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Percutaneous Transcatheter Treatment for Massive Pulmonary Embolism

Tratamiento percutáneo de la tromboembolia pulmonar aguda masiva

To the Editor,

Massive pulmonary thromboembolism (PTE) is characterized by sustained hypotension or cardiogenic shock, or both, and has high in-hospital mortality. In addition to hemodynamic and respiratory support, treatment includes anticoagulation and systemic fibrinolysis. Thrombolysis is contraindicated in between one third and one half of patients, mainly due to recent major surgery or trauma, etc., and is unsuccessful in approximately 8% of cases.[1] In these situations, the treatment options are surgical embolectomy, in select centers, or alternatively, percutaneous treatment.

In 2013, a protocol was implemented in our hospital for percutaneous intervention in patients with massive PTE and contraindication for thrombolysis. Since then, 24 such patients have been admitted and 5 of them (20%) received percutaneous intervention, performed by the interventional cardiologist (on-call available 24 hours). Prior to 2013, intervention had been performed, sporadically, in 3 patients. Thus a total of 8 patients have received attempted percutaneous treatment. Six patients (75%) had cardiorespiratory arrest with pulseless electrical activity. In 3 patients, the initial suspected diagnosis was cardiogenic shock secondary to acute coronary syndrome, with definitive diagnosis of PTE in the catheterization laboratory; in 2 patients, diagnosis was established by transesophageal echocardiography in the operating room; and in the remaining patients, diagnosis was confirmed on CT angiography. The angiographic and catheterization findings are described in the Table. Six patients had thrombotic occlusion of at least 1 pulmonary branch, and the mean pulmonary systolic pressure was 56 mmHg (standard deviation, 16 mmHg); in 2 patients, the pressures were not recorded due to hemodynamic instability. Five patients received variable doses of thrombolytic, administered as in situ intra-arterial boluses, divided between both pulmonary arteries according to the thrombus size.

Table
Clinical Data, Angiographic and Catheterization Details, Type of Percutaneous Intervention, In Situ Thrombolysis Dose, and Clinical Outcome

	Age	Sex	Diagnostic technique	Thrombolysis contra-indication	Angiographic findings	Preintervention PAP	In situ TL, dose	Transcatheter treatment	Postintervention PAP	Outcome
1	79	Female	CT-angio: bilateral PTE	HI	Bilateral segmental artery thrombus	35/18 (24)	No	No		Asymptomatic (15 months)
2	67	Female	Catheterization suspected ACS	HI	Complete occlusion RPA	Not recorded	Alteplase 25 mg RPA	Balloon fragmentation	Not recorded	In-hospital death due to ICH
3	44	Male	CT-angio: bilateral PTE	Knee surgery	Complete occlusion RPA	70/30 (45)	No	14 F aspiration	40/20 (26)	In-hospital death
4	33	Female	TEE: dilatation/ dysfunction RV	Surgery, hand replant	Occlusion RPA and inferior lobar branches LPA	60/20 (34)	Alteplase 10 mg RPA and 5 mg LPA	8 F aspiration	35/15 (16)	Asymptomatic (6 months)
5	42	Female	TEE: dilatation/ dysfunction RV and RPA thrombus	Surgery, skin graft	Occlusion RPA	51/21 (31)	Alteplase 20 mg RPA	Pigtail fragmentation 8 F aspiration	31/13 (19)	Asymptomatic (2 years)
6	71	Male	Catheterization suspected ACS	No	Bilateral occlusion of RPA and LPA	Not recorded	Alteplase 50 mg PT	8 F aspiration	Not recorded	Died in catheterization laboratory
7	68	Male	CT-angio: bilateral PTE	Hip surgery	Occlusion superior lobar artery	43/18 (26)	No	8 F aspiration	35/15 (22)	Asymptomatic (7 years)
8	70	Male	Catheterization suspected ACS	Hip surgery	Complete occlusion RPA	80/40 (53)	Alteplase 20 mg + 20 mg RPA	Balloon fragmentation	45/25 (31)	Asymptomatic (8 years)

ACS, acute coronary syndrome; CT-angio, computed tomography angiography; HI, head injury; ICH, intracranial hemorrhage; LPA, left pulmonary artery; postinterv. PAP, pulmonary artery pressure; PT, pulmonary trunk, PTE, pulmonary thromboembolism; RPA, right pulmonary artery; RV, right ventricle; TEE, transesophageal echocardiography; TL, thrombolytic.

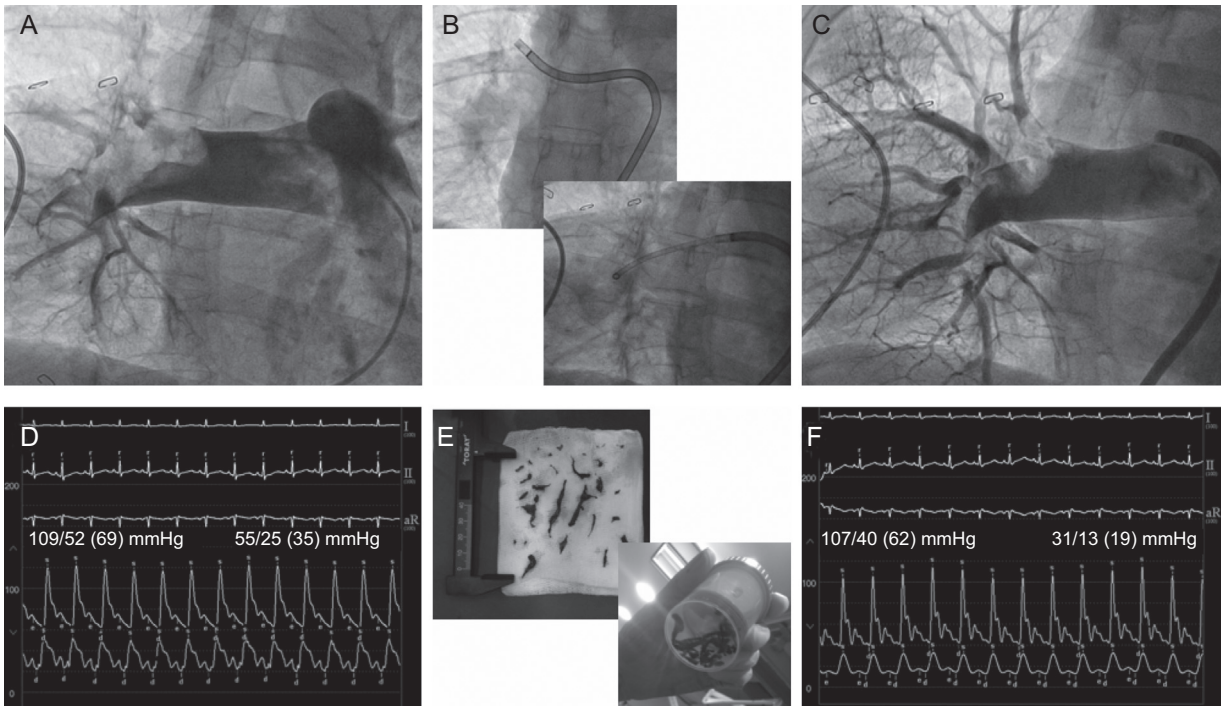

Figure. Patient 5. A: Angiography showing a large thrombus lodged in the right pulmonary branch. B: Thrombus aspiration with a deflectable catheter that allowed the passage of an 8 F guidewire-catheter through the thrombus. C: Final angiography, after mechanical/fibrinolytic treatment, showing residual thrombus but good distal perfusion. D: Baseline aortic and pulmonary pressures. E: Gross samples of aspirated thrombus. F: Final aortic and pulmonary pressures.

Given that most patients had a contraindication for systemic thrombolysis, the average dose was approximately one quarter of the systemic dose. Seven patients underwent mechanical treatment with thrombus fragmentation or aspiration (or both), either after intra-arterial thrombolysis if there was no hemodynamic improvement, or simultaneously if the patient's condition was very serious. One patient, with thrombosis in the segmental arteries and normal pulmonary pressure, did not receive percutaneous treatment. Five patients underwent aspiration with an 8 F guidewire-catheter using a Judkins right coronary catheter or multipurpose catheter introduced through an 8.5 F deflectable catheter (Agilis, St Jude Medical), allowing the catheter to be directed to the main affected branches or lobes. In all patients, thrombus was extracted, in variable amounts. Upon thrombus extraction, the lumen of the 8 F guidewire-catheter became occluded and had to be completely withdrawn. Use of the Agilis catheter allowed withdrawal of the 8 F catheters as many times as necessary without losing the position in the pulmonary tree. The Figure shows the deflectable catheter in use. Following mechanical/thrombolytic treatment, pulmonary systolic pressure decreased significantly (final pressure, 37 mmHg; standard deviation, 6 mmHg; $P = .007$). The aim of the procedure was to reduce pulmonary pressure and increase systemic pressure and pulmonary oxygenation. One patient died in the catheterization laboratory, although the entire procedure was performed in cardiac arrest (patient 6), and there were 2 in-hospital deaths: 1 patient died of intracranial hemorrhage despite the use of just one quarter of the systemic dose of thrombolytic, and 1 patient had a cardiac arrest in the vascular operating room. This patient, following successful percutaneous treatment of the PTE, required vascular repair to control an arteriovenous fistula hemorrhage caused by femoral vein puncture during catheterization.

Mortality from massive PTE is very high (approximately 30%) and is 3 to 7 times higher in patients who have undergone cardiopulmonary resuscitation. In our study, mortality was 33%, taking into account that 1 patient did not undergo intervention and that another patient underwent the entire procedure in prolonged cardiac arrest. Currently, there are no randomized studies comparing endovascular treatment with thrombolysis or with surgical embolectomy, and therefore the existing evidence comes from observational studies. A systematic analysis that included 594 patients with massive PTE (from 35 studies) found a success rate, defined as resolution of hypoxia, hemodynamic stabilization, and discharge from hospital, of 85.5% (between 40% and 100% depending on the series), and a major complication rate of just 2.4%.[1] This difference in mortality compared with our study is probably due to the profile of the patients included, considering that most patients in our series had had a cardiac arrest. In addition to reducing the thrombotic load by thrombus fragmentation and aspiration, endovascular treatment has the advantage of being able to administer the thrombolytic in situ, increasing its effectiveness and reducing the risk of hemorrhage because low doses can be administered. Fragmentation and aspiration were performed only in the main arteries and lobar arteries, not in the segmental arteries, and the procedure was ended as soon as hemodynamic and respiratory improvement were obtained, independently of the angiographic result. There was 1 serious procedural complication, which was a femoral arteriovenous fistula requiring vascular repair, and the patient died of a probable rethrombosis when anticoagulation was withheld.

This single-center study shows that percutaneous treatment of massive PTE is effective and offers an alternative to surgical embolectomy when fibrinolysis is contraindicated or has failed. In Spain, urgent percutaneous treatment of PTE could be easily implemented in a large number of hospitals with on-call teams of interventional cardiologists or radiologists.

Angel Sánchez-Recalde,[a,*] Raúl Moreno,[a] Belén Estebanez Flores,[a] Santiago Jiménez-Valero,[a] Abelardo García de Lorenzo y Mateos,[b] and José L. López-Sendón[a]

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Maximum Low-density Lipoprotein Cholesterol Lowering Capacity Achievable With Drug Combinations. When 50 Plus 20 Equals 60

Máxima reducción de colesterol unido a lipoproteínas de baja densidad alcanzable con combinaciones farmacológicas. Cuando 50 más 20 suma 60

To the Editor,

The results from the IMPROVE-IT trial and data from Mendelian randomization studies reinforce the causal role of low-density lipoprotein (LDL) cholesterol in atheromatous cardiovascular disease.[1,2] The "lower is best" concept has robust evidence-based support, and high-intensity cholesterol-lowering strategies ought to be implemented instead of high-intensity statin therapy.[3]

A clinically relevant question is "What is the maximum LDL-lowering capacity that will be achieved by combination therapy after the introduction of the new proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors?"

Statins have accumulated the most scientific evidence in cardiovascular prevention. Their average cholesterol-lowering effect ranges from 30% to 50%. By adding ezetimibe, their LDL-lowering capacity increased by 20% (22% in the IMPROVE-IT trial).[1] New PCSK9 inhibitors add an LDL reduction capacity of approximately 60%.[4,5] It must be taken into account that these reduction percentages are average values that may vary due to individual response. In addition, these percentages are achieved from the starting LDL values. Therefore, when calculating the overall impact of drug combinations, the effect of previous drugs must be taken into account. The absolute effect of adding drugs is lower than the addition of their relative effects.

For example, in a patient with LDL levels of 200 mg/dL, a high potency statin will decrease LDL cholesterol by 50% to 100 mg/dL. By adding ezetimibe, we expect a 20% incremental LDL reduction; therefore, LDL concentrations of 100 mg/dL will decrease to 80 mg/dL (20% less). Thus, this patient will have a final reduction of 120 mg/dL, which is a 60% reduction from the starting point (200 mg/dL). Therefore, by adding a drug that reduces LDL by 50% and another that reduces it by 20%, we will have a final absolute reduction of 60% instead of 70%. The same principle can be applied to PCSK9 inhibitors. In this patient, we can expect an incremental LDL reduction of 60%, so the LDL cholesterol level of 80 mg/dL will decrease to 32 mg/dL. This is exactly an 84% reduction, 24% more from the baseline value. This is indeed the maximum LDL-lowering capacity according to available drugs.

The efficacy of different drug combinations can be calculated by the formula in the Figure.

Several points should be stressed. The maximum LDL-lowering capacity obtained with a statin plus ezetimibe was 60%. The maximum LDL-lowering capacity when combining the more potent statin plus a PCSK9 inhibitor was 80%. The maximum LDL-lowering capacity using the 3 drugs in combination was 84% (Table).

This theoretical exercise has implications for clinical decision-making and should also be taken into account in clinical guidelines.

For example, when statins are used as monotherapy (a maximum LDL lowering effect of 50%), only patients with LDL levels below 140 mg/dL will reach secondary prevention targets (LDL < 70 mg/dL). With a statin plus ezetimibe (maximum LDL lowering capacity of 60%), only patients with LDL below 175 mg/dL will reach secondary prevention targets.

With triple therapy (LDL lowering capacity of 84%), almost anyone with LDL levels up to 437 mg/dL could achieve secondary prevention LDL targets.

It seems reasonable to adapt clinical guidelines and recommendations to clinical feasibility.

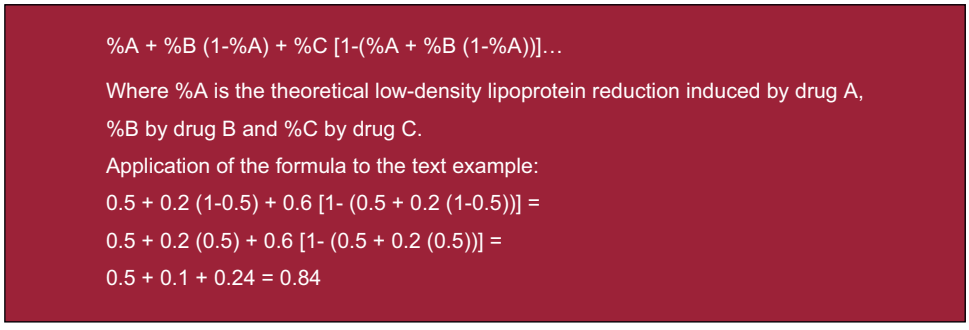

Figure. Formula to calculate the percentage of low-density lipoprotein lowering efficacy of drug combinations.