'Clot-busting' drugs reduce deaths from pulmonary embolism by nearly half

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Bringing clarity to a decades-long debate, a national team of researchers led by experts from the Perelman School of Medicine at the University of Pennsylvania has found that adding clot-busting medications known as thrombolytics to conventional approaches when treating sudden-onset pulmonary embolism patients is associated with 47 percent fewer deaths than using standard intravenous or under-the-skin anticoagulant medications alone. A pulmonary embolism is a blockage of one or more arteries in the lungs, primarily because of blood clots that travel there from the legs.

The meta-analysis of 16 published, randomized, controlled trials over the past 40 years assessed 2,115 pulmonary embolism patients, approximately half of whom received both thrombolysis and conventional anticoagulation treatment, namely IV-administered and injectable blood-thinners such as heparin; and half of whom only received the conventional treatment. The findings are published online in the *Journal of the American Medical Association*.

The authors found a 2.17 mortality rate among patients undergoing thrombolysis in addition to the other drugs. This compares to a 3.89 percent mortality rate for patients receiving the conventional blood-thinning regimen alone. Thus, the addition of thrombolysis was associated with 47 percent less mortality than standard anticoagulant therapy.

While the exact number of instances of pulmonary embolism is not known, experts estimate that 300,000 to 600,000 people in the United States are affected each year. More than 100,000 of these cases may result in death each year.

Thrombolysis involves the injection of clot-busting drugs such as alteplase and tenecteplase, usually through an intravenous line. In addition to sudden onset pulmonary embolism, patients may undergo emergency thrombolysis if they are having a stroke.

Using such criteria as low blood pressure, heart damage as revealed by diagnostic testing, and shortness of breath, physicians classify patients as being at high-risk, intermediate-risk, and low-risk of dying from pulmonary embolism. All patients diagnosed with sudden-onset pulmonary embolism are administered blood thinning medications such as heparin. These drugs prevent clot extension and put the body in a position to better break down the clot on its own. High-risk patients are usually also considered for more aggressive therapies such as thrombolysis or surgery to remove the clot, while low-risk patients generally are only maintained on oral blood-thinning medications such as warfarin. There has been extensive debate about whether the third group of patients, those at intermediate-risk, could benefit from thrombolysis as well, especially in light of the fact that the procedure could put them at greater risk for bleeding in their brains. Indeed, the reduction in death rate observed in the study was partially balanced by significant, associated increases in intracranial hemorrhage: 1.46 percent with thrombolysis vs. 0.19 percent with blood-thinners alone. But the study also revealed patterns in where those side effects may be more common: According to the meta-analysis, patients 65 and younger might be at less bleeding risk from thrombolysis than those above age 65.

"We discovered that thrombolysis was associated with a clear reduction in deaths in grey-area, intermediate-risk, pulmonary embolism patients," said the study's senior author, Jay Giri, MD, MPH, assistant professor of Clinical Medicine in the division of Cardiovascular Medicine at Penn. "Of course, this potential benefit must be balanced against potential bleeding risks, which we also attempted to clarify. With this knowledge, future research can help identify subgroups of patients who are most likely to obtain this mortality benefit and least likely to be harmed by bleeding, particularly intracranial hemorrhage."

"Additionally, research should focus on standardization of dosages of medication in thrombolysis as well as explore the optimal method of administration, namely intravenous versus catheter-directed therapy into the pulmonary arteries, to determine maximal clinical benefits with minimization of bleeding risk."

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