

Preventive therapy in brain-injured patients lowers risk of pulmonary embolism and DVT

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People who sustain a traumatic brain injury (TBI) are at high risk for developing deep vein thrombosis (DVT) and pulmonary embolism (PE). PE is a leading cause of death in these patients. But blood-thinning medications started within 72 hours of hospital arrival have a significant protective effect against these conditions in patients with severe TBI, and do not increase risk of bleeding complications or death, according to study results published online as an "article in press" on the *Journal of the American College of Surgeons* website in advance of print publication.

"Physicians have traditionally been hesitant to initiate pharmacological blood clot prophylaxis early in [patients](#) with severe brain injuries because, while thinning the blood might prevent PE and DVT, it might also increase the risk of complications related to worsening intracranial hemorrhage," according to lead study author James P. Byrne, MD, a general surgery resident and PhD student at the University of Toronto (Ontario, Canada). "We performed this study because there wasn't clear evidence that starting prophylaxis early actually prevented blood clots, or whether this benefit would outweigh the risk of complications from intracranial hemorrhage. Current evidence-based guidelines don't address the optimal timing for starting prophylaxis in patients with severe TBI."

Traumatic [brain injury](#) is common, affecting one in five patients treated for major injury at [trauma centers](#). Patients with TBI are at higher risk of forming blood clots because of hypercoagulability related to their

injuries and long-term immobility. DVT occurs when the blood in the veins pools and forms a clot in the arms or the legs. PE occurs when a clot breaks loose and travels to the lungs.

For the study, researchers looked at data on 3,634 adult patients with severe traumatic brain injury who were treated at 186 trauma centers participating in the American College of Surgeons Trauma Quality Improvement Program (ACS TQIP). TQIP works to elevate the quality of care for trauma patients in participating trauma centers across the United States and Canada.

The researchers looked at TQIP data for all patients who had received prophylaxis with either low-molecular weight heparin or unfractionated heparin between 2012 and 2014. The aim of the study was to compare the effectiveness of early versus late prophylaxis, and to evaluate the potential risks of worsening intracranial hemorrhage.

For the analysis, patients were divided into two groups: early prophylaxis (started within 72 hours of arrival at hospital) or late prophylaxis (started after 72 hours). The primary outcomes investigated were PE or DVT.

"Focusing on PE as an outcome was especially important for our study, because PE can occur in patients who don't have a demonstrated DVT, and carries an attributable mortality risk of 10 to 50 percent," Dr. Byrne said. "By limiting our cohort to patients with isolated severe traumatic brain injury, we were able to minimize confounding due to other injuries in multiple body regions, while ensuring that our results are generalizable to patients with the most severe head injuries," Dr. Byrne said.

The research team also wanted to characterize complications related to intracranial hemorrhage, so they included two secondary outcomes for that purpose: late neurosurgical interventions (performed after 72 hours) or in-hospital death.

An analytic method called *propensity score matching* was used in this study to emulate the design of a randomized controlled trial and minimize selection bias. This method took into account a large set of patient baseline and injury factors, and yielded a cohort of 2,468 patients. Outcomes were then compared between early and late prophylaxis groups.

Researchers found that early initiation of prophylaxis was associated with significantly lower rates of PE and DVT. The odds of both PE and DVT were 50 percent lower in the early prophylaxis group than in the late prophylaxis group. Importantly, there was no difference with respect to rates of late neurosurgical interventions or in-hospital death between early prophylaxis and late prophylaxis groups.

"No previous study has shown that patients who receive early prophylaxis have lower rates of [pulmonary embolism](#), which is important because this complication is a potentially fatal one," Dr. Byrne reported. "We also found that trauma centers that most frequently used early prophylaxis in their patients had significantly lower rates of [deep vein thrombosis](#), compared with counterparts where fewer patients received early prophylaxis, with no difference in rates of late neurosurgical intervention or mortality."

To date, this is the largest study comparing the effectiveness and safety of early versus late venous thromboembolism prophylaxis in patients with severe traumatic brain injuries. Study limitations included the fact that statistical methods could not account for confounding factors that were not measured in the study dataset. One important such factor was changes in patterns of intracranial hemorrhage on head CT scan, which would influence physician decision-making.

"The takeaway message is that early prophylaxis really does matter in patients with severe [traumatic brain injury](#), in terms of reducing a

patient's risk of pulmonary embolism or deep vein thrombosis," Dr. Byrne said. "Our findings suggest that this is possible without increasing the risk of the most feared complications, such as the need to take a patient to the operating room to evacuate [intracranial hemorrhage](#), or death. In other words, it's possible to prevent PE or DVT with early prophylaxis, without putting patients at risk of bad outcomes, and we should be striving to achieve this," he concluded.

More information: www.facs.org/publications/jacs/inpress

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