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Case Reports

Use of Ultrasound-Assisted, Catheter-Directed Thrombolysis in a Patient With High-Risk Pulmonary Embolism

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Abstract

High-risk pulmonary embolism (PE) is a complex clinical entity associated with high mortality rates. Ultrasound-assisted, catheter-directed thrombolysis, typically used for intermediate-risk PE, may be a viable treatment approach for high-risk PE, particularly in patients at increased risk for major bleeding. This report describes a case in which ultrasound-assisted, catheter-directed thrombolysis was successfully used to treat high-risk PE in a female patient with extensive peritoneal metastases from gastric adenocarcinoma. Other examples from the literature, in which ultrasound-assisted, catheter-directed thrombolysis was used to treat high-risk PE, are also provided.

Case Report

Presentation and Physical Examination

A 54-year-old woman presented at the emergency department for a presyncopal episode. While at home, she felt suddenly nauseous and experienced an episode of nonbloody, nonbilious emesis. Upon standing, she became lightheaded and almost fell to the floor. She denied chest pain, abdominal pain, shortness of breath, heart palpitations, and recent illness.

On presentation, she was found to be tachycardic but normotensive and without hypoxia. The cardiopulmonary examination revealed no abnormality. The electrocardiogram demonstrated a new right bundle-branch block (Fig. 1). Bedside ultrasound imaging found right ventricular (RV) free wall akinesis with apical sparing. While in the emergency department, she developed hypoxia, requiring the support of 3 L oxygen by nasal cannula, and hypotension. Her blood pressure did not improve following administration of 2 L normal saline, and an infusion of norepinephrine was started.

Medical History

The patient had a medical history of stage IV gastric adenocarcinoma for which she had previously undergone chemotherapy. On follow-up with oncology, she was found to have peritoneal nodularity consistent with metastatic disease.

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Differential Diagnosis

The differential diagnosis for this patient's presyncope included myocardial infarction, arrhythmia, sepsis, and pulmonary embolism (PE).

Technique

Computed tomography with angiography of the pulmonary artery revealed a large saddle embolus at the right mainstem bronchus, with portions of the thrombus extending to the left mainstem bronchus without obstruction (Fig. 2A and Fig. 2B). Computed tomography of the head without contrast revealed no acute abnormality.

Given the recent computed tomography of the patient's abdomen and pelvis, which showed peritoneal nodularity consistent with metastasis of her gastric adenocarcinoma, she was deemed to be at high risk of bleeding from systemic thrombolytics, and the decision to proceed with ultrasound-assisted, catheter-directed thrombolysis (USAT) was made, given her tenuous clinical picture and extensive distal thrombus burden. Aspiration thrombectomy devices such as Angiovac (Vortex Medical, Inc) and the Inari Flowtriever (Inari Medical) were not considered because they were not available at the treating institution. The patient was taken to the cardiac catheterization laboratory, where EkoSonic Endovascular System (Boston Scientific) catheters were placed in the pulmonary arteries. She received 1 mg tissue plasminogen activator (tPA)/h through each catheter for a total of 3 hours while simultaneously receiving 500 units/h systemic heparin (half her steady-state dose). Systemic heparin was reinitiated 6 hours after the end of tPA infusion.

Key Points

- The present case illustrates the current guidelines regarding the management of high-risk PE.
- The report describes a case in which USAT was used to successfully treat high-risk PE in a patient at high risk for major bleeding.
- The report provides a compilation of similar cases that can be used to help clinicians decide when to proceed with USAT to treat high-risk PE.

Abbreviations and Acronyms

PE	pulmonary embolism
RV	right ventricular
tPA	tissue plasminogen activator
USAT	ultrasound-assisted, catheter-directed thrombolysis

Outcome

The patient was weaned off norepinephrine within 2 hours of completion of the tPA infusion. The following day, her oxygenation was normal without supplementation. A transthoracic echocardiogram was performed, revealing normalization of the right ventricle to left ventricle ratio and mildly reduced RV systolic fraction. She was discharged home with therapeutic enoxaparin on hospital day 4.

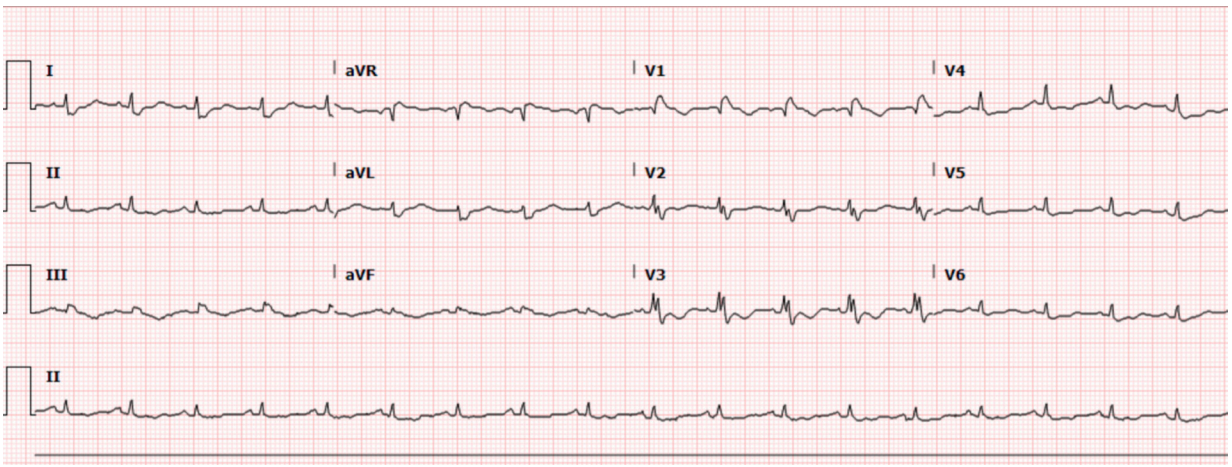

Fig. 1 Electrocardiogram on presentation shows new right bundle-branch block.

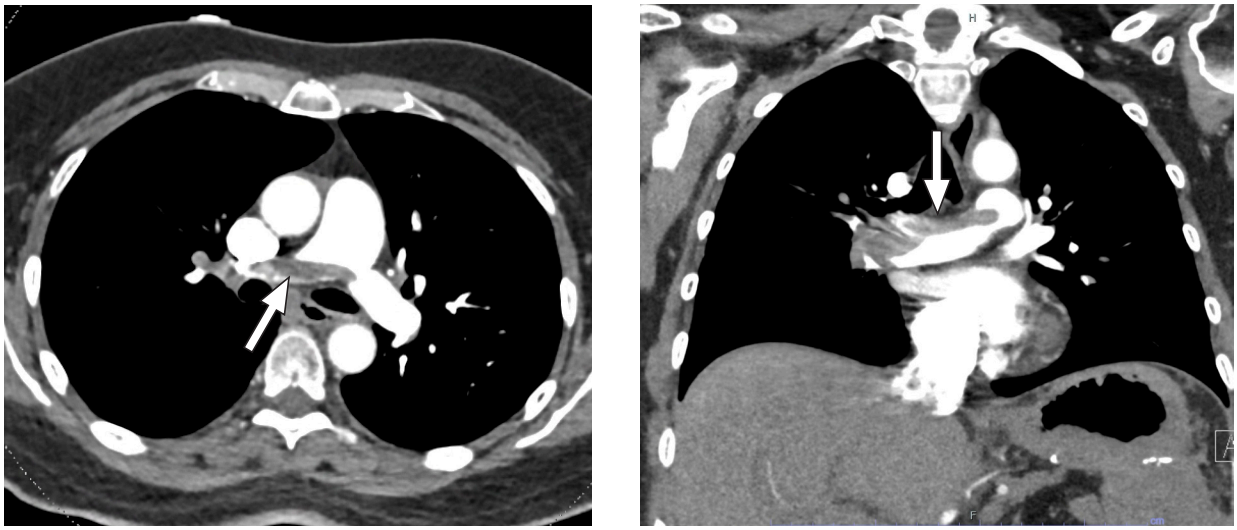

Fig. 2 A) Transverse and **B**) coronal computed tomography with angiography images of the pulmonary artery show a large pulmonary embolus extending from the left pulmonary artery to the right pulmonary artery (arrows).

Latest Follow-Up

Six months after discharge, the patient remains well, without cardiopulmonary symptoms and with stable oncologic disease.

Discussion

High-risk PE is a complex clinical entity requiring the treatment determined by a multidisciplinary team. High-risk PE is defined as a PE that causes hemodynamic compromise (hypotension or evidence of shock). Mortality rates associated with high-risk PE are estimated to be as high as 14%, considerably higher than the mortality rates of patients presenting with intermediate-risk PE, which is defined as PE without hemodynamic compromise but with evidence of right heart strain.[1] Therapy for high-risk PE centers on the use of systemic thrombolytics in patients without contraindications to their use[2]; the decision to use thrombolytics can be fraught with difficulty in patients at high risk for major bleeding, but it is not an absolute contraindication to their use.

The most recent American Heart Association guidelines regarding the treatment of both high-risk PE and intermediate-risk PE with signs of respiratory failure or severe RV dysfunction recommend the use of systemic thrombolytics unless there is a contraindication to their administration.[3] In the presence of absolute contraindications, catheter-based or surgical embolectomy is a reasonable alternative.[3] The European Society of Cardiology suggests percutaneous-directed treatments for cases of failed thrombolysis and in patients who have a contraindication to the use of systemic thrombolytics, but this is not addressed in the most recent American College of Chest Physicians guidelines.[2,4] These guidelines do not differentiate between the modalities of catheter-directed therapy, and the evidence supporting their use is limited. No specific recommendations exist for the use of these therapies in patients at high risk for major bleeding without absolute contraindication to systemic thrombolytics.

Ultrasound-assisted, catheter-directed thrombolysis has been shown to be an effective therapy for reducing right ventricle size in patients with intermediate-risk PE without increasing bleeding risk,[4] but limited data exist for its use in high-risk cases. That said, USAT allows for the delivery of thrombolytics directly to the site of the clot with the assistance of ultrasound acoustic waves to improve penetration of the clot, leading to a reduced required dose of thrombolytic. This approach may present an alternative treatment option for high-risk PE in patients who are at risk for major bleeding without absolute contraindication for systemic thrombolytics, as highlighted in this case.

The patient in this report developed both RV dysfunction and hypotension requiring vasopressor support because of a saddle pulmonary embolus. Her extensive peritoneal metastases were determined to be a precluding factor to

systemic thrombolysis, and she promptly underwent USAT with EkoSonic Endovascular System catheters. Because of her high bleeding risk, shorter-duration tPA infusion was chosen based on the Optimum Duration of Acoustic Pulse Thrombolysis Procedure in Acute Pulmonary Embolism (OPTALYSE PE) trial, which found that low-dose, shorter-duration tPA infusions are efficacious in improving RV function and reducing clot burden in intermediate-risk PE.[5] Hemodynamic stability was restored soon after termination of tPA infusion, and the patient had no substantial bleeding events. An echocardiogram performed shortly after tPA infusion noted only mild RV dysfunction, despite her presentation with RV free wall akinesis.

Determining whether a patient is at higher risk for major bleeding and whether USAT is a viable treatment option are complex clinical questions that a multitude of individual patient factors affects. Table I provides examples of previously described case reports in which USAT was used to treat high-risk PE that may aid in clinical decision-making.[6-12] A case series by He et al[6] describes 3 cases in which high-risk PE was treated with USAT. In the first case, a 73-year-old woman who had undergone retromastoid craniectomy 1 week prior was found to have emboli in bilateral proximal pulmonary arteries; he underwent USAT with substantial improvement in hemodynamics and no major bleeding. He was discharged home on hospital day 8. A second case describes the successful use of USAT in a patient with high-risk PE in the bilateral proximal pulmonary arteries who was at increased risk for bleeding as a result of localized bowel perforation secondary to malignancy with a history of chronic hemorrhage. The third case details the use of USAT in a patient with a recent cesarean delivery complicated by disseminated intravascular coagulation and bleeding that required a hysterectomy. The patient was weaned off inotropic support by the end of the procedure and had no major bleeding. Giuffrida et al,[7] Nelson et al,[8] and Lindsey et al[9] all reported the use of USAT in patients following cardiac arrest with concerns for trauma as a result of cardiopulmonary resuscitation. Gowda et al[10] illustrated the application of USAT in a pregnant patient at 9 weeks gestation. Shokr et al[11] and Shammas et al[12] both described the successful use of USAT in patients with high-risk PE and no specific contraindication to systemic thrombolysis. These cases encompass multiple degrees of hemodynamic instability, from single vasopressor shock to cardiac arrest and extracorporeal membrane oxygenation. Reasons cited for proceeding with USAT in place of systemic thrombolysis included recent cardiopulmonary resuscitation, pregnancy, and recent major surgery, though in some cases, USAT was used despite the patient not having risk factors for major bleeding. In a majority of cases, no major bleeding occurred, and hemodynamic stability was restored soon after the procedure. In a single case (Lindsey et al[9]) major bleeding was documented, and the patient was fully anticoagulated for extracorporeal membrane oxygenation at the time USAT was performed. At follow-up, patients often had no sequelae from their previous high-risk PE.

The use of USAT was studied in patients with intermediate-risk PE in the Ultrasound Accelerated Thrombolysis of PE (ULTIMA) trial, a randomized clinical trial in which USAT was used in conjunction with systemic anticoagulation and compared with systemic anticoagulation alone, but no randomized clinical trials have evaluated USAT for use in high-risk PE.[13] The present case and the collection of cases presented here provide preliminary data demonstrating a use for USAT in this setting. Further studies are needed to better define which populations of patients with high-risk PE may benefit from USAT and how its outcomes compare with the outcomes of systemic thrombolysis. It is hoped that further descriptions of the successful use of USAT in patients with high-risk PE may prompt such research in the future.

Article Information

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TABLE I. Case Reports Detailing the Use of Ultrasound-Assisted, Catheter-Directed Thrombolysis for High-Risk PE

Case	Age, y	Sex	Absolute or relative contraindication to systemic thrombolysis	Hemodynamic status	RV function	PE location	Procedural complications	Dose	Major bleeding	Neurologic outcome	Disposition
Shammas N, et al[12] (2015)	69	Female	None stated	Systolic blood pressure of 80 mm Hg on presentation	RV enlarged (3.6 cm)	Bilateral PE	None	1 mg/h per catheter of tPA for 12 h	None	No deficits noted	Discharged on rivaroxaban 1 wk following procedure; at 2-mo follow-up, the patient was without symptoms from PE
Lindsey J, et al[9] (2018)	38	Male	Following cardiac arrest with prolonged cardiopulmonary resuscitation	Cardiac arrest in computed tomography scanner at time of diagnosis, placed on extracorporeal membrane oxygenation	Not stated	Bilateral proximal pulmonary arteries	Fully anticoagulated for extracorporeal membrane oxygenation at time of procedure; developed hemothorax; EkoSonic Endovascular System (Boston Scientific) stopped early; chest tube placed	2-mg bolus alteplase followed by 1 mg/h for 10 h	Hemothorax, bilateral occipital lobe hemorrhages	Alert, able to follow commands and move all extremities	Hospital course complicated by hemothorax; later in hospital course, while on anticoagulation for extracorporeal membrane oxygenation, developed bilateral occipital lobe hemorrhages and underwent hemicraniectomy with hemorrhage evacuation; discharged hospital day 22
Nelson S, et al[8] (2018)	24	Female	Post-trauma with recent orthopedic surgery requiring blood products, subarachnoid hemorrhage, and laboratory findings of international normalized ratio of 1.8 and platelet count of 89,000/μL	Following cardiac arrest, required vasopressor support to maintain mean arterial pressure >65 mm Hg	Dilated right ventricle with septal flattening; right ventricle to left ventricle ratio, 2.5	Saddle embolus with distal extension	None	12 mg tPA over 12 h	None	Not stated	Weaned off vasopressors by end of procedure; follow up 1 y after procedure without substantial morbidity related to PE
Shokr M, et al[11] (2018) case 1	52	Female	None stated	Blood pressure 85/55 mm Hg on presentation; required dobutamine infusion to maintain mean arterial pressure >65 mm Hg	Severely dilated, hypokinetic right ventricle; right ventricle to left ventricle ratio, 2.2	Left and right main pulmonary arteries extending to the lobar branches	None	11 mg alteplase over 6 h	None	No deficits noted	Despite reduction in thrombus size and inotropic support, poor cardiac output from right-sided heart failure continued; an Impella (Abiomed) heart pump was placed in the left pulmonary artery, with intake in the inferior vena cava; weaned off support over 5 d; discharged home in stable condition
Shokr M, et al[11] (2018) case 2	72	Male	None stated	Hemodynamically stable (not necessarily massive)	Severely increased RV size; RV ejection fraction, 0.10%; right ventricle to left ventricle ratio, 1.2	Saddle embolus	Became hypotensive and tachycardic during procedure; cardiac index of 2 L/min/m^2 despite dobutamine infusion	35 mg alteplase over 14 h	None	No deficits noted	Became hypotensive during procedure; found to have a low cardiac index despite dobutamine infusion; an Impella device was placed in the left pulmonary artery, with intake in the inferior vena cava; weaned off support over 4 d; RV function substantially improved, and the patient was discharged home

Continued

TABLE I. Case Reports Detailing the Use of Ultrasound-Assisted, Catheter-Directed Thrombolysis for High-Risk PE (continued)

Case	Age, y	Sex	Absolute or relative contraindication to systemic thrombolysis	Hemodynamic status	RV function	PE location	Procedural complications	Dose	Major bleeding	Neurologic outcome	Disposition
Gowda N, et al[10] (2019)	27	Female	Pregnant at 9 wk gestation	Systolic blood pressure of 70 mm Hg on presentation	RV function decreased	Bilateral PE	None	1 mg tPA/h per catheter for 4 h	None	No deficits noted	Discharged home on hospital day 5 on therapeutic enoxaparin; presented 2 wk later for subacute chest pain and was found to have a pulmonary infarction' had a normal spontaneous vaginal delivery at 39 wk gestation
Giuffrida S, et al[7] (2020)	Not stated	Male	Possible liver laceration as a result of rib fracture sustained during cardiopulmonary resuscitation	Following pulseless electrical activity arrest, required metaraminol (20 mg/h) to maintain perfusing blood pressures	Unspecified RV strain noted	Bilateral proximal pulmonary arteries	Pulseless electrical activity arrest, 10 mg tPA given into main pulmonary trunk with return of spontaneous circulation	Dose not stated, given over 15 h	None	No deficits noted	Weaned off vasopressors within 48 h and discharged by hospital day 9
He J, et al[6] (2021) case 1	73	Female	Retromastoid craniectomy and mass excision performed 1 wk before presentation	Required vasopressor support to maintain mean arterial pressure >65 mm Hg	Dilated	Bilateral proximal pulmonary arteries	None	9 mg alteplase over 5 h	None	No new deficit (previous diplopia)	Discharged home 8 d after procedure
He J, et al[6] (2021) case 2	70	Female	Localized bowel perforation as a result of underlying malignancy with chronic hemorrhage	Hypotensive, with blood pressure of 90/50 mm Hg (mean arterial pressure, 63 mm Hg)	Severely dilated; right ventricle to left ventricle ratio, 1.8	Bilateral proximal pulmonary arteries	None	9 mg alteplase over 4.5 h	None	No deficits noted	Underwent right hemicolectomy 2 wk later, discharged 8 d postoperatively
He J, et al[6] (2021) case 3	33	Female	Recent cesarean delivery, with substantial bleeding as a result of disseminated intravascular coagulation requiring hysterectomy	Required inotropic support to maintain mean arterial pressure >65 mm Hg	Dilated; right ventricle to left ventricle ratio, 1.2	Saddle embolus	None	14 mg alteplase over 24 h	None	No deficits noted	Weaned off inotropic support by end of procedure; extubated on day 5; discharged home on day 10; normal RV function and pulmonary artery systolic pressure at 1 y
Current case	54	Female	Gastric adenocarcinoma with substantial peritoneal metastasis	Required norepinephrine to maintain mean arterial pressure >65 mm Hg	RV free wall akinesis with apical sparing	Saddle embolus	None	1 mg alteplase per h per catheter for 3 h	None	No deficits noted	Weaned off vasopressor support 2 h after completion of infusion; repeat transthoracic echocardiogram with normalization of right ventricle to left ventricle ratio; discharged home on hospital day 4

PE, pulmonary embolism; RV, right ventricle; tPA, tissue plasminogen activator.

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