Pulmonary Embolism in Heart Failure
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Case Presentation: A 71-year-old man with coronary artery disease, left ventricular (LV) systolic dysfunction (ejection fraction, 30%), and recent admission for heart failure presented with acute dyspnea and hypoxemia. A pro-brain–type natriuretic peptide level was elevated at 2450 pg/mL (normal <350 pg/mL). Chest x-ray demonstrated cardiomegaly and small bilateral pleural effusions. After an hour of diuresis, the patient developed systemic arterial hypotension and worsened hypoxemia, prompting cardiology consultation. Based on the absence of rales on physical examination and lack of pulmonary edema on chest x-ray, an alternative diagnosis of pulmonary embolism (PE) was suggested, and contrast-enhanced chest tomography (CT) was obtained. Chest CT demonstrated large bilateral proximal PE.

Overview
Venous thromboembolism (VTE), which encompasses deep vein thrombosis and PE, is an increasingly common and challenging complication of heart failure. The relative risk of PE is at least double that of patients without heart failure and increases as LV systolic function declines. PE patients with heart failure have a higher overall mortality rate than those without heart failure (17% versus 10%). In addition, PE is an independent predictor of death or rehospitalization among heart failure patients.

Pathophysiology
Risk Factors
Heart failure patients often have a high medical acuity and multiple risk factors that amplify the risk of VTE. The increased risk of VTE observed with heart failure itself has been attributed to reduced flow caused by low cardiac output and abnormalities of hemostasis, platelet function, and endothelial function. Central venous catheters and leads from implantable cardiac defibrillators and pacemakers are common among heart failure patients and have been shown to increase the risk of upper-extremity deep vein thrombosis. Heart failure patients tend to be older, and VTE in the elderly is problematic.

Hemodynamics
Acute PE increases pulmonary vascular resistance and right ventricular (RV) afterload through direct physical obstruction, hypoxemia, and pulmonary vasoconstrictors. Many heart failure patients with LV systolic dysfunction, diastolic dysfunction, or a combination of both suffer from some degree of RV pressure overload and RV dysfunction. A sudden superimposed increase in RV afterload from acute PE leads to worsening RV dilatation and hypokinesis, tricuspid regurgitation, and ultimately acute RV failure. Heart failure patients rely on relatively preserved RV function to maintain LV preload and systemic cardiac output. RV pressure overload caused by PE may result in interventricular septal deviation toward the LV in diastole and decreased RV systolic function, thereby limiting LV filling and left-sided cardiac output (see the Movie in the online Data Supplement). In addition, RV pressure overload may result in increased wall stress and ischemia by simultaneously increasing myocardial oxygen demand while decreasing supply (Figure 1).

Diagnosis
Evaluation of heart failure patients with suspected acute PE is challenging because of the substantial overlap in symptoms and signs of both disorders. Although dyspnea is the most commonly reported symptom in both PE and heart failure, severe dyspnea out of proportion to objective findings of pulmonary vascular congestion suggests that another process such as PE is compromising gas exchange (Table 1).

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(Circulation. 2008;118:1598-1601.)
© 2008 American Heart Association, Inc.
Circulation is available at http://circ.ahajournals.org DOI: 10.1161/CIRCULATIONAHA.108.803965

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Systemic arterial hypotension, cardiogenic shock, or cardiac arrest may be observed in decompensated heart failure or massive PE. Submassive PE should be considered in normotensive heart failure patients with evidence of right heart failure such as elevated jugular venous pressure, tricuspid regurgitation, and an accentuated sound of pulmonic closure (P2). However, heart failure patients often demonstrate signs of right ventricular dysfunction in the absence of PE. Findings consistent with new or worsened right greater than left heart failure such as lower-extremity edema, hepatomegaly, and elevated jugular venous pressure in the absence of significant pulmonary rales should raise concern for subacute or chronic PE.

Laboratory testing of heart failure patients with suspected acute PE is complicated because elevated D-dimer levels may be present in heart failure alone. Similarly, cardiac biomarkers, including troponin, brain-type natriuretic peptide, and pro-brain-type natriuretic peptide, may be difficult to interpret because they often are abnormally elevated in heart failure. Nevertheless, heart failure patients with elevated cardiac biomarkers and findings of new or worsened RV failure should undergo further evaluation for PE. Elevated cardiac biomarkers in the setting of PE correlate with the presence of RV dysfunction, a powerful independent predictor of early mortality.

Contrast-enhanced chest CT is the preferred imaging modality to evaluate suspected PE in heart failure patients. However, use of intravenous contrast-enhanced chest CT may be problematic for heart failure patients with chronic kidney disease who will have increased susceptibility to contrast nephropathy. In addition, the rapid bolus administration of intravenous contrast may cause a sudden increase in intracardiac pressures and pulmonary edema. Heart failure patients presenting with pulmonary vascular congestion or systemic hypertension should be stabilized before undergoing chest CT.

**Table 1. Clinical Pearls for the Evaluation of Suspected PE in Heart Failure Patients**

Dyspnea and hypoxemia out of proportion to findings of pulmonary vascular congestion on physical examination or chest x-ray should warrant evaluation for acute PE. New or worsened right greater than left heart failure such as lower-extremity edema, hepatomegaly, and elevated jugular venous pressure in the absence of significant pulmonary rales should raise concern for subacute/chronic PE.

Inpatient heart failure patients should proceed directly to imaging because almost all heart failure patients ill enough to be hospitalized have elevated D-dimer levels. Because it may be difficult to discern whether elevations in troponin or brain-type natriuretic peptide are due to heart failure or PE, transthoracic echocardiography should be performed to evaluate for new or worsened RV dysfunction in heart failure patients with acute PE and elevated cardiac biomarkers.

**An Integrated Approach to Diagnosis**

An algorithm for the diagnosis of acute PE in heart failure patients should integrate clinical probability with appropriate use of D-dimer testing and imaging studies (Figure 2). Both the Christopher Study and the Prospective Investigation of Pulmonary Embolism Diagnosis II (PIOPED II) trial have validated a simplified clinical decision rule, known as the Wells criteria, in combination with D-dimer testing and chest CT to evaluate suspected PE.

**Management**

**Risk Stratification**

RV dysfunction demonstrated on echocardiography and RV enlargement detected by chest CT identify a population of PE patients at increased risk of adverse events, including early mortality. Risk stratification using these parameters can be challenging because many heart failure patients have some degree of RV dilatation or hypokinesis at baseline. However, review of previous echocardiographic and chest CT data may reveal interval
worsening in RV function suggestive of an intercurrent PE.

**Primary Therapy**
Options for primary therapy in heart failure patients with acute PE include fibrinolysis, surgical pulmonary embolectomy, or catheter-assisted pulmonary embolectomy. Primary therapy is reserved for patients presenting with either massive or submassive PE. Many heart failure patients will have comorbid conditions and contraindications that preclude the consideration of primary therapy.

**Supportive Management of Massive PE**
Coexisting left ventricular systolic dysfunction and diastolic dysfunction complicate the management of heart failure patients with massive PE. Although a common strategy in response to systemic arterial hypotension is to prescribe a fluid bolus, volume loading may worsen biventricular failure, pulmonary edema, and hypoxemia. An initial trial of volume expansion, limited to 250 to 500 mL, may be attempted in those heart failure patients without evidence of increased right-sided filling pressures or pulmonary edema.

Although non–heart failure patients generally respond well to pure vasopressors for hemodynamic support in massive PE, many heart failure patients will not tolerate the isolated increase in systemic vascular resistance. PE patients with heart failure may require an agent with mixed vasopressor and inotropic properties such as norepinephrine, epinephrine, or dopamine. Whereas LV function often becomes hyperdynamic to compensate for RV failure, the presence of underlying LV systolic dysfunction in heart failure patients may limit the patient’s ability to maintain normal systemic cardiac output and may necessitate the addition of inotropes.

**Anticoagulation**
Options for anticoagulation include intravenous unfractionated heparin, low-molecular-weight heparin, and fondaparinux. Hepatic congestion will slow the metabolism of unfractionated heparin in heart failure patients, resulting in lower-than-usual doses to achieve therapeutic anticoagulation. Renal impairment, a common comorbid condition among heart failure patients, may result in excessive anticoagulation and bleeding when low-molecular-weight heparins and fondaparinux are used, both of which are cleared by the kidney.

The management of warfarin therapy can be problematic in heart failure patients who have comorbidities and take numerous medications that affect its metabolism and amplify the risk of bleeding. Bowel congestion and poor hepatic function resulting from liver congestion or low cardiac output can impair warfarin metabolism. Frequently prescribed medications in heart failure patients such as amiodarone and clopidogrel potentiate the effect of warfarin, whereas others, like spironolactone, accelerate its metabolism.

For heart failure patients with contraindications to anticoagulation or who suffer recurrent PE despite therapeutic anticoagulation, inferior vena cava filter insertion should be considered. Inferior vena cava filters reduce the risk of PE but increase the long-term risk of deep vein thrombosis.

**Prevention**
The eighth American College of Chest Physicians Conference on Antithrombotic and Thrombolytic Therapy classifies VTE prophylaxis as a 1A recommendation for hospitalized heart failure patients. In an analysis of the
Table 2. Regimens for VTE Prophylaxis in Heart Failure Patients

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<th>Regimen</th>
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<tr>
<td>Unfractionated heparin 5000 U SC 3 times daily</td>
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<tr>
<td>Enoxaparin 40 mg SC daily</td>
</tr>
<tr>
<td>Dalteparin 5000 U SC daily</td>
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<tr>
<td>Fondaparinux 2.5 mg SC daily</td>
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<tr>
<td>Warfarin if administered for another indication</td>
</tr>
<tr>
<td>Graduated compression stockings/pneumatic compression devices for patients with contraindications to anticoagulation</td>
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<tr>
<td>Consider combination pharmacological and mechanical prophylaxis for high-risk heart failure patients</td>
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Acute Decompensated Heart Failure National Registry, fewer than one third of eligible heart failure patients received VTE prophylaxis.13

Options for VTE prophylaxis include pharmacological prophylaxis with subcutaneous unfractionated heparin, low-molecular-weight heparin, or fondaparinux and mechanical prophylaxis with graduated compression stockings or pneumatic compression devices (Table 2). Heart failure patients at high risk of PE may benefit from combined pharmacological and mechanical modalities. Whereas prophylactic anticoagulation with low-molecular-weight heparin or fondaparinux is generally associated with a low risk of bleeding, the frequency of bleeding complications may increase in heart failure patients with renal impairment.

Case Presentation: The patient received an intravenous bolus of unfractionated heparin followed by continuous infusion titrated to a target activated partial thromboplastin time of 60 to 80 seconds. An echocardiogram demonstrated new RV dilatation and hypokinesis, as well as moderate to severe elevation in pulmonary artery systolic pressure compared with a prior study. His systemic arterial hypotension resolved after a 250-mL intravenous bolus of normal saline. He was eventually discharged on oral anticoagulation with a goal international normalized ratio of 2.0 to 3.0. Six weeks later, a follow-up echocardiogram demonstrated improved RV function and return of pulmonary artery systolic pressure to baseline. This case presentation highlights the challenge of diagnosing PE in patients with heart failure. Dyspnea and hypoxemia out of proportion to findings of pulmonary vascular congestion on physical examination or chest x-ray should raise concern for acute PE. The case also identifies PE as a preventable complication of heart failure and emphasizes the importance of VTE prophylaxis in this vulnerable patient population.

Disclosures

None.

References

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Circulation. 2008;118:1598-1601
doi: 10.1161/CIRCULATIONAHA.108.803965

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