On the value of routine prothrombin time screening in elective neurosurgical procedures

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Object. The authors performed a study to evaluate whether preoperative assessment of prothrombin time (PT) is mandatory in patients undergoing routinely planned neurosurgical procedures.

Methods. The charts of all patients admitted to general wards of the authors’ department for routinely planned surgery (excluding trauma and ICU patients) between 2006 and 2010 were retrospectively reviewed. The authors assessed preoperative PT and the clinical courses of all patients, with special consideration for patients receiving coagulation factor substitution. All cases involving hemorrhagic complications were analyzed in detail with regard to pre- and postoperative PT abnormalities. Prothrombin time was expressed as the international normalized ratio, and values greater than 1.28 were regarded as elevated.

Results. Clinical courses and PT values of 4310 patients were reviewed. Of these, 33 patients (0.7%) suffered hemorrhagic complications requiring repeat surgery. Thirty-one patients (94%) had a normal PT before the initial operation, while 2 patients had slightly elevated PT values of 1.33 and 1.65, which were anticipated based on the patient’s history. In the latter 2 cases, surgery was performed without prior correction of PT. Preoperatively, PT was elevated in 78 patients (1.8%). In 73 (93.6%) of the 78 patients, the PT elevation was expected and explained by each patient’s medical history. In only 5 (0.1%) of 4310 patients did we find an unexpected PT elevation (mean 1.53, range 1.37–1.74). All 5 patients underwent surgery without complications, while 2 had received coagulation factor substitution preoperatively, as requested by the surgeon, because of an estimated risk of bleeding complications. None of the 5 patients received coagulation factor substitution postoperatively, and later detailed laboratory studies ruled out single coagulation factor deficiencies. There was no statistically significant association between preoperatively elevated PT levels and the occurrence of hemorrhagic complications (p = 0.12). Before the second procedure but not before the initial operation, 4 (12%) of the 33 patients had elevated PT.

Conclusions. The findings suggest that the value of preoperative PT testing is limited in patients in whom a normal history can be ascertained. Close postoperative PT control is necessary in every neurosurgical patient, and better tests need to be developed to identify patients who are prone to hemorrhagic complications.

Key Words • prothrombin time • Coumadin • warfarin • screening

Abbreviations used in this paper: aPTT = activated partial thromboplastin time; INR = international normalized ratio; PT = prothrombin time; PTT = partial thromboplastin time.
Methods

The PT values of 4310 consecutive patients admitted to our neurosurgical service between 2006 and 2010 to undergo electively planned surgery were analyzed using the INR (developed in 1983 by Kirkwood20). Patients directly admitted to our ICU were excluded from this analysis because a complete medical history could not be obtained immediately. We selected patients with a PT greater than 1.28, which is considered “abnormal” at our institution. Furthermore we determined if elevated PT values could be explained and expected by patient history (for example, in patients receiving prior warfarin/Coumadin medication or in those with liver cirrhosis, and so on).

To elucidate the role of preoperative PT assessment in the prevention and/or prediction of postoperative hemorrhage, we retrospectively reviewed all patients with hemorrhagic complications that led to a reoperation with regard to pre- and postoperative PT abnormalities.

Institutional Policy for Preoperative Coagulation Testing and Factor Substitution

We screened every patient admitted to our service for coagulation factor abnormalities using laboratory testing of PT, aPTT, and fibrinogen. Using a questionnaire, we routinely obtained a specific history on bleeding problems. We checked levels of coagulation factor XIII in patients undergoing craniotomies because reduced levels have been shown to be associated with postoperative bleeding.20 If coagulation testing showed increased PT (INR > 1.28), patients were usually given prothrombin complex concentrate (PPSB-human, Octapharma) before surgery until PT normalized, and this was followed by further hemostaseological workup for specific coagulation factor deficits.

Statistical Analysis

Statistical analyses were performed using commercially available software (BIAS for Windows). Binomial dichotomized data were compared using the Fisher exact test, and categorical data were compared using the chi-square test. A p value < 0.05 was considered statistically significant.

Results

Preoperative PT Screening

A total of 4310 patients were screened (Fig. 1). Of these, 170 patients (3.9%) had a PT greater than 1.28 once during their hospital stay. Preoperatively, PT was elevated in 78 patients (1.8%). In 73 (93.6%) of the 78 patients the PT elevation was expected and explained by the patient’s history (Table 1). In only 5 (0.1%) of 4310 patients did we find an unexpected PT elevation (mean 1.53, range 1.37–1.74) (Table 2).

Two of these 5 patients received coagulation factor substitution preoperatively by means of prothrombin complex concentrates in a dose-dependent fashion until PT normalized. These patients had only a slightly elevated INR, but the risk of postoperative bleeding in that specific surgery demanded substitution as requested by the surgeon. One patient had a vertebral body metastasis (preoperative INR 1.74) and the other patient had a spondylodiscitis (preoperative INR 1.55). Both patients underwent spinal instrumentation and stabilization procedures. Because none of these 5 patients had single coagulation factor deficits in later detailed laboratory studies, PT elevation was unexplained. It remained elevated in the patients in whom coagulation factor substitution was not administered throughout their hospital stay.

Postoperatively, none of the 5 patients with unexplained PT elevation received coagulation factor substitution. All surgeries and postoperative courses were uneventful.

Retrospective Analysis of Hemorrhagic Complications

In total, 33 patients (0.77%) suffered bleeding compli-

TABLE 1: Summary of the known diseases or medications that caused coagulation disturbance in the 73 patients with preoperatively elevated PT*

<table>
<thead>
<tr>
<th>Underlying Illness Causing Coagulation Disturbance</th>
<th>No. of Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>atrial fibrillation (warfarin medication)</td>
<td>36 (49)</td>
</tr>
<tr>
<td>aortic valve replacement (warfarin medication)</td>
<td>14 (19)</td>
</tr>
<tr>
<td>liver cirrhosis</td>
<td>13 (17)</td>
</tr>
<tr>
<td>status after deep vein thrombosis (warfarin medic</td>
<td>4 (5)</td>
</tr>
<tr>
<td>status after lung embolism (warfarin medication)</td>
<td>5 (7)</td>
</tr>
<tr>
<td>renal artery stenosis (warfarin medication)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>recovery phase after sepsis with DIC</td>
<td>1 (1)</td>
</tr>
</tbody>
</table>

* DIC = disseminated intravascular coagulation.
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TABLE 2: Overview of the 5 patients with elevated preoperative PT not explained by the patient’s medical history or current medication

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs), Sex</th>
<th>Disease</th>
<th>Underlying Disease</th>
<th>Op Delayed</th>
<th>Coagulation Factor Substitution (INR)</th>
<th>Bleeding Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>75, F</td>
<td>vertebral body metastasis</td>
<td>prostate cancer</td>
<td>no</td>
<td>yes (1.74)</td>
<td>no</td>
</tr>
<tr>
<td>2</td>
<td>61, M</td>
<td>vertebral body metastasis</td>
<td>prostate cancer</td>
<td>no</td>
<td>no (1.37)</td>
<td>no</td>
</tr>
<tr>
<td>3</td>
<td>78, F</td>
<td>spondylodiscitis</td>
<td>no</td>
<td>no</td>
<td>yes (1.55)</td>
<td>no</td>
</tr>
<tr>
<td>4</td>
<td>77, M</td>
<td>spondylodiscitis</td>
<td>no</td>
<td>no</td>
<td>no (1.56)</td>
<td>no</td>
</tr>
<tr>
<td>5</td>
<td>61, F</td>
<td>hemiated lumbar disc</td>
<td>no</td>
<td>no</td>
<td>no (1.47)</td>
<td>no</td>
</tr>
</tbody>
</table>

* Only 2 patients subsequently received coagulation factor substitution. In these patients, risk of postoperative bleeding in the specific surgery they underwent demanded substitution as requested by the surgeon. One patient (Case 1) had a vertebral body metastasis (preoperative INR 1.74) and the other patient (Case 3) had a spondylodiscitis (preoperative INR 1.55). Both had spinal instrumentation implanted. None of the 5 patients received factor substitution postoperatively. All surgeries were uneventful. Specific reason for the elevated INR was not found.

The evaluation of the PT as a measure of bleeding risk in patients undergoing invasive procedures has been investigated thoroughly. Some authors have argued that the relationship between PT and bleeding risk is remote at best. Even though evidence is growing that PT thresh-

TABLE 3: Incidence of postoperative hemorrhage stratified by elevated versus normal preoperative PT

<table>
<thead>
<tr>
<th>Variable</th>
<th>Postop Hemorrhage</th>
<th>Total No. of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>elevated PT prep</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>76</td>
</tr>
<tr>
<td>normal PT prep</td>
<td>31</td>
<td>4201</td>
</tr>
<tr>
<td>total</td>
<td>33</td>
<td>4277</td>
</tr>
</tbody>
</table>

* Patients with elevated preoperative PT were not at a higher risk of hemorrhagic complications. See Results for full details.
caused by disturbances of thrombocyte function, which gets disturbed through an operation. From an epidemiologic point of view, hemorrhagic complications are postoperative PT control, because surgery is the main reason for depletion of coagulation factors. From the time that tissue has been damaged—that is, when surgery has started—the coagulation system is activated. Coagulation factors are consumed and levels decline. Depending on the extent, type, and duration of surgery, levels may decline to the extent that secondary coagulation is also impaired.

Therefore, better tests should be developed to broaden the existing testing armamentarium. These tests need to be tailored to the needs of the surgeon. In view of our results, they should be readily available intraoperatively to assess whether a formerly normal coagulation system gets disturbed through an operation. From an epidemiologic point of view, hemorrhagic complications are caused by disturbances of thrombocyte function, which is not tested by measuring PT. Furthermore, preoperatively new concepts of hemostasis should be reflected. These tests should be able to mimic the complex interplay between activated thrombocytes and the coagulation system from tissue injury to forming a blood clot.

The main limitation of our study is its retrospective design. Generally, if we discovered an abnormal PT value, we chose to substitute coagulation factors. Therefore, one may not conclude from this study that PT testing should per se be abandoned for elective neurosurgical patients. To fully determine the value of PT testing and coagulation factor substitution, a randomized trial would be necessary; it is doubtful, however, whether an ethics committee would ever approve such a study. In a series of more than 4000 elective patients, however, we found only 5 with unexpectedly elevated PT.

From a cost perspective, one may argue that it is not essential to refrain from PT testing: At our institution, laboratory costs for PT testing are low, approximately $7.50 per test. The estimated annual amount needed to screen all elective patients preoperatively is around $8100, which is arguably negligible given the overall department costs. On the other hand, none of the 5 patients with unexpected PT elevations experienced hemorrhagic complications, even if admittedly 2 of them received coagulation factors. Yet, all 5 patients’ PT values were within the limits that Matevosyan et al. considered safe, so we may have exposed these patients to the potential risk of coagulation activation by administering prothrombin complex. Five patients are, however, too small a group to draw solid conclusions in this respect.

The positive predictive value of 2.5% is also limited by the fact that we provided coagulation factor substitution in most patients in whom we found elevated PTs, but again the necessity for substitution was anticipated based on patient history in the vast majority. The rate of unexpectedly elevated PTs that do not affect the bleeding tendency would be strongly diminished if testing were focused on elective patients with a higher pretest probability for PT abnormalities only—patients with current or previous anticoagulation medication, liver disease including alcoholism, or longer-lasting inflammatory or malignant illnesses. Subsequent studies might reveal specific conditions in which PT testing remains mandatory.

We conclude that it may be justified to refrain from routine PT testing in otherwise healthy individuals scheduled to undergo elective neurosurgical procedures who do not have a history of bleeding complications, known coagulopathies, liver disease (including alcoholism), or metastatic disease. If, however, PT testing reveals impaired coagulation capacity, thorough testing should nonetheless be performed to exclude single coagulation factor deficits, and PT should be corrected to reduce the risk of periprocedural hemorrhage.

Conclusions

The results of our study suggest that the yield of preoperative PT testing in routine elective cases in a neurosurgical population excluding trauma and ICU patients is trifling. Our data highlight the importance of surgery per se in initiating the coagulation cascade, consumption of coagulation factors, and bleeding complications in elective patients. Better tests need to be developed to broaden the existing testing armamentarium, aiming at identifying patients at risk for postoperative hemorrhagic complications.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Dützmann, Marquardt, Senft. Acquisition of data: Dützmann. Analysis and interpretation of data: Dützmann. Drafting the article: Dützmann. Critically revising the article: Gefeller, Senft. Statistical analysis: Dützmann. Administrative/technical/material support: Seifert. Study supervision: Senft.

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