Clinical Case

Do we know everything about intermediate risk pulmonary embolism? A case report at a high complexity hospital in Medellin 2024.

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ABSTRACT

Venous thromboembolic diseases such as pulmonary embolism and deep vein thrombosis are the third more prevalent cause of cardiovascular syndrome. Pulmonary embolism has an incidence of 39 to 115 in 100,000 inhabitants annually and a mortality of approximately 300,000 people every year in the United states. Some risk factors of the disease are infections, trauma, lower limb fractures, venous thromboembolic disease and major surgeries. People have symptoms like dyspnea, syncope, chest pain, dizziness and abdominal pain. It is classified according to the risk of the patient into low, low-intermediate, high-intermediate and very high; the last one saved for patients with hemodynamic instability defined by the presence of cardiac arrest, obstructive shock and persistent hypotension. Antithrombotic therapy is the best treatment option, but in very high-risk patients, thrombolytic therapy is an option too.

CLINICAL CASE

Female, 34-year-old patient with history of tibial fracture, who consulted due to syncope, dyspnea, diaphoresis, vomiting and oppressive chest pain; ECG with sinus tachycardia and McGinn-White pattern. Wells score of high risk (9 points). CT angiography of pulmonary arteries leads to diagnosis of acute bilateral pulmonary thromboembolism, with saddle embolism in pulmonary arteries, lobar, segmental and subsegmental arteries *(Figure 1).* Transthoracic echocardiogram showing right ventricular dilatation with basal diameter of 5.5 cm, RV/LV ratio of 2.2, McConnell's sign, TAPSE of 14 mm, dilated RA with a volume of 37 ml/m2, tricuspid valve with severe secondary regurgitation with vena contracta width of 0.7 cm and regurgitation of 10 cm2, maximum gradient of tricuspid regurgitation of 39 mmHg, and thrombus in right chamber of 2.1 cm x 0.6 cm with area of 1.7 cm2 in the right branch of the pulmonary artery. Pulmonary trunk of 2.6 cm, right pulmonary branch of 1.7 cm, left pulmonary branch of 1.5 cm. PASP of 49 mmHg and tricuspid regurgitation velocity estimated in 303 cm/sec. Admission tests with troponin T 47.5 ng/ml (positive), arterial blood gas with hyperlactatemia and lactic acidosis compensated with 2.49 mMol/L lactate. She was classified as in intermediate-high risk according to the 2019 European guidelines criteria on the diagnosis and management for pulmonary thromboembolism, and she was anticoagulated with unfractionated heparin infusion. In spite of the analgesic, anticoagulant and support treatment, she remained with tachycardia, tachypnea, WHO function class deterioration from I to IV, and progressive increase of lactate in blood. In spite of not meeting the criteria for hemodynamic instability, taking into account the high risk of clinical deterioration and compromise of quality of life, besides the acute right heart compromise evident in transthoracic echocardiogram, a multidisciplinary meeting was conducted, and the choice was made to apply thrombolysis in situ. Seventy-two hours after admission, catheters were



FIGURE 1.
CT angiography of pulmonary arteries

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advanced into each pulmonary artery, the location was verified by pulmonary arteriography and in situ infusion was administered of alteplase, at a dose of 1 mg/h for 3 hours and 35 minutes with no complications. Four days after the procedure, control transthoracic echocardiogram was made, showing normal RV size, with basal diameter of 3.5 cm, TAPSE 18 mm, right atrium with 12 cm2 area and volume of 13 ml/m2, tricuspid valve with mild regurgitation, pulmonary valve with normal morphology and flows by Doppler, pulmonary trunk of 1.7 cm, right pulmonary artery of 1.2 cm, left pulmonary branch of 1.0 cm, PASP 36 mmHg with tricuspid regurgitation velocity of 280 cm/sec. The patient presented adequate clinical course and tolerated supplemental oxygen weaning.

DISCUSSION

Reperfusion therapies, particularly in systemic thrombolysis, is the treatment of choice for high-risk pulmonary embolism. The question has been raised that in patients with intermediate risk, these therapies may entail a bleeding risk exceeding the benefit of the intervention; however, it is known that within the group of patients with intermediate-high risk, they represent a significant mortality in the short term, suggesting the need for a more aggressive treatment.

Catheter-directed thrombolysis is a management strategy by which a slow infusion of a thrombolytic agent is administered into the pulmonary artery through a catheter with multiple holes, which is locally introduced into the thrombus/embolus. The dose of the thrombolytic agent is approximately 25% of the systemic dose, seeking to maintain therapeutic effectiveness with less bleeding risk.

Therapies such as surgical embolectomy or catheter-directed therapy could be management alternatives, but their use is limited due to their low availability.

In the USAT IH-PE study, a multicenter, retrospective and prospective registry carried out in 5 centers in Italy, including 102 patients with pulmonary embolism of intermediate-high and high risk, who were treated by catheter-directed thrombolysis facilitated by ultrasound, from March 2018 to July 2023, the incidence of pulmonary embolism was studied. It was defined as medium pressure of the pulmonary artery ≥20 mmHg in rest during right heart catheterization performed in patients presenting PASP ≥40 mmHg in echocardiographic follow-up. For secondary outcomes, the following were evaluated: parameters of RV function (TAPSE, RV/LV ratio, pulmonary artery systolic pressure, TAPSE/PASP ratio), in the short and mid-term, all-cause in-hospital mortality, and bleeding associated to the procedure as safety outcome.

From the 102 patients, 86% presented pulmonary embolism of intermediate-high risk, with an average age of 63 years. In 70 of the analyzed patients, an improvement was verified in RV function parameters within 24 hours after thrombolysis, with 44.1% of patients presenting sings of RV insufficiency (TAPSE ≤16 mm and/or PASP ≥40 mmHg and/or RV/LV >1), which during the subsequent follow-up (3-6 months), it was just 5.9%, with an incidence of residual pulmonary hypertension of 1.43%.

Mortality rate during follow-up was 11%, with in-hospital mortality of 3.9% and mortality upon discharge unrelated to pulmonary embolism.

In the KNOCOUT PE study, a prospective cohort including 489 patients from 64 centers, with acute pulmonary embolism of intermediate-high and high risk, treated by catheter-directed thrombolysis facilitated by ultrasound (USCDT), using reduced thrombolytic doses and shorter infusion durations, 94.7% were classified as in intermediate-high risk. The total medium dose of r-tPA administered was 18.1 mg, with a mean duration of infusion of 10.5 hours.

The patients received USCDT performed by an endovascular specialist; the dose and treatment durations were determined according to the criterion of the individual investigator. The follow-up terms were carried out during hospital stay, before discharge and within 3 and 12 months after the treatment. The echocardiographic follow-up was carried out within 3 months for those with initial abnormal echocardiogram after the procedure, with the aim of assessing chronic pulmonary hypertension signs, and within 12 months for all patients. In regard to the analyzed outcomes, 8 major bleeding events occurred within the first 72 hours after the treatment, with a single episode of intracranial bleeding, which represented a rate of major bleeding of 1.6%. Five patients died during the first 30 days after the treatment; all of whom were intermediate-high risk patients. The assessment of echocardiographic changes showed a modification in the RV/LV ratio of 1.35 to 0.98 within the first 24 hours, and of the estimated medium RV systolic pressure from 50.35 mmHg to 35.77 mmHg within 24-48 hours.[1,2,3,4,5]

In a retrospective cohort conducted in 2022 including 74 patients with diagnosis of pulmonary thromboembolism with intermediate risk, clinical variables were evaluated, in association with adverse outcomes in patients with pulmonary thromboembolism; namely, brain natriuretic peptide, leukocytes and RV/LV ratio, which were all greater in patients with adverse outcomes in comparison to controls. The patients that presented adverse outcomes presented higher rates of syncope, negative T waves in V1-V3, and low arterial oxygen saturation (SaO2 <90%) upon admission.[6]

In the PEITHO study, the efficacy and safety of systemic thrombolysis with 50 mg of tenecteplase was evaluated in patients with intermediate-high risk. No statistically significantly differences were found related to mortality, and for this reason, it is not a therapy used frequently in our area; however, given the variable behavior of patients, there are no other therapeutic strategies with evidence supporting an improvement in the outcomes of patients.

In a meta-analysis of observational studies and clinical trials, including 12 studies, most used the Ekosonic device for the thrombolytic treatment of patients; where the effectiveness of catheter-directed thrombolysis was compa-

red with systemic anticoagulation, which is the standard management according to the 2019 European guidelines in patients with submassive PTE or of intermediate-high risk. The primary outcome that evaluated this study was in-hospital mortality within 30 days, 90 days and one year. Additionally, secondary significant outcomes were evaluated, such as major bleeding (defined as the presence of intracranial bleeding or any source of bleeding that may produce hemodynamic instability), minor bleeding and blood transfusion. Patients with hemodynamic instability were ruled out. From the 7 studies analyzed, only 1 found a real difference in terms of mortality when the odds ratio was compared with other studies. Possibly, this difference is due to the size of the sample. Additionally, in terms of heterogeneity, this was low among groups. However, a tendency to lower mortality within one year was identified, and to the recovery of RV function in patients who had underwent thrombolysis. When evaluating the secondary outcome of major bleeding, there were no statistically significant differences. It is then believed that the intervention seems to reduce mortality without increasing the risk of major or minor bleeding.[6]

Currently, the PEITHO-3 TRIAL is ongoing; this is a study evaluating the outcomes of efficacy and safety when administering reduced doses of IV alteplase at 0.6 mg/kg in 15-minute infusion, not exceeding the total dose of 50 mg.[7]

Finally, in the HI-PEITHO study, an ongoing study, the usefulness of catheter-directed thrombolysis is being evaluated in comparison with anticoagulation in patients with pulmonary thromboembolism with intermediate-high risk.[8]

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