber et al., 2003; Wood, 2002).

The hemodynamic cascade provides an appreciation in understanding the roles the various imaging modalities and biomarkers play in the risk assessment of patients with acute PE.

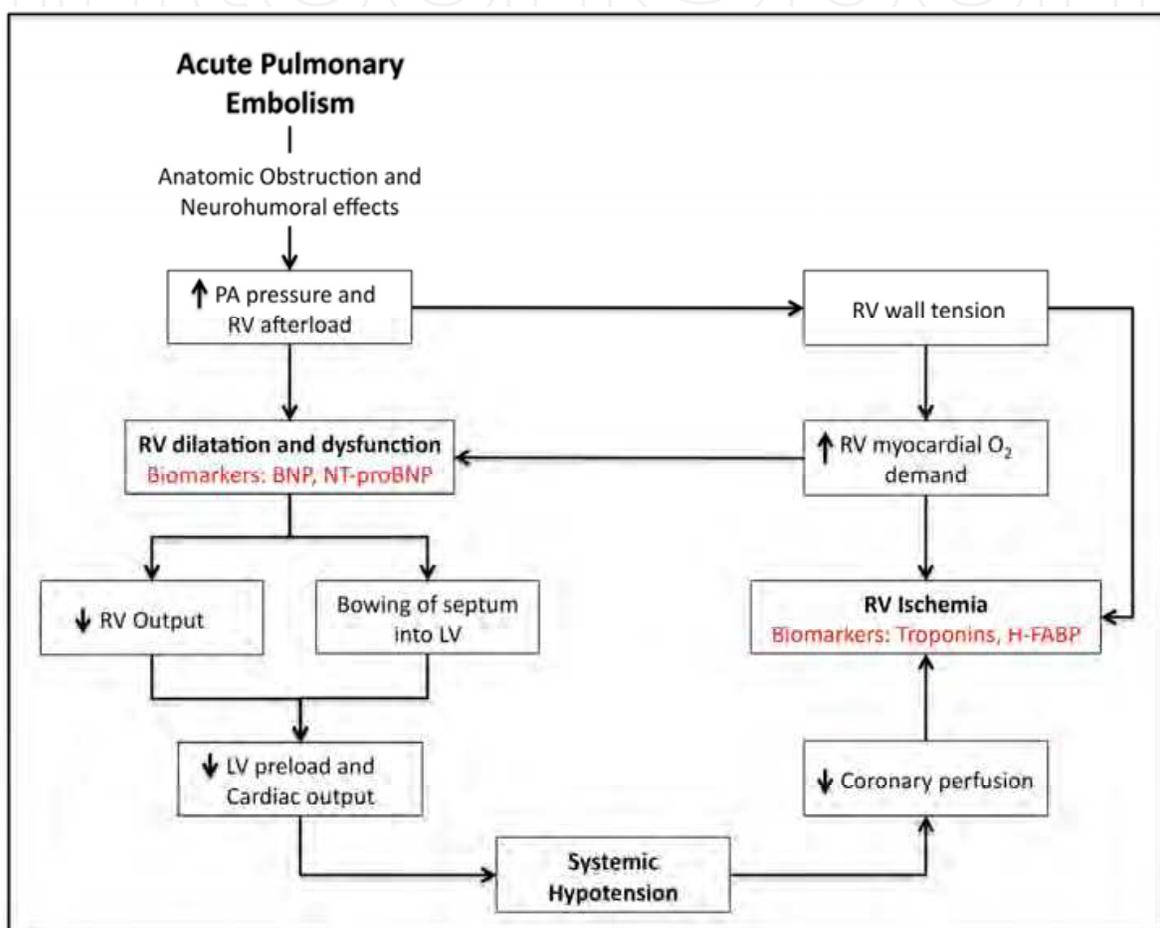


Fig. 1. Hemodynamic consequences due to acute pulmonary embolism and mechanism of biomarkers detection (PA, pulmonary artery; RV, right ventricle; LV, left ventricle; BNP, brain natriuretic peptide; NT-proBNP, NT-pro brain natriuretic peptide; H-FABP, heart-type fatty acid binding protein)

### 3. Classification of risk

The prognosis of acute PE correlates most directly with the degree of hemodynamic compromise and RV dysfunction.

The European Society of Cardiology recommends an individual risk assessment of early PE-related deaths (Torbicki et al, 2008). Based on the clinical presentation, presence of RV dysfunction and elevated biomarkers, high-risk PE has a short-term (in-hospital or 30-day)

mortality risk of > 15%. Non high-risk patients are more heterogenous and are further stratified into intermediate risk (short term mortality risk of 3 to 15%) and low risk (short term mortality risk of less than 1%) (Figure 2).

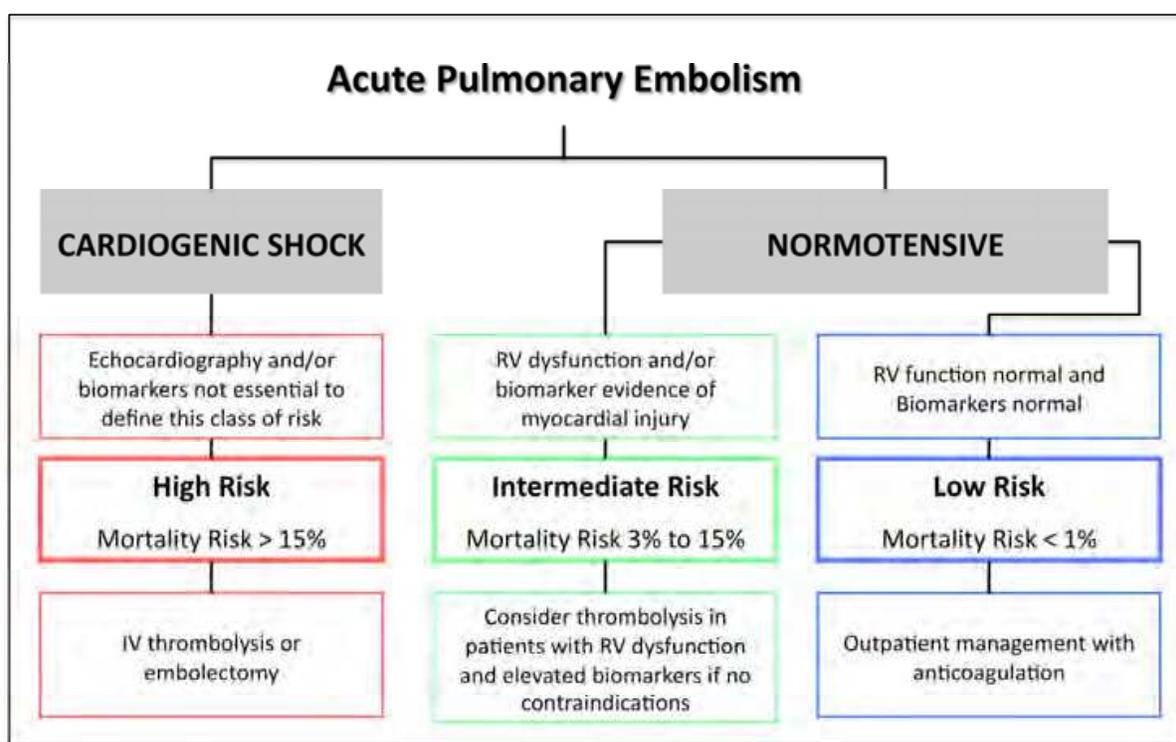


Fig. 2. Risk stratification based on pulmonary embolism-related adverse outcomes

#### 4. Risk assessment based on clinical parameters and risk models

The presence of co-morbidities increases the risk of adverse events, even with a small PE. Advanced age (more than 70 years old), congestive heart failure, cancer, or chronic lung disease were identified as independent predictors of 3-month mortality from PE (Goldhaber, 1999).

The clinical manifestations of acute PE are non-specific and often overlap with other cardiac and pulmonary conditions. Chest pain is one of the most frequent presentations of PE. Pleuritic chest pain, with or without dyspnea, is usually caused by pleural irritation due to distal emboli which may be associated with pulmonary infarction. Individuals may also present with retrosternal angina-like chest pain, reflecting right ventricular ischemia. Isolated dyspnea of a rapid onset is suspicious of a more central and hemodynamically significant PE. Occasionally, the onset of dyspnea is more insidious especially in patients with co-existing heart failure or pulmonary disease.

Cardiogenic shock occurs in less than 5% of acute PE, and these patients have a high risk of death. Conversely, patients with non-massive PE present with stable blood pressure and have a lower risk of death. In the International Cooperative Pulmonary Embolism Registry,

the death rate was about 58% in hemodynamically unstable patients and about 15% in patients who were hemodynamically stable (Goldhaber et al., 1999).

Despite the limited sensitivity and specificity of individual symptoms, and signs, clinical risk models consisting of a combination of clinical variables makes it possible to identify patients with suspected PE into risk categories. The Geneva prognostic index and the Pulmonary Embolism Prognostic Index (PESI) are two standardized prognostic scores that incorporated systolic blood pressure, amongst other clinical parameters, to predict risk of PE-related adverse outcomes. These scores have been well validated to identify low-risk, clinically stable patients for outpatient treatment.

The Geneva prognostic index is based mainly on findings from the past medical history and the clinical examination (Table 1). Risk stratification was performed using the score with a maximum of 8 points. Patients with a score of 2 or less are considered at low risk for PE-related adverse events. Of the 180 low risk patients identified, only 4 experienced an adverse outcome at 3 months (Wicki et al., 2000).

The PESI score uses 11 weighted clinical parameters commonly available on presentation (Table 2). Patients are stratified by their scores into five classes of increasing risk of death and adverse outcomes. Patients classified as low risk (score of 85 or less corresponding to PESI Class I or II) have a 30-day mortality of 1.0% (Aujesky et al., 2006).

Of the two, the PESI score appears to be more accurate at predicting low-risk patients. In a head-to-head comparison, the two models were retrospectively applied in a cohort of 599 patients with PE. The 30-day mortality in the Geneva low-risk patients was 5.6% compared to the PESI low-risk mortality rate of 0.9%. The PESI score classified fewer patients as low-risk than the Geneva model (36% vs. 84%), but the area under the receiver operating curve was higher for the PESI (0.76 vs. 0.61) (Jiménez et al., 2007).

Unfortunately, the major limitation of the PESI is the difficulty to apply in a busy clinical environment. There are many variables to be considered, each with its own weight. To address this limitation, a simplified PESI has been developed with similar prognostic accuracy (Jiménez et al., 2010). However, prospective validation of the simplified PESI is lacking.

Risk Factor	Geneva Risk Scale (Points)
Active cancer	2
Systolic blood pressure < 100mmHg	2
Concomitant deep venous thrombosis at diagnosis	1
History of venous thromboembolism	1
Congestive heart failure	1
Hypoxia (arterial PaO <sub>2</sub> < 60mmHg)	1
<b>Geneva Risk Categories</b>	
Low risk: 2 or fewer points; High risk: 3 or more points	

Table 1. Geneva Pulmonary Embolism Prognostic Index

Variable	Points
Age	1 point/year
Male gender	10
Cancer	30
Congestive heart failure	10
Chronic lung disease	10
Heart rate > 110/min	20
Systolic blood pressure < 100mmHg	30
Respiratory rate $\geq$ 30/min	20
Body temperature < 36°	20
Disorientation, lethargy, stupor or coma	60
Oxygen saturation < 90% (pulsoximetry)	20

Risk category	Points	30-day mortality risk
Class I	< 65	0 %
Class II	66 to 85	1.0 %
Class III	86 to 105	3.1 %
Class IV	> 125	24.4 %

Table 2. Pulmonary Embolism Severity index (Low risk = Class I and II)

## 5. Risk assessment based on presence of right ventricular dysfunction

The majority of patients with acute PE are stable at time of diagnosis, but this may not necessarily imply a benign course. Patients may appear stable initially because the development of RV failure and cardiogenic shock can be delayed as the vicious cycle of elevated pulmonary resistance, RV dilatation, and the RV hypokinesia unfolds. In stable patients with acute PE, the presence of RV dysfunction is associated with a high mortality rate (Sanchez et al., 2008).

In addition, RV dysfunction in acute PE predicts recurrent thromboembolic events. During a mean follow-up of three years, patients with persistent RV dysfunction were more likely to have a recurrent PE, deep venous thrombosis or higher PE-related deaths compared with patients without RV dysfunction or had RV dysfunction that resolved at discharge (Grifoni et al., 2006).

### 5.1 Echocardiography

Echocardiography is non-invasive and able to provide very useful information promptly. However, it is not recommended as a routine imaging test to diagnose PE because an echocardiogram can appear normal in about 50% of the patients with suspected PE. Despite its limitations, a bedside echocardiogram in a hemodynamically unstable patient is an

invaluable first-line tool to diagnose other conditions that mimic an acute PE such as myocardial infarction, proximal aortic dissection or a pericardial tamponade. These emergency conditions require management very different from an acute PE.

More importantly, the main role of echocardiography in the setting of an acute PE is to identify a sub-group of stable, non-high-risk patients with RV dysfunction for more aggressive management. The prognostic implications of RV dysfunction detected with echocardiography, even in stable acute PE patients, are clear and this has been illustrated in two separate meta-analyses. In all studies, patients with normal RV function have very good prognosis, with low in-hospital mortality (ten Wolde et al., 2004; Sanchez et al., 2008). Unfortunately, unlike the left ventricle, the anatomy of the RV is complex and assessment of RV function is challenging. Thus, the criteria of RV dysfunction are not well established and differ among published studies (Table 3).

Echocardiography detects both direct and indirect hemodynamic consequences of acute PE (Figure 1). Direct evidence of RV dysfunction includes a dilated RV cavity as compared to the LV. More convincingly, the concomitant presence of RV hypokinesia suggests a failing RV. However, qualitative assessment of RV wall motion is subjective and insufficient in this era of standardization. There is a distinctive two-dimensional echocardiographic finding of regional RV dysfunction that has been described in acute PE. This abnormality is characterized by the presence of normal or hyperdynamic RV apex despite moderate to severe RV free-wall hypokinesia (McConnell sign, Figure 3). Echocardiography may also show flattened inter-ventricular septum or paradoxical motion towards the LV during systole to suggest RV pressure overload (Figure 4).

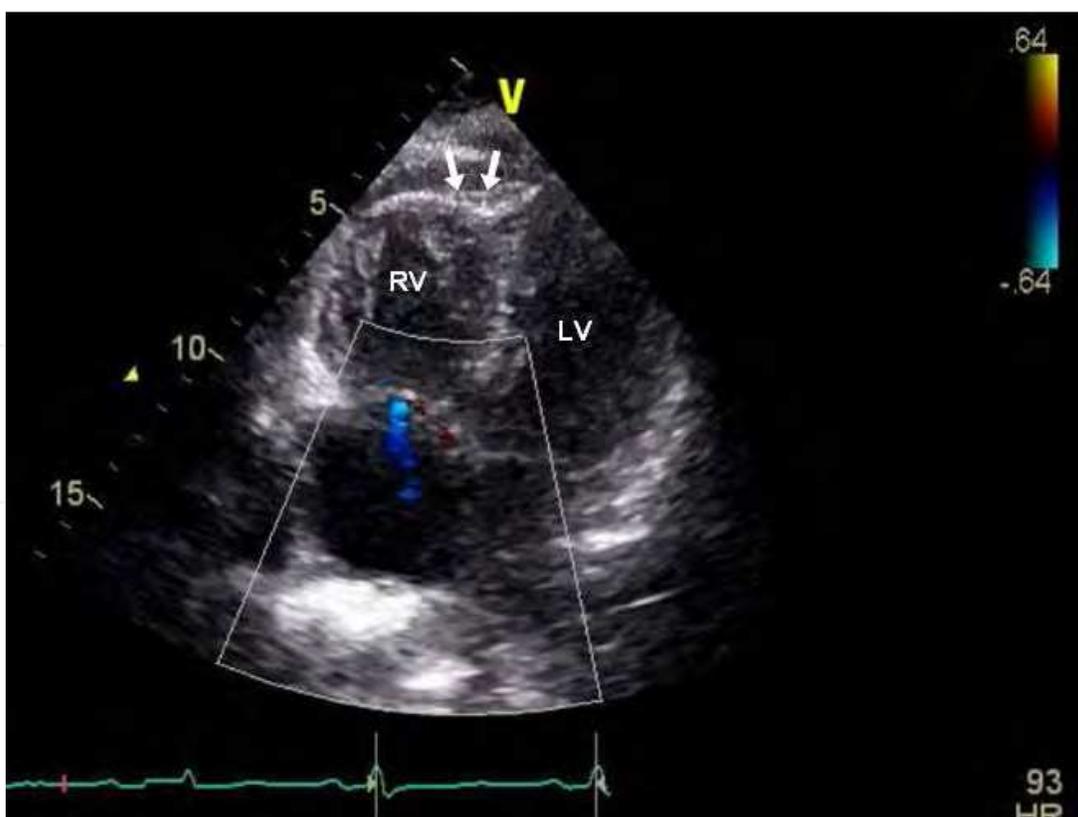


Fig. 3. Apical four-chamber view demonstrating McConnell sign: hypokinesia of the right ventricle (RV) free wall sparing the apex (arrows). The RV is markedly dilated.

Authors	Definition of RV dysfunction
Goldhaber et al, 1993, 1999 Ribeiro et al, 1997, Jerjes-Sanchz et al, 2001, Kucher et al, 2003, 2005	RV hypokinesia by qualitative assessment of the RV wall motion
Kasper et al, 1997	Dilated RV cavity (qualitative assessment of RV compared to left ventricle) or RVEDD > 30mm; or when 2 of the following were present: <ol style="list-style-type: none"> <li>1. TR velocity &gt; 2.8m/s</li> <li>2. TR velocity &gt; 2.5m/s in the absence of inspiratory collapse of the IVC</li> <li>3. Dilated RPA (&gt; 12mm/m<sup>2</sup>)</li> <li>4. RV wall thickness &gt; 5mm</li> <li>5. Loss of inspiratory collapse of the IVC</li> </ol>
Grifoni et al, 2000, 2001	Presence of any 1 of the following: <ol style="list-style-type: none"> <li>1. Dilated RV (RVEDD/LVEDD &gt; 1 or RVEDD &gt; 30mm)</li> <li>2. Septal dyskinesia</li> <li>3. Pulmonary hypertension (Doppler PAT &lt;90ms or RV-RA gradient &gt;30mmHg)</li> <li>4. Absence of RV hypertrophy (thickness &gt; 7mm)</li> </ol>
Pieralli et al, 2006	Presence of any 1 of the following: <ol style="list-style-type: none"> <li>1. Dilated RV (RVEDD/LVEDD &gt; 1 or RVEDD &gt; 30mm)</li> <li>2. Septal dyskinesia</li> <li>3. Pulmonary hypertension (Doppler PAT &lt;90ms or RV-RA gradient &gt;30mmHg)</li> </ol>
Vieillard-Baron et al, 2001	RVEDA/LVEDA > 0.6 with septal dyskinesia
Kostrubiec et al, 2005	Presence of any 1 of the following: <ol style="list-style-type: none"> <li>1. RVEDD/LVEDD &gt; 0.6 with RV hypokinesia</li> <li>2. Pulmonary hypertension (Elevated TVPG &gt;30mmHg with PAT &lt;80ms)</li> </ol>

(RVEDD/LVEDD, right to left end-diastolic diameter ratio; RVEDA/LVEDA, right to left ventricular end-diastolic area ratio; RV-RA gradient, right ventricular-right atrial gradient; PAT, pulmonary arterial flow acceleration time; TVPG, tricuspid valve pressure gradient; IVC, inferior vena cava; TR, tricuspid regurgitation).

Table 3. Studies evaluating RV dysfunction with echocardiography

Indirect evidence of RV dysfunction from echocardiography includes raised pulmonary artery systolic pressure (PASP). This can be estimated from the right ventricular systolic pressure (RVSP) according to the formula:  $PASP = RVSP + \text{estimated right atrial pressure}$  (Figure 5). The RVSP is obtained from the velocity of the tricuspid regurgitant jet ( $v$ ), such that  $RVSP = 4v^2$  and the right atrial pressure is estimated from the size and respiratory variation of the inferior vena cava.

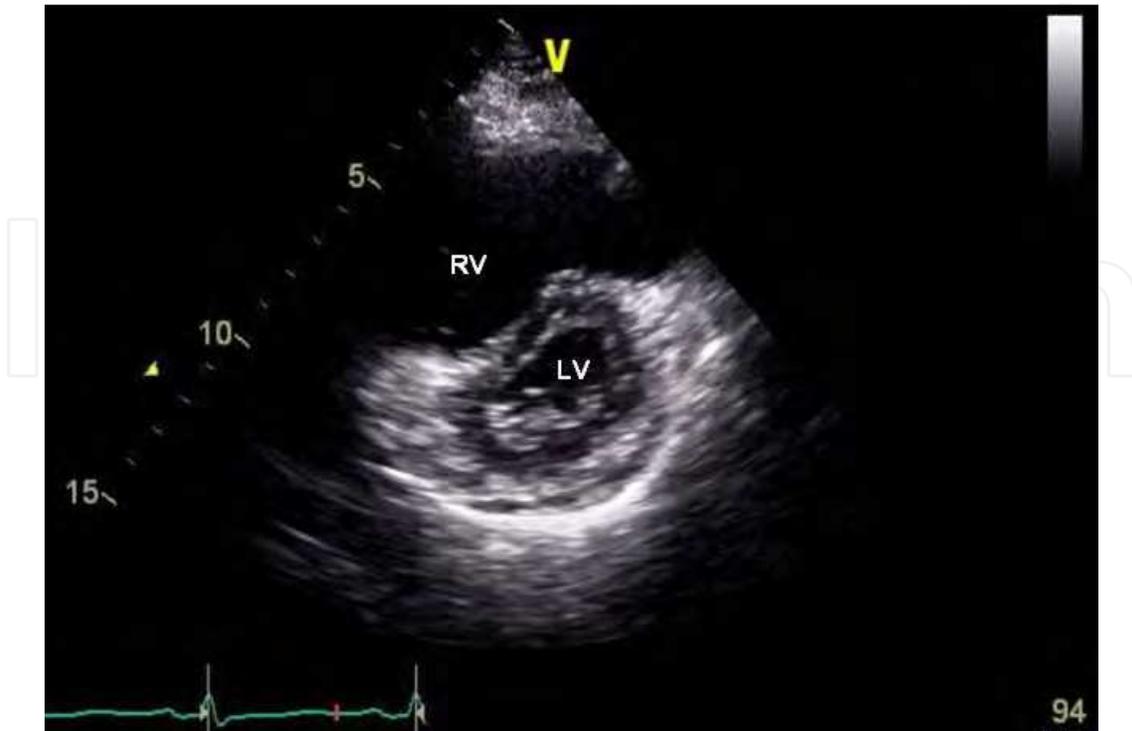


Fig. 4. Parasternal short axis view showing an enlarged right ventricle (RV) with a “D” shaped septum, suggesting RV pressure overload.

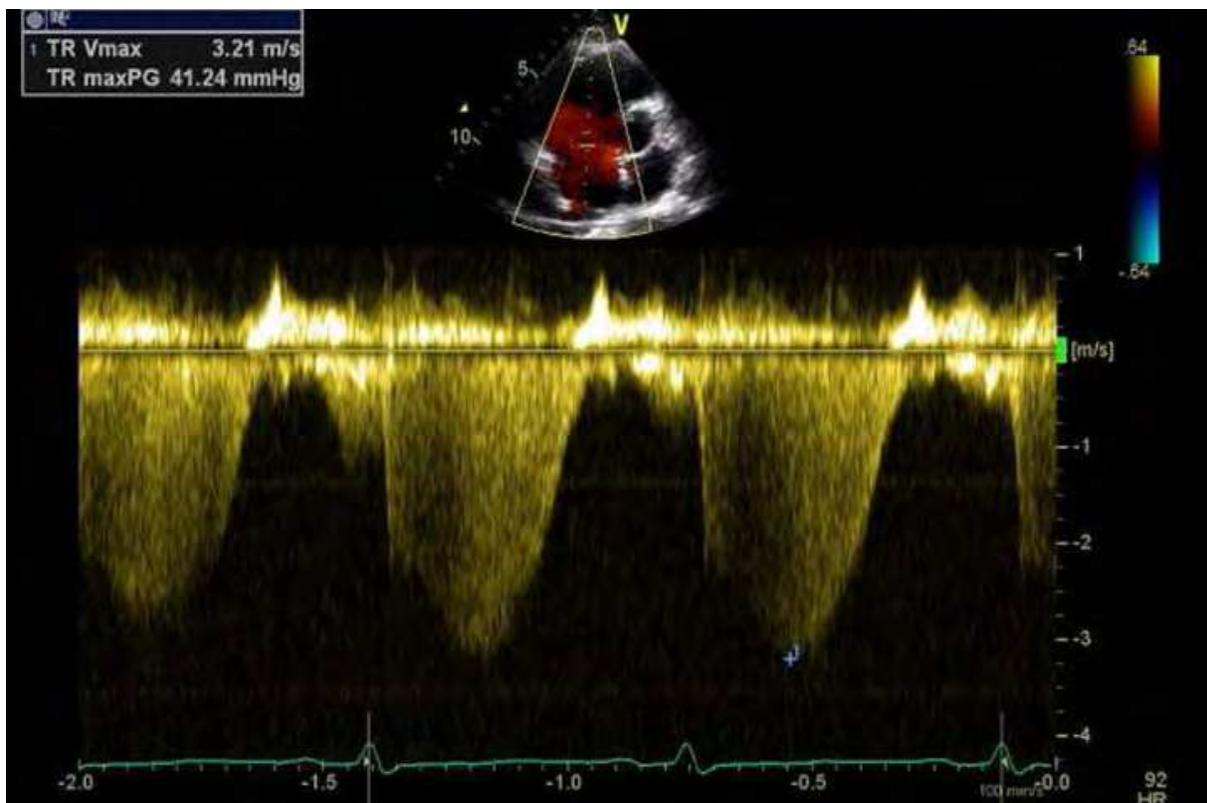


Fig. 5. Continuous wave Doppler demonstrating peak tricuspid velocity of 3.2m/s, corresponding to a right ventricular systolic pressure of 41mmHg.

An elevated pulmonary artery systolic pressure of more than 50mmHg at time of diagnosis is associated with persistent pulmonary hypertension at 1 year (Ribeiro et al., 1999). In patients with acute PE, the absence of any significant tricuspid regurgitation makes the severe pulmonary hypertension less likely.

Besides the evidence of RV dysfunction and elevated pulmonary arterial pressures, other echocardiographic features with prognostic implications include:

1. A right-to-left shunt, such as a patent foramen ovale (PFO). In a prospective study of 139 consecutive patients with acute PE, PFO was diagnosed in 48 patients by contrast echocardiography. Evidence of a PFO in patients with acute PE was associated with higher mortality rate (33% vs. 14%) and higher incidence of peripheral thromboembolic events (Konstantinides et al., 1998). These patients are particularly prone to paradoxical embolism due to increased right-to-left shunt from elevated right-sided pressures.
2. A free-floating right heart thrombus (Figure 6). The prevalence of patients with a right heart thrombus visualized during echocardiography was about 4% (Torbicki et al., 2003). Thrombus from the right heart usually arises from the lower limb veins. These thrombi are highly mobile and often described as having the appearance of a worm, or snake. Free-floating thrombus can embolize at any time and have a dismal prognosis regardless of therapeutic option (Chin et al., 2010). The mortality rate of about 20% within 24 hours of diagnosis, and mortality is significantly linked with the occurrence of cardiac arrest (Chartir et al., 1999).

## 5.2 Computed tomography

Contrast enhanced computer tomography (CT) of the pulmonary arteries is increasingly used as a first-line imaging modality for PE diagnosis. The anatomical distribution and burden of embolic occlusion of the pulmonary arterial bed can be assessed easily by CT (Figure 7). However, the anatomical assessment seems less relevant for risk stratification than assessment based on functional (hemodynamic) consequences of PE.

Most scanners allow reconstruction of standardized cardiac views and direct measurements of ventricular dimensions can be made. RV enlargement based on RV-to-LV dimension ratio,  $RV_d/LV_d$ , (Figure 8) on the reconstructed CT four-chamber view correlated with RV dysfunction on echocardiogram. Using  $RV_d/LV_d > 0.9$  as cut-off, the sensitivity and specificity for predicting PE-related adverse events were 83% and 49% on the reconstructed CT, respectively. Comparatively, the sensitivity and specificity of  $RV_d/LV_d > 0.9$  on echocardiography were 71% and 56%, respectively (Quiroz et al., 2004).

In addition to having good correlation with RV dysfunction on echocardiography, assessment of RV enlargement on chest CT in acute PE also predicted patients at risk of death from RV failure (Van der Meer et al., 2005; Schoepf et al., 2004). The greatest role appears to be the identification of low-risk patients due to its high negative predictive value (Table 4).

Author	CT equipment (Cutoff)	Sensitivity (%)	Specificity (%)	NPV (%)	PPV (%)
Van der Meer et al., 2005	SDCT (RV/LV >1)	100	45	100	10
Schoepf et al., 2004	4 - 16 MDCT (RV/LV > 0.9)	78	38	92	16

Table 4. Trials reporting RV/LV diameter ratio assessed by CT as a risk marker for 30-day all cause mortality in acute pulmonary embolism.

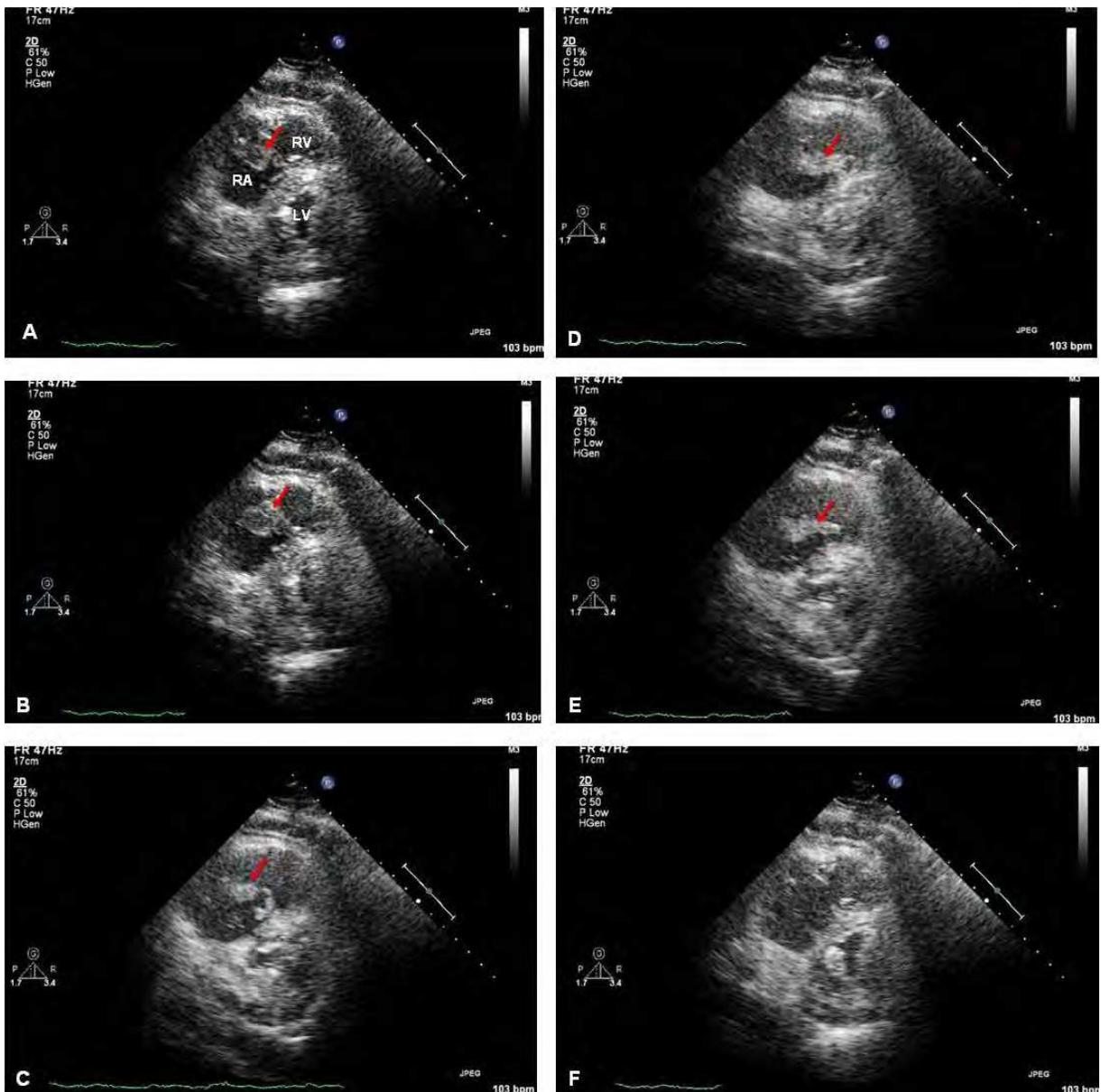


Fig. 6. Free floating thrombus (red arrow) transiting from the RA causing acute pulmonary embolism (RA, right atrium; LA, left atrium; LV, left ventricle).

Other CT-derived parameters have also been investigated. The presence of interventricular septal bowing is predictive of PE-related deaths but has low sensitivity and high inter-observer variability (Araoz et al., 2007), scores to quantify the extent and location of pulmonary artery obstruction have been developed but not shown to be of prognostic relevance yet (Qanadil et al., 2001; Ghanima et al., 2007).

### 5.3 Ventilation-perfusion scintigraphy

Lung ventilation-perfusion scintigraphy (V/Q scan) is a well-established diagnostic test used in patients suspected of PE. Interpretation of the scans can vary, depending on the algorithms used (PIOPED criteria, modified PIOPED criteria, McMaster Clinical criteria and PisaPED criteria) and the experience of the reader. The diagnostic roles and limitations of V/Q scan are beyond the scope and will not be discussed in this chapter.

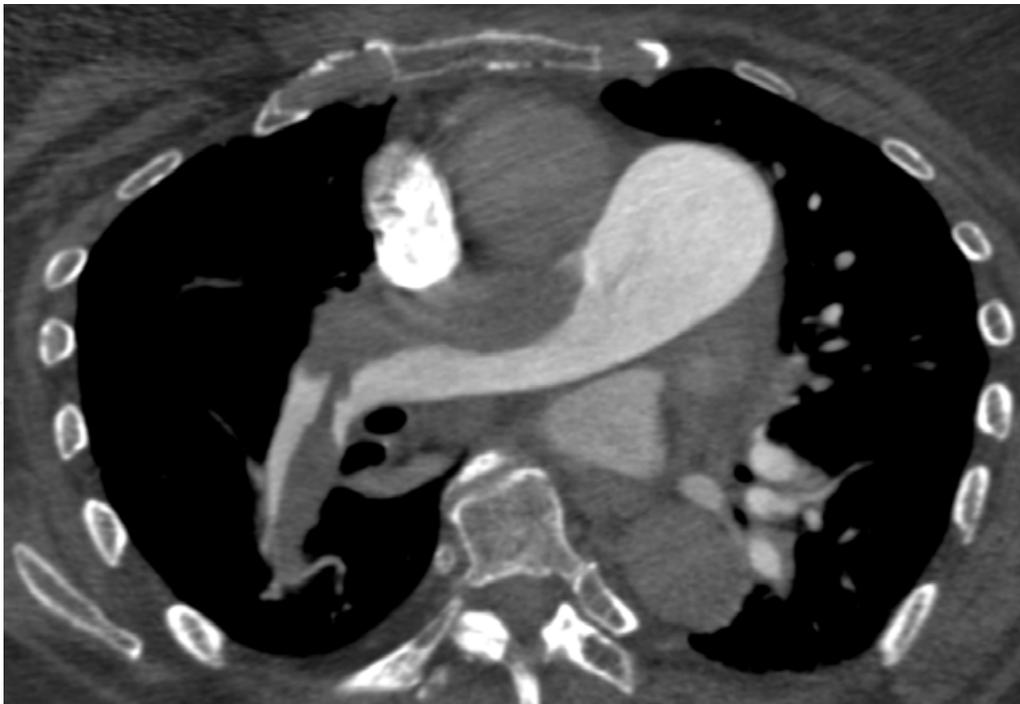


Fig. 7. Computed tomography pulmonary angiogram showing a large embolus within the right main pulmonary artery, extending to the main right upper lobe.

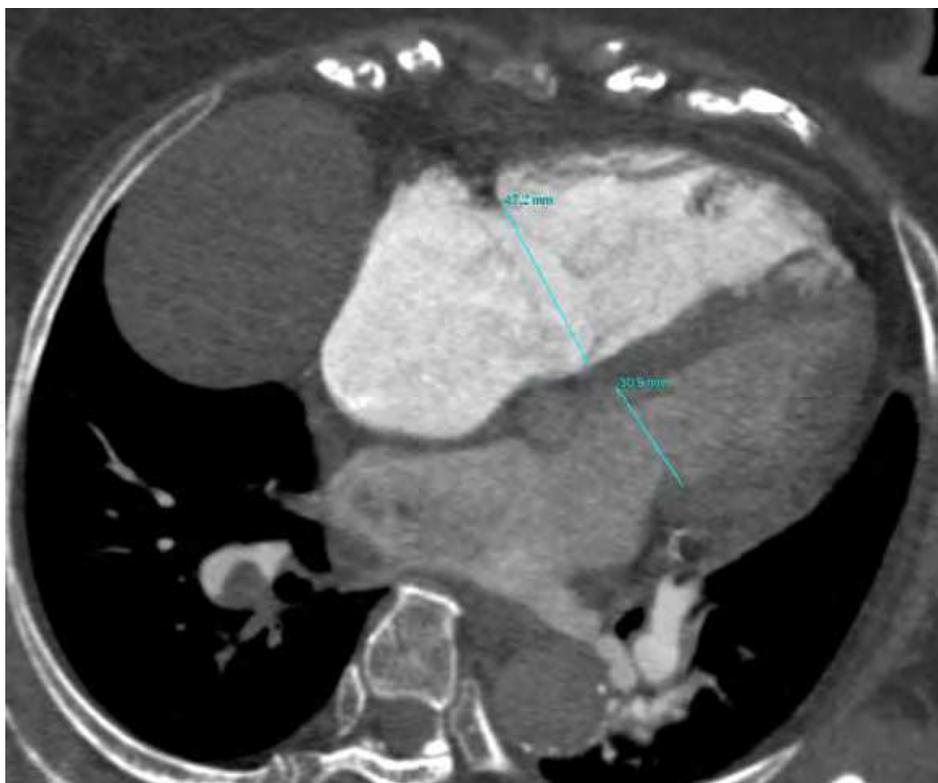


Fig. 8. Measurement of the short axes of the RV (47 mm) and LV (39 mm) on computed tomography pulmonary angiogram of the same patient (RV, right ventricle; LV, left ventricle)

Perfusion defects due to PE increase with the number and size of emboli, without corresponding ventilation compromise ("mismatch" defects). However, the prognostic implications of the number and size of defects on a V/Q scan have not been investigated.

## 6. Risk assessment based on biomarkers of myocardial injury

Cardiac troponins I and T as well as NT-pro brain natriuretic peptide (NT-proBNP) and brain natriuretic peptide (BNP) have emerged as promising tools for risk stratification.

### 6.1 Cardiac troponins

Cardiac troponins may be increased in patients with PE, even in the absence of coronary artery disease. The presumed mechanism is acute right heart overload attributed to myocardial ischemia and from oxygen supply-demand mismatch. The elevation usually resolves within 40 hours following PE in contrast to more prolonged elevation after an acute myocardial infarction. The peak level is usually lower than in acute myocardial infarction (Müller-Bardorff et al., 2002).

Patients with an elevated troponin I or troponin T levels had an increased risk for short-term mortality (OR 5.24, 95% CI 3.28 – 8.38) or PE-related deaths (OR 9.44, 95% CI 4.14 – 21.49). Elevated troponin levels even among patients who are hemodynamically stable are associated with higher mortality (Becattini et al., 2007; Jimenez et al., 2008).

Irrespective of various methods and cut-off values applied, most trials reported a low positive predictive value for PE-related mortality in the range of 12% to 44%, but with a very high negative predictive value between 99% and 100%.

### 6.2 Brain natriuretic peptide

Right ventricular dysfunction is associated with increased myocardial stretch which leads to the release of BNP and its amino terminal portion, NT-proBNP.

In acute PE, increasing levels of BNP or NT-proBNP predict the severity of RV dysfunction and mortality (Cavallazzi et al., 2008; Klok et al., 2008; Lega et al., 2009). Although elevated concentrations are related to worse outcome, the positive predictive value is low. On the other hand, low levels of BNP or NT-proBNP can be used reliably to identify patients with a good prognosis (Table 5).

### 6.3 Novel biomarker

Heart-type fatty acid binding protein (H-FABP), a protein released earlier than troponins during myocardial ischemia, has been evaluated as a prognostic marker in acute PE. The studies have reported a high sensitivity (78% to 100%) and negative predictive value (96% to 100%), but these studies are small and such measurements are not widely available (Puls et al., 2007; Kaczynska et al., 2006).

### 6.4 Summary of evidence on the prognostic value of biomarkers

Many studies did not perform an extensive comparison between all the available biomarkers, thus it remains debatable which biomarker will yield the best prognostic value. Another limitation is biomarker thresholds were determined retrospectively, thus no consistent cut-off values were used in the studies. Despite this, it appears BNP/NT-proBNP and cardiac troponins could be used as rule-out tests.

Author	Test used (Threshold)	Outcome Definition	Sensitivity (%)	Specificity (%)	NPV (%)	PPV (%)
Ten Wolde et al, 2003	BNP Shionoria <sup>a</sup> (21.7 pmol/L)	PE-related deaths	86	71	99	17
Kucher et al, 2003a	NT-proBNP <sup>b</sup> (500 pg/mL)	In-hospital death or adverse events <sup>e</sup>	95	57	97	45
Kucher et al, 2003b	BNP Triage <sup>c</sup> (50 pg/mL)	In-hospital death or adverse events <sup>e</sup>	95	60	97	48
Pruszczyk et al, 2003	NT-proBNP <sup>b</sup> (600 pg/mL)	In-hospital mortality	100	33	100	23
Binder et al, 2005	NT-proBNP <sup>b</sup> (1000 pg/mL)	In-hospital mortality	100	49	100	10
Kostrubiec et al, 2007	NT-proBNP <sup>b</sup> (7500 pg/mL)	30-day all cause mortality	65	93	94	61

(<sup>a-c</sup>Tests used: <sup>a</sup>Shionoria, CIS Bio International; <sup>b</sup>Elecsys, Roche Diagnostics; <sup>c</sup>Triage, Biosite Technologies. <sup>e</sup>Adverse events include the need for resuscitation, mechanical ventilation, inotropic support, thrombolytics, or embolectomy)

Table 5. Prognostic value of BNP or NT-proBNP in acute pulmonary embolism

Due to the high negative predictive value for PE-related mortality and adverse events, a potential approach consists of a combination of biomarker testing and echocardiography. In the setting of an acute PE, further risk stratification with echocardiography is warranted in patients with elevated cardiac biomarkers due to limited specificity of the assays for predicting RV dysfunction. Conversely, in patients with levels below cut-off, echocardiography will likely not add prognostic information.

This approach was demonstrated in a prospective study of 124 patients diagnosed with acute PE. The presence of RV dysfunction on echocardiography in patients with elevated NT-proBNP (cut-off of 1000 pg/mL) or cardiac troponins (cut-off of 0.04 ng/mL) is associated with a 10-fold increase in complication risk compared with patients biomarker levels below threshold (Binder et al., 2005).

## 7. Risk of recurrence

Recurrent PE can occur despite adequate anticoagulation therapy in patients who had survived an acute PE.

Patients with unprovoked PE (PE occurring in the absence of established risk factors or predisposing illnesses) are at a higher risk for recurrent PE compared to patients with risk factors for PE. In contrast, patients with risk factors of PE have a higher mortality risk (Klok

et al., 2010). In addition, patients who presented with a first symptomatic PE are at a 4-fold increased risk of recurrent symptomatic PE compared to patients who presented with deep venous thrombosis without symptoms of PE (Eichinger et al., 2004).

In patients with recurrent PE or progressive deep venous thrombosis (DVT) despite adequate anticoagulation therapy, inferior vena cava (IVC) filters may be indicated. IVC filter placement is generally accepted in patients with massive PE or limited cardiopulmonary reserve and DVT. Current evidence indicates that IVC filters are largely effective, with breakthrough PE occurring in only 0% to 6.2% cases. Recurrent PE, IVC thrombosis, filter migration, filter fracture, or penetration of caval wall can sometimes occur with long-term use (Chung et al., 2008).

## 8. Conclusion

Risk stratification of acute PE is fundamental not only to select an appropriate treatment strategy, but also to potentially reduce costs of management (Figure 2). An appropriate risk stratification algorithm would include clinical, imaging and biomarkers. High risk PE is diagnosed in the presence of shock or persistent hypotension and should warrant urgent management. Thrombolysis with alteplase (rtPA), streptokinase, or urokinase is the recommended therapy. Embolectomy could represent an alternative therapy for patients with shock in the acute setting when thrombolysis has been unsuccessful.

Hemodynamically stable patients without RV dysfunction or myocardial injury are at low-risk for PE-related adverse events. These patients may be eligible for early hospital discharge or even outpatient treatment.

In the remaining normotensive patients, a plausible strategy is to combine biomarkers with echocardiography. The presence of RV dysfunction and myocardial injury identifies patients at intermediate risk.

Whether intermediate risk patients will have any survival benefit with early initiation of reperfusion therapy (and what type of therapy) is not well accepted. Current recommendations proposed thrombolysis be instituted in selected patients at high risk for adverse events without contraindications (Grade IIB ESC and ACCP VIII Edition), and intravenous unfractionated heparin should be reserved to conditions in which thrombolysis is contraindicated (Grade IA ESC and ACCP VIII Edition). An ongoing study assessing the benefit of thrombolysis as compared with anticoagulation in hemodynamically stable patients with evidence of RV dysfunction and an elevated troponin levels will hopefully provide some insights (NCT00639743).

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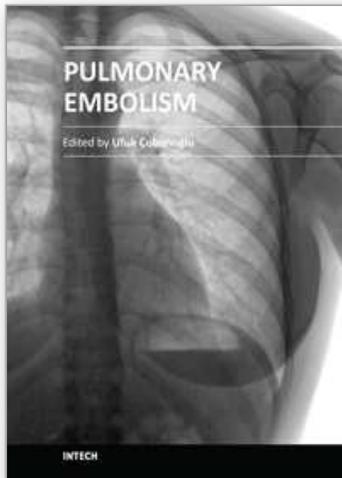
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## **Pulmonary Embolism**

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Pulmonary embolism is a serious, potentially life-threatening cardiopulmonary disease that occurs due to partial or total obstruction of the pulmonary arterial bed. Recently, new improvement occurred in the diagnosis and treatment of the disease. The aim of this disease is to re-review pulmonary embolism in the light of new developments. In this book, in addition to risk factors causing pulmonary embolus, a guide for systematic approaches to lead the risk stratification for decision making is also presented. In order to provide a maximum length of active life and continuation of functional abilities as the aim of new interventional gerontology, the risk factors causing pulmonary embolus in elderly individuals are evaluated, and the approach to prevention and treatment are defined. The risk of the development of deep vein thrombosis and pulmonary embolism, combined with obesity due to immobility, the disease of this era, irregular and excessive eating, and treatment management are highlighted. Non-thrombotic pulmonary emboli are also covered and an attempt is made to constitute an awareness of this picture that can change the treatment and prognosis of the disease to a considerable extent. In addition to the pathophysiological definition of pulmonary embolus, the priority goal of quick and definitive diagnosis is emphasized, and diagnostic strategies are discussed in the book. A numerical analysis of the vena cava filters, which is a current approach to prevent pulmonary emboli recurrences, is presented in the last chapter.

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