Standard Coagulation Tests or Viscoelastic Testing in Patients with Massive Transfusion.

Bruce D. Spiess, MD, FAHA
Virginia Commonwealth University Reanimation Engineering Science institute (VCURES)
Richmond, Virginia

Massive transfusion is relatively uncommon in cardiac surgery—thankfully. The question as it was worded for this lecture denotes that these tests should be exclusive of each other and somehow one might be the best. It should rather be considered that they are complimentary and one needs not to examine the advantages of one type of testing over the other. Rather the audience should consider how human systems (our laboratories and hospital support systems) can give us as much information as possible quickly and allow us to use appropriate coagulation algorithms (decision trees) to make the best decisions. Also, the wording “standard” coagulation tests somehow connotes that viscoelastic tests are not standard. Nothing is farther from the truth (thousands of papers are published upon them—they are standard). We as a group should stop using this incorrect nomenclature and fight back against the past jargon that perpetuates bad medicine.

The prothrombin time (PT) and activated partial thromboplastin time (aPTT) were devised in the 1950’s as screening tests to detect congenital coagulopathies of insufficient or dysfunctional proteins. They later became of use in monitoring either vitamin K factor depletion through warfarin/Coumadin therapy (PT) or anticoagulation with unfractionated heparin. For heart surgery neither technique has been shown to individually predict peri-operative bleeding or to be particularly useful in guiding treatment for micro-vascular bleeding. Because these two tests were created at the evolutionary time when the protein coagulation cascades were biochemically investigated, they have persisted within laboratory medicine and clinical usage. They have been widely criticized for focusing only upon isolated plasma protein function with artificial activators.

Coagulation is not a pure protein chemical reaction nor does it occur in vivo without cell signaling. Coagulation and thrombosis formation happens in the microenvironment of the endothelial cells with flow, shear forces, platelets, white cells and even red cells having key interactions. The platelet surface is where the biochemistry of protein cascade reactions takes place. But a little known fact is that red cells trade eicosinoids and must be present for platelets and white cells to function normally and that erythrocytes have GpIIb/IIIa binding sites and do cross link with fibrinogen. So a more wholistic view of coagulation is a contemporary understanding.

Viscoelastic tests utilize whole blood. These tests have included thromboelastography (TEG), Rotational Thromboelastometry (ROTEM) and Platelet Elastic Modulus (Hemodyne Inc). The Sonoclot can also be considered a whole blood viscoelastic test but the accent there should be upon it as a viscometer, because that is what it does exactly measure. Whole blood clot strength is quite important. It is the strength of the clot that creates a dam against the pressure of arterioles and venules thereby stopping bleeding. But equally important (perhaps) is the speed at which clot formation occurs as well as whether the clot stays intact or breaks down (fibrinolysis). The viscoelastic tests do assess
each of these key parts of coagulation. But one can and should argue that the PT and aPTT might under some circumstances get better information with regards the onset of clot formation. Other tests, now available, such as the Verify Now (Accumeterics) PFA-100, Platelet Works and others (automated platelet aggregometry, or flow cytometry) can tell a great deal more about both native platelet dysfunction, inhibition or drug effects on platelets.

The use of individual tests with a claim that one is best is fraught with failure. Several studies have shown that the PT, aPTT and even the “coagulation profile” (PT, aPTT, fibrinogen, Platelet count, plus D-dimer) have a less than 50% accuracy in predicting abnormal bleeding. Think about that, these “standard tests” in heart surgery are worse than flipping a coin. But we should not abandon them. The viscoelastic tests have shown between 70-95% predictive value in a number of studies. A few studies have criticized the viscoelastic studies because there is not a direct correlation between changes in a clot strength and chest tube bleeding as collected in a postoperative measuring device. Such studies seem to miss the biology of how bleeding occurs. Blood loss after heart surgery is not a bell shaped curve and gradations of prolongation of clot onset time or decreased clot strength will not translate into incremental increases in bleeding. There must exist a threshold of clot dysfunction beyond which blood simply will not clot and the chest tubes will fill more and more. Likewise such research does not take into account the effects of surgical bleeding (the cause of over 90% of bleeding). But, many of the studies do agree that if the viscoelastic tests are normal and the patient is bleeding then it almost certainly is a surgical bleed that has not been found.

Recently, and pertinent to this lecture some literature has arisen regarding the use of viscoelastic testing in massive bleeding both for poly-trauma (the wars in Iraq and Afghanistan) as well as in cardiac surgery. Examination of that contemporary literature is very useful. First one must understand that hemorrhagic shock due to polytrauma, especially in a war with IED explosions, or in civilian blunt (motor vehicle crash) is different than in cardiopulmonary bypass. Similarly it is wrong to translate the evolving literature of polytrauma and massive transfusion protocols to early intervention in the cardiac suites.

In trauma the PT/INR has a direct correlation to both the ISS score as well as morbidity (multi-system organ failure) and mortality. TEG has gained interest in trauma both in war zones and in civilian medicine. In a recent data bank analysis of 1,230,422 trauma patients the prevalence of warfarin drugs in trauma patients was as high as 12.8%. Clearly its use in heart surgery is higher and we know that the bypass machine/inflammation/heparin-protamine prolongs the PT/INR. So, which test is better. The TEG R-value looks at the onset of clotting (a protein platelet interaction). In a Canadian study of 628 adult trauma patients simultaneous TEG and PT/INR tests were drawn on arrival to the trauma center and then over the next 48 hours. Clotting factor assays were also performed with specific examinations of factors II, V, VII, X and IX. From this trauma study 13 and 9% of the patients had levels of INR prolonged beyond 1.3 and 1.5 INR. Only 6% had a TEG R value prolonged beyond the outer limit of normal. When one looks the specificity, positive predictive value and negative predictive value of the PT v. the TEG r value in this study to determine the presence of low levels of vitamin K dependent coagulation factors some interesting things show up. The INR > 1.5 seems to be the best with a specificity of 98%, PPV-84% and NPV-96%. The TEG
R-value with a cut off of 8 minutes had a specificity of 95%, PPV of 47% and NPV of 92% (not terrible dissimilar to the INR> 1.5). The real question is who had more bleeding and which groups of patients required more transfusion. Unfortunately the study was not structured to answer that question and a blood management/transfusion algorithm was not followed. The use of blood products between groups seems rather muddy and similar. Of note, the study was set up to try to ferret out which patients had been on warfarin drugs prior to presenting to the ED. Those patients on warfarin had rather low transfusion utilizations and that was not predictive of how much they would bleed/use transfusion. This study did however show that the TEG in that Canadian center in trauma took as long as 55 minutes to run, get data back. This study shows a problem with all such research, the TEG was run with Kaolin as an activator and it was run according to "manufacturer’s instructions that the citrated whole blood be held for 45 minutes prior to running the TEG. Therefore the TEG was already going to perform poorly in terms of timing. The use of Kaolin activates the aPTT-like contact activation. As so often this data means that apples to oranges were compared.

Perhaps a more useful study was smaller in size (only 26 Patients) but examined ROTEM and "standard coagulation tests (PT, aPTT, fibrinogen level, ATIII, thrombin generation and platelet count). The ROTEM is more robust than the TEG and does have pre-packaged cuvettes with activators for the extrinsic system (EXTEM0 and the intrinsic system (INTEM). In contrast to the above study, it makes sense that using the right activator when comparing PT and aPTT is critical. In addition the ROTEM has the capability of examining the fibrinogen level through use of platelet blocking agents (FIBTEM). All of these types of studies can be performed with the TEG but to do so requires the user to pipette and measure reagents. The ROTEM is supplied with these cuvettes and is therefore partially automated to create this data analysis.

The study of the 26 patients did find the ROTEM –FIBTEM measurement having a good correlation coefficient( r=0.87, p<0.001) compared to laboratory derived fibrinogen levels. The FIBTEM followed the expected dilution and consumption of fibrinogen during he bypass run. This study did not have enough patients to see if the FIBTEM could pick up particularly low levels of fibrinogen that might well be highly related to postoperative bleeding. Recently some have said that fibrinogen should be as much as 200mg/dl to decrease post CPB bleeding. It has been this authors opinion to accept lower levels such as 100 mg/dl. But the FIBTEM seems to be accurate in those ranges.

The EXTEM and INTEM through their MCF (or maximum clot firmness) had significant correlations with the platelet count (r=.69 and .63 respectively p<0.001. Why one would expect anything higher is hard to understand. The maximum clot firmness is dependent upon platelet count, platelet function (the GP ligands), fibrinogen concentration and factor XIII. The fact that there was a statistical correlation is interesting.

The thrust of this study was that could one use the ROTEM and substitute it as a guide for the transfusion decisions by eliminating the “standard” coagulation tests. The study neither answers that question nor discards it. Clearly changes that are expected in a rather small number of cardiac patients can be followed and found by the ROTEM. Will the
widespread use of the ROTEM lead to reduction in blood product utilization? That question has been answered by a growing literature showing it is capable of doing that. Should we eliminate the use of the “standard “coagulation tests? That should not be answered by a study of only 26 patients.

Lastly we should look at the question of how fast can these tests perform and give us useful information. Again, so much of this answer is dependent upon the “systems” in place within hospitals. If a ROTEM, TEG or coagulation testing laboratory is immediately in the vicinity of the operating rooms, and if the “system” is sensitive to the importance of these data with computer links, rapid test sample intake processing, then data can be very quickly acquired. If however laboratories are in distant buildings and excuses are made for why the laboratory medicine service cannot provide ultra-fast results in critical situations then the tests are doomed to failure.

In a study of rapid TEG in Colorado during massive transfusion and trauma an algorithm for treatment was agreed upon. The R-TEG uses both kaolin and tissue factor along with buffers, and phospholipids, essentially creating a massive turn on of the intrinsic and extrinsic systems. This system sacrifices some of the discriminating power of the R-value to get as rapidly as possible a maximum amplitude. The R-TEG gave data within minutes and interestingly in this study the use of blood products dropped and mortality went form 65-29% with the use of the r-TEG algorithm. To date, I am not aware of similar work in cardiac surgery. This group did note that the r-TTEG was far more useful than the “standard” coagulation tests.

In conclusion, there is gathering data that viscoelastic test could replace “standard” coagulation tests, but we cannot fully claim that yet. Furthermore, there is so much data showing that the use of coagulation algorithms in conjunction with all types of coagulation testing and particularly ROTEM and r-TEG not only makes sense, decreases blood utilization and may improve morbidity and mortality. Indeed the STS/SCA guidelines for blood transfusion in heart surgery call for such algorithm usage. That should be our stress- that all centers institute the guidelines and embrace real time, fast as complete as possible coagulation monitoring.

Recommended Reading: