

D-dimer plasma level: A reliable marker for venous thromboembolism after craniotomy

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The D-dimer test is often used to rule out the presence of venous thromboembolism; however, the test has been considered unreliable in postoperative patients because D-dimer levels may rise after surgery. Researchers from the Department of Neurosurgery at the University of Halle in Germany hypothesized that this rise might be systematic and predictable, in which case a feasible postoperative threshold of D-dimer indicating venous thromboembolism could be determined. The results of this study show that the researchers were able to determine such a threshold. Complete findings are reported and discussed in "D-dimer plasma level: a reliable marker for venous thromboembolism after elective craniotomy. Clinical article," by Julian Prell, M.D., and colleagues, published today online, ahead of print, in the *Journal of Neurosurgery*.

Following craniotomy, up to 50% of <u>patients</u> experience <u>deep vein</u> <u>thrombosis</u> (DVT), the formation of <u>blood clots</u> (<u>thrombosis</u>) in veins lying deep below the <u>skin surface</u>—predominantly in the leg (not to be confused with <u>varicose veins</u>). In some of these patients a blood clot will break apart and a portion may travel to the lung, resulting in <u>pulmonary</u> <u>embolism</u> (PE), a medical emergency that is lethal in 50% of affected neurosurgical patients.

The presence of DVT or PE—both manifestations of venous thromboembolism—can be detected by performing the D-dimer test. Ddimer is a fibrin degradation product, which is produced when a blood clot (thrombus) dissolves. Under normal conditions, more than 0.5



milligrams of D-dimer in a liter of plasma (0.5 mg/L) indicates the presence of venous thromboembolism. For this reason the D-dimer test is often used when physicians suspect that a patient has this condition.

Following craniotomy and other surgeries, <u>blood coagulation</u> is activated and D-dimer plasma levels may become elevated. For this reason, the Ddimer test has been deemed unreliable in postoperative patients. Dr. Prell and colleagues hypothesized that after craniotomy, the plasma level of D-dimer would rise in a systematic and predictive manner in persons without venous thromboembolism, and that the D-dimer levels in persons with venous thromboembolism would rise to even higher levels. On the basis of these postoperative levels, a new postoperative D-dimer threshold for venous thromboembolism could be determined.

To pursue their hypothesis, the researchers conducted a single-center prospective study between April 2010 and February 2012 in patients undergoing elective surgery that involved craniotomy. The study sample consisted of 101 patients (59 female and 42 male) ranging in age from 18 to 82 years. All patients were outfitted with compression stockings from the day of surgery until the 5th postoperative day, and all received daily prophylactic doses of heparin postoperatively. If venous thromboembolism was diagnosed, the amount of heparin was increased. Doppler ultrasonography was used to directly detect the presence of thrombus in the patient's lower extremities. If DVT was identified, the location of this disorder was also noted to determine the associated risk of PE. In patients showing signs or symptoms indicative of PE, diagnostic computed tomography (CT) was also performed. Plasma levels of D-dimer in all patients were evaluated preoperatively and on the 3rd, 7th, and 10th days postoperatively.

Following surgery, the researchers noted that the D-dimer levels in plasma had risen systematically compared with preoperative levels. A substantial number of patients (42.6%) were found to have venous



thromboembolism (39.6% of patients with DVT [symptomatic or asymptomatic] and 8.9% with symptomatic PE). The researchers compared the values of D-dimer found preoperatively and on the 3rd, 7th, and 10th days postoperatively in patients with venous thromboembolism with values in patients without venous thromboembolism. Although there were no significant differences between groups with respect to D-dimer values preoperatively, there were significant differences in the D-dimer values obtained on all three postoperative testing days.

To determine the D-dimer threshold level indicating venous thromboembolism in patients who have undergone craniotomy, the researchers focused on D-dimer values obtained on the 3rd postoperative day. They focused on this time point because values obtained on subsequent days in patients affected by the disorder reflected the effects of therapeutic anticoagulation. The researchers found that a D-dimer threshold of 2 mg/L indicated venous thromboembolism with a sensitivity of 95.3%, a specificity of 74.1%, a negative predictive value of 95.6%, and a positive predictive value of 73.2%. Only two patients with venous thromboembolism had D-dimer levels lower than 2 mg/L. The D-dimer threshold for PE would appear to be even higher; in this small group of nine patients the mean D-dimer level was 7.14 mg/L (range 4.11-.33 mg/L).

To the best of the researchers' knowledge, "this is the first systematic study to evaluate a specific threshold of D-dimer plasma levels for a postoperative patient cohort." They conclude their paper by stating, "using a threshold of 2 mg/L, D-dimer levels will indicate VTE [venous thromboembolism] in patients after craniotomy with high sensitivity and specificity." These researchers expect that a postoperative D-dimer threshold for venous thromboembolism can be found for other types of surgery, although the precise level may differ from the one found in this study. Future studies are indicated.



An additional important finding of this study is that ventilation time and duration of surgery are highly significant risk factors for the development of venous thromboembolism.

When asked for his view on the study findings, Dr. Julian Prell stated, "We were honestly surprised by the clarity of our own results, which strongly contradict the established doctrine. Before this study, D-dimer plasma levels were considered to be completely unreliable in the postoperative period. Now, screening for venous <u>thromboembolism</u> using D-dimer <u>plasma levels</u> appears to be very straightforward and clinically applicable. We feel that utilizing this method as a routine measure in the perioperative management of neurosurgical patients has great potential to make their surgery safer, and we hope that similar studies will be conducted in other surgical fields."

More information: Prell J, Rachinger, J, Smaczny R, Taute BM, Rampp S, Illert J, Koman G, Marquart C, Rachinger A, Simmermacher S, Alfieri A, Scheller C, Strauss C. D-dimer plasma level: a reliable marker for venous thromboembolism after elective craniotomy. Clinical article. Journal of Neurosurgery, published online, ahead of print, August 6, 2013; <u>DOI: 10.3171/2013.5.JNS13151</u>

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