Comparison of thromboelastography with routine laboratory coagulation parameters to assess the hemostatic profile and prognosticate postoperative critically ill patients

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ABSTRACT
Background: Patients undergoing surgery often demonstrate coagulopathy. Usually, this derangement in coagulation is assessed by the laboratory based evaluation of blood samples. However, collection of samples, their transportation to the lab, and the analyses can result in several errors and as such these tests may not be representative of the complete coagulation process. In our study, we compared the lab coagulation parameters with the point of care TEG indices and attempted to compare the outcome prediction of our patients based on the TEG indices and the various practiced ICU scores.

Methods: A prospective, observational study was conducted between May 2014 and May 2015. Fifty adult patients who had undergone noncardiac surgery and had developed new onset 2 or more than 2 system involvement in the postoperative period were enrolled in the study. They were sampled simultaneously for lab coagulation parameters (PT, APTT, INR, fibrinogen, and platelet count) and TEG on days 1, 3, and 5 post admission.

Results: There were significant differences between TEG and lab coagulation parameters on day 1 of the study (P = 0.004) but not on days 3 and 5. On days 1 and 3 of our study, the ICU scores (SOFA and APACHE II) were significantly higher in the group with deranged TEG parameters (P = 0.003, 0.02). The patient subpopulation with deranged TEG parameters had significantly higher mortality at median survival time (P = 0.014). Such a difference was not found in patients with higher ICU scores or deranged lab coagulation times. We constructed a ROC curve and arrived at a cutoff value of the reaction time to predict the median survival day mortality.

Conclusions: The agreement between TEG and conventional lab parameters remains poor but the TEG parameters seem to be more deranged in sicker patients. As the relationship between the overall severity of illness and derangement in the hemostatic system has been well explored in medical literature, TEG may be a more appropriate modality in such patients.

Keywords: ICU Scores, lab coagulation parameters, postoperative patients, prognostication, TEG

INTRODUCTION
Surgical patients often demonstrate coagulopathy in the postoperative period.[1] The common reasons can be prolonged surgery, enormous fluid shifts, bleeding, hypothermia, tissue damage, and subsequent edema and inflammation due to surgical handling.[2] Usually, this derangement in coagulation is assessed by the laboratory-based evaluation of blood samples. But collection of samples, their transportation to the lab, and analyses can result in several errors and as such these tests may not be representative of the complete coagulation process. In our study, we compared the lab coagulation parameters with the point of care TEG indices and attempted to compare the outcome prediction of our patients based on the TEG indices and the various practiced ICU scores.
ultimately their analyses are error-prone and as such these tests may not be representative of the complete coagulation process. However, viscoelastic tests like TEG can assess the entire hemostatic system, including the contribution of platelets and other cellular elements to the development of the clot as well as its strength and integrity. They also evaluate the fibrinolytic system and can be done at point of care.

Literature search resulted in very few studies that have compared lab coagulation studies and TEG indices in postoperative patients; however, none had used these indices for prognostication in these patient subset. In our study, we attempted to compare the lab coagulation parameters with the TEG indices and attempted to explore the value of these indices in predicting the outcomes.

**Aims of the study**

**Primary objective**

To assess whether the thromboelastography (TEG) parameters correlate with the standard lab-based coagulation parameters in the evaluation of hemostatic functions in postsurgical patients who develop 2 or more than 2 system involvement in the postoperative period.

**Secondary objectives**

To compare the outcome (mortality at median survival time) between groups with low and high ICU scores and groups with deranged and normal admission TEG indices and lab coagulation parameters.

**METHODS**

After approval from the Institutional Ethical Committee (IEC code: 2014-74-MD-76), a prospective, observational study was conducted between May 2014 and April 2015, a period of 12 months at the postoperative ICU of a tertiary care hospital in North India. Adult patients who had new onset 2 or more than 2 system involvement or decompensation in the postoperative period were enrolled in the study. Exclusion criteria were age under 18 years, cardiac surgical patients, pre-existent hematological disorders, currently under oral anticoagulants, or therapy to inhibit platelet aggregation, patients who have received heparin in the previous 6 hours or blood transfusion in the past 24 hours, death within 6 hours following surgery, postpartum or pregnant patients.

For routine coagulation profile, citrated anticoagulated blood samples were tested for prothrombin time (PT), international normalized ratio (INR), activated partial thromboplastin time (APTT), total platelet count, and fibrinogen level (using fully automated coagulation analyser). In our study, we used TEG 5000 thromboelastographic hemostasis analyzer system (Haemonetics) using kaolin with heparinized cuvettes to evaluate the following viscoelastic parameters: activated clotting time (R), kinetics (K), the alpha angle, the maximum amplitude (MA), LY -30, and the clot index (CI). Samples for the lab-based tests and the TEG-based evaluation were simultaneously obtained in the morning of the day 1, 3, and 5 of the study. The tests at the bedside as well as at the laboratory were performed by the same two dedicated technicians at all three time points of the study. In addition to the above, parameters pertaining to each system involved were recorded on days 1, 3, and 5 of the ICU stay of the patient. Samples for analyses were drawn from an arterial or central venous catheter connected to a transducer with an auto flush system with pressurized bags of 500-ml 0.9% sodium chloride solution. The point of care TEG was done immediately at the bedside whereas the conventional tests were sent to the laboratory which had an approximate turnover time of two hours. The patients’ conditions were evaluated on days 1, 3, and 5 on the basis of APACHE II and SOFA score. The study population was followed up for 30 days post inclusion into the study. All decisions regarding treatment were taken by an independent team of treating physicians and the patients were transfused with blood products as per the standard ICU transfusion protocol.

The organ systems considered were the respiratory system, the cardiovascular system, the renal system, the neurological system, the hepatobiliary system, and the platelet count. We defined ‘new’ system involvement as the involvement of an organ system that was completely unaffected in the preoperative period and showed involvement in the postoperative period or an acute on chronic decompensation (GCS for CNS involvement, creatinine, and urine output for the renal system, mean arterial pressure and the vasopressor support for CVS, the PAO2/Fio2 ratio for the respiratory system, bilirubin levels for the hepatobiliary system, and platelet count for coagulation system).

We were able to enrol 50 patients in the study who fulfilled the inclusion criteria [Figure 1].

Statistical comparisons were accomplished with SPSS software (version 20, IBM SPSS statistics 20.0). A P value of ≤0.05 was considered to be statistically significant. Both TEG and lab coagulation parameters evaluated the coagulation system in different manners and the parameters obtained were not comparable. So they were converted into categorical binomial variables and the McNamara test was used for comparison. Any value of reaction time beyond...
the reference parameter for our device [4–8], angle [47–74], maximum amplitude [54–72], and for lysis 30 [0–8], was considered a deranged TEG. Similarly, any value in platelet count, INR, and fibrinogen that was beyond the reference values of our lab were considered to be deranged.

The study population was subdivided into two groups on the basis of normal and deranged TEG parameters and their median ICU scores (SOFA, APACHE II, and SAPS II) were compared on each of the study days by unpaired t tests. A Kaplan–Meyer survival analysis was run and the survival distribution of the above two groups (normal and deranged TEG) were plotted. A log rank test was run to determine the differences in the survival distribution for the groups with deranged and normal TEG. The mean and median survival times were calculated from the curves. A receiver operating characteristic (ROC) curve was drawn by plotting the sensitivity and specificity of the reaction time (R) (the TEG parameter) in predicting median mortality [Figure 2]. The area under the curve was calculated. In addition, a suitable cutoff value of reaction time (R) was determined for predicting median mortality and sensitivity, specificity, false positive, and false negative.

RESULTS

The mean age of our study population was 52, with 30% of our patients being elderly. We had a balanced sex-ratio in our study population. The mean BMI was 23.2 although we had 12 obese patients, the majority of whom had undergone bariatric surgical procedures. We had 19 patients who have undergone emergency surgical procedures and developed multiorgan dysfunction. Of our patient population, the largest number of patients had undergone GI surgical procedures followed closely by oncosurgical procedures. Most patients (76%) had more than one of the Charlson comorbidities [Table 1].

Our first aim in this study was to compare the coagulation status of the patients as assessed by TEG and lab parameters on the three study days. On day 1, 86% of the patients had a deranged coagulation as per lab studies versus 46% as per TEG. On day 3, 90% of the patients had deranged lab values versus a 70% who had deranged TEG. On day 5, the figures were 69% versus 64% for TEG. Lab parameters were consistently more deranged than the TEG parameters. However, when we compared the lab coagulation status and the coagulation status as per TEG, on days 1, 3, and 5 by McNemar test, there was a

Table 1: Patient demographics

| Parameter                  | Value |
|---------------------------|-------|
| Age (range)               | 52    |
| Patients >65              | 15    |
| Sex (male/female)         | 28/22 |
| BMI (mean)                | 23.2  |
| BMI >30                   | 12    |
| Type of surgery           |       |
| Emergency                 | 19    |
| Elective                  | 31    |
| Type of surgery           |       |
| GI surgery                | 11    |
| Thoracic                  | 6     |
| Urological procedures     | 7     |
| Endocrine                 | 3     |
| ENT                       | 2     |
| Bariatric surgery         | 5     |
| Gynaecological            | 6     |
| Onco-surgery              | 10    |
| >1 Charlson comorbidity   | 38 (76%) |

Figure 1: Flow diagram of inclusion and exclusion criteria of study subjects

Figure 2: Receiver operating curve of the reaction time in predicting mortality at the median survival time
significant difference in the coagulation status as assessed by TEG and lab parameters on day 1 \((P = 0.004)\) but not on days 3 and 5.

We then subdivided the study population into two groups based on deranged and normal TEG parameters and compared the ICU scores between them. The SOFA score in the group with deranged TEG was significantly higher on days 1 and 3 \((P = 0.002\) and \(P = 0.012\)) but not on day 5. The APACHE II score showed a similar pattern with significantly higher APACHE II score in the deranged TEG group on days 1 and 3 \((P = 0.03)\) but not on day 5 [Table 3].

We subdivided our cohort into low and high ICU scores on the basis of the median score and also into normal and deranged coagulation on the basis of TEG parameters and lab coagulation values. A Chi-square test yielded a significant difference in the mortality of the two groups with normal and deranged TEG values \((P = 0.014)\). No difference could be found in the patient population with low and high coagulation scores, both SOFA \((P = 0.694)\) and APACHE \((P = 0.066)\), and also in the patient population with deranged and normal lab coagulation values \((P = 0.886)\).

A receiver operating curve was charted to determine the sensitivity and specificity of R value in predicting the mortality at median survival time, at different cutoff values. The median survival of our study population was eight days. The area under the curve was 0.695 \((P = 0.08)\). We examined the coordinates of the curve, that is, the sensitivity and specificity of the reaction time at different cutoffs in predicting the median mortality. At a cutoff value of 8.35 for the reaction time, we found that it had a sensitivity of 70% and a specificity of 80% in predicting the median mortality. Also, the false positive at this cutoff was 20%, the false negative was 30%, the positive likelihood ratio was 3.5, and the negative likelihood ratio was 0.37.

We followed up our patient population for 30 days. At 30 days, we had 17 mortalities.

**DISCUSSION**

Our first aim in this study was to detect whether there was any significant difference in the coagulation status as evaluated by TEG and lab coagulation parameters. We found significant differences between days 1 and 3 of the study. However, on day 5, we could not demonstrate any significant difference. Considering the theoretical superiority of TEG over the conventional assays, this could point toward a major lacuna in our conventional understanding of patient coagulation status.

Adamzik and colleagues recently demonstrated, in an observational cohort study of 56 patients with severe sepsis and 52 patients after major surgery, that the thromboelastometry-derived lysis index was a more reliable biomarker of severe sepsis than were procalcitonin, IL-6, and C-reactive protein (CRP).\[6\] A multivariate analysis of another cohort study of 98 septic patients by the same author\[7\] revealed that the absence or presence of at least one pathological thromboelastometry variable allowed better prediction of 30-day survival in severe sepsis patients than did the simplified acute physiology system (SAPS) II and sequential organ failure assessment SOFA scores.

In our study, based on patient subgroups of low and high ICU scores and normal and deranged lab coagulation parameters, there was no significant difference in mortality at the median survival time of eight days. However, we found a significant difference in mortality between the patient subgroups with normal and deranged TEG. We could arrive on a cut off value of reaction time to predict mortality at our median survival time of eight days. This could be of immense aid in prognostication in the ICU. Since coagulation plays a pivotal role in postoperative patients having multiorgan dysfunction, the possibility of adding thromboelastometry parameters to the established scoring systems could be explored.

We had two mortalities in the first five days of follow up. The SOFA score on admission of the first of these two

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**Table 2: Frequency of derangement of TEG and lab parameters on days 1, 3, 5**

| Day   | Deranged TEG | Deranged lab |
|-------|--------------|--------------|
| Day 1 | 23 (46%)     | 43 (86%)     |
| Day 3 | 35 (70%)     | 45 (90%)     |
| Day 5 | 30 (64%)     | 34 (69%)     |

**Table 3: ICU scores of the study population on the 3 days**

|          | Minimum | Maximum | Mean  | Median | Mean score in group with normal TEG | Mean score in group with deranged TEG | \(P\)  |
|----------|---------|---------|-------|--------|------------------------------------|---------------------------------------|------|
| SOFA day 1 | 4       | 16      | 6.97  | 5      | 5.19                               | 9                                     | 0.002|
| SOFA day 3 | 2       | 20      | 7.47  | 6      | 4.33                               | 8.81                                  | 0.012|
| SOFA day 5 | 0       | 15      | 7.07  | 6      | 5.45                               | 8.12                                  | 0.32 |
| APACHE day 1 | 4       | 25      | 13.57 | 12     | 11.06                              | 16.43                                 | 0.03 |
| APACHE day 3 | 6       | 30      | 13.97 | 11     | 9.89                               | 15.71                                 | 0.03 |
| APACHE day 5 | 4       | 28      | 12.75 | 10     | 6.65                               | 8.22                                  | 0.21 |
patients being considered was 10 and 15 (predicted mortality 50% and 90% respectively) and remained at 11 and 15 on day 3. For one of the patients, the APACHE II score was 22 on admission (predicted mortality 57%) and rose up to 30 (predicted mortality of 81%) on day 3. For the second patient, the apache scores predicted a mortality of 74% on day 1 which rose up to 81% on day 3. The coagulation profile of both the patients was deranged as per TEG and lab parameters on both days.

We could enrol only 50 patients in our study due to the limited time duration of the study. All our patients were postoperative patients and the type, duration, and complexity of surgeries that our cohort underwent were inhomogeneous. We did not perform any subgroup analysis based on the number of organ systems affected or the severity of involvement. However, in spite of these shortcomings, our study hopes to prove that this particular subset of population deserves our attention for larger and perhaps better structured studies.

CONCLUSION

Postoperative patients are precious in the sense that most of them might have had no or only minor preoperative underlying medical illnesses. Also, they are at a precarious stage of biodynamics especially with regards to the coagulation system. Thromboelatometry in any form can render more insight in prognostication of the outcome but more multi-institutional research work ought to be focused on this subset of population.

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Conflicts of interest
There are no conflicts of interest.

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