Anaesthetists may be involved in the management of patients with a bleeding diathesis in the preoperative, intraoperative or during the postoperative period in the intensive care ward. Complex surgical procedures, including liver and cardiac surgery, are associated with a potential for significant perioperative blood loss and the development of postoperative bleeding disorders. The inherent risks of the use of homologous blood and blood products [25, 41], allied to the scarcity of these resources, make it important that treatment with blood products is based on scientific evidence of need.

Monitoring of anticoagulation in the intraoperative period is performed most commonly by the activated clotting time (ACT) using an automated method such as the Hemochron (International Technidyne Corporation, Edison, NJ, USA). This method uses disposable glass tubes containing diatomaceous earth 12 mg as a coagulation activator and a small cylindrical magnet which, when bound up in the developing clot, activates the detector to stop the counter of the machine. This method is effective for monitoring heparin therapy, but it is not specific to a particular part of the coagulation cascade and is therefore less effective in the patient with a coagulopathy from other causes, such as impaired platelet function or fibrinogen deficiency. After operation, a variety of coagulation tests are used to assess whole blood coagulation, including prothrombin (plasma thromboplastin) time (PT), activated partial thromboplastin time (APTT), platelet count and plasma fibrinogen concentration. Each of these tests measures a different aspect of the clotting process, but even in combination they do not provide a complete picture of the status of the coagulation system.

Several recent studies have emphasized platelet dysfunction as a major cause of postoperative bleeding after cardiopulmonary bypass [9, 13, 23, 39], and yet evaluation of platelet function remains insensitive and time consuming [29]. The platelet count provides only a quantitative, not qualitative, index of platelet status. Template bleeding times are notoriously inaccurate [27]. Standard laboratory tests of platelet function are complex, and in most hospitals are impractical for the acute perioperative management of the patient who is bleeding.

At present the treatment of postoperative bleeding remains empirical because of the perceived need for immediate correction of the haemostatic defect and the lack of readily available measures of all phases of clot formation and breakdown, including the strength of the clot. Patients are often given fresh frozen plasma and platelets with little scientific basis. There is therefore a requirement for a simple, reproducible method that allows specific diagnosis of coagulation defects.

Recently, interest has been shown in the perioperative use of viscoelastic methods of assessing the clotting mechanism [5, 15, 29, 34]. Two such methods exist: these are Sonoclot analysis (SCT) and thrombelastography (TEG). Both methods evaluate all phases of clot formation and retraction from a single sample of blood, and allow assessment of coagulation factor, fibrinogen and platelet activity, in addition to measures of clot maturation and lysis. SCT and TEG have been shown to be of clinical value in assessing the haemostatic process during liver transplantation and cardiac surgery [5, 35, 38]. Thrombelastography has been reviewed recently in this journal [21]; we present a review of the Sonoclot method.

Sonoclot analysis

In 1889 Hayem suggested that changes in the viscosity of blood might form the basis for a test of coagulation function [12]. It was not until 1910, when Koffmann introduced his coaguloviscometer, that continuous measurement of changes in blood viscosity during blood coagulation were possible [17]. In 1923 Kugelmass [18] introduced an alternative viscosimeter which formed the basis of the modern thrombelastograph, and in 1975 von Kaula, Ostendorf and van Kaula described the Sonoclot analyser, a device which measures the changing impedance to movement imposed by the developing clot on a small probe vibrating at an ultrasonic frequency in a coagulating blood sample [40].

Key words

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OPERATING PRINCIPLE

The Sonoclot analyser (Sienco Inc., Morrison) has a hollow, open-ended disposable plastic probe, mounted on an ultrasonic transducer. The probe vibrates vertically a distance of $1 \mu m$ at a frequency of $200 \text{ Hz}$, and is immersed to a fixed depth in a cuvette containing a 0.4-ml sample of whole blood or plasma (fig. 1). The same exerts a viscous drag on the probe, mechanically impeding its free vibration. The drag increases as the sample clots and fibrin strands form on the probe tip, and between the probe and the wall of the cuvette, effectively increasing the mass of the probe. The increasing impedance to vibration of the probe as the sample clots is detected by the electronic circuits driving the probe and converted to an output signal, on a paper chart recorder, which reflects the viscoelastic properties of the developing clot [40]. The continuous output curve, or “signature” (see fig. 2), describes the whole coagulation process in vitro, from the start of fibrin formation, through polymerization of the fibrin monomer, platelet interaction and eventually to clot retraction and lysis.

A plain cuvette, containing no activator, is usually used to derive the SCT signature. Two other types of cuvette are also available which are better suited to intraoperative coagulation monitoring. Both contain a celite activator: the cuvettes with a low concentration of activator (“red cap” tubes) speed up the analysis but still allow assessment of platelet function, while the cuvettes with a high concentration of activator (“white cap” tubes) merely measure ACT which is comparable with the ACT obtained with the Hemochron method.

INTERPRETATION OF THE SONOCLOT SIGNATURE

Several measurements (fig. 2) can be made from the Sonoclot signature [29] and a normal trace is reproduced in figure 3. Immersion of the vibrating probe in the sample cuvette initially causes a small increase in the signal because the liquid presents an increased impedance to vibration compared with free vibration in air. The onset time, also known as the Sonoclot ACT or SonACT, is the time in seconds until the beginning of fibrin formation. This is defined as an upward deflection of 1 mm on the 100-mm wide recorder chart and is calculated automatically by the machine. This measurement corresponds to the conventional ACT measurement using the Hemochron method, provided cuvettes containing a high concentration of activator are used to derive the SCT. The rate of fibrin formation from fibrinogen is indicated by the gradient of the primary slope (R1). The rate is expressed as a percentage of the peak amplitude per unit time; R1 values between 15 and 45 % are considered normal. An inflection point, or shoulder, on the upstroke is often seen between the R1 and R2 slopes, although this is a variable feature of the trace. The shoulder represents the start of contraction of the fibrin strands by the action of the platelets. As contraction proceeds, the developing clot starts to break away from the inner wall of the cuvette and the impedance to vibration of the probe decreases briefly. The secondary slope (R2) reflects further fibrinogenesis, fibrin polymerization and platelet–fibrin interaction. During the R2 slope, the increase in probe mass caused by deposition of fibrin still exceeds the decrease in clot mass resulting from expulsion of serum during clot retraction. The peak impedance (PEAK) reflects completion of fibrin formation and has two variables. The time to peak amplitude is an index of the rate of conversion of fibrinogen to fibrin, although the R2 slope is modified by the dynamic combination of fibrin formation and early clot retraction. The amplitude of the peak is an index of fibrinogen concentration; the
signatures in SCT analysis, producing progressively anticoagulant is a potential source of poor platelet platelets within sample tubes which contain citrate using fresh whole blood. Contact activation of the bedside, or as close to the patient as possible, usable as a measure of fibrinolysis. decrease in the signal after the R3 slope is clinically ever, in patients with accelerated fibrinolysis the not seen on the average Sonoclot signature. How- pre-immersion value. Usually this is very slow and fibrinolysis takes place, returning eventually to the forms a plateau at the peak value [34]. no inflection in the R1/R2 upstroke, and the signal is small, there is minimal, or protracted, inflection in the R1/R2 upstroke and a shallow R3 gradient with platelet function is poor, or the number of platelets therefore key determinants of the R3 value. When platelet function is poor, or the number of platelets is small, there is minimal, or protracted, inflection in the R1/R2 upstroke and a shallow R3 gradient with little decrease in the signal after the peak (fig. 5). An extreme case of this type of trace may be seen when plasma samples, rather than whole blood, are used to measure the SonACT. The signature then represents only the conversion of fibrinogen to fibrin; there is no inflection in the R1/R2 upstroke, and the signal forms a plateau at the peak value [34].

Much later, the signal decreases still further as fibrinolysis takes place, returning eventually to the pre-immersion value. Usually this is very slow and not seen on the average Sonoclot signature. However, in patients with accelerated fibrinolysis the decrease in the signal after the R3 slope is clinically usable as a measure of fibrinolysis.

Ideally, Sonoclot analysis should be performed at the bedside, or as close to the patient as possible, using fresh whole blood. Contact activation of platelets within sample tubes which contain citrate anticoagulant is a potential source of poor platelet signatures in SCT analysis, producing progressively shorter SonACT times and steeper R1 slopes with increasing storage time [personal communication, J. L. Francis]. The problem is worse with glass rather than polypropylene tubes. When transfer of the blood sample to the point of analysis takes longer than 3 min, a platelet protective anticoagulant is recommended, such as the Diatube H (Diagnostica Stago, France). This tube contains a 3.2 % citrate anticoagulant, combined with theophylline, adenosine and dipyridamole, which protects platelet function and allows better reproducibility of results.

Comparison of Sonoclot with conventional clotting studies

Conventional clotting studies are usually performed on centrifuged plasma fractions and therefore only provide information on isolated parts of the coagulation cascade. There are several interactions between constituent parts of the clotting cascade, and proper clinical evaluation of clotting and bleeding problems requires information regarding these interactions which is not provided routinely by haematology laboratories [24]. Most of the conventional tests end when fibrin strands are formed but viscoelastic techniques such as Sonoclot begin as the first fibrin strands become evident and continue through to clot lysis and retraction.

No studies have shown a direct correlation between abnormalities in the conventional clotting tests and perioperative blood loss, probably because adequate platelet function is required before normal haemostasis can occur. A normal platelet count does not imply that platelet function is normal, but platelet function tests are complex and unsuitable for acute perioperative situations requiring rapid diagnosis and treatment. SCT distinctly differentiates between platelet-rich and platelet-poor plasma [34] and has been used primarily for assessing platelet function [29].

Tuman and colleagues [38] found that the sensitivity of SCT in predicting postoperative bleeding after cardiopulmonary bypass was 74 %, with no false negatives and 33 % false positives. This compares well with a predictive accuracy of 33 % using routine coagulation tests, with 44 % false negative results and 73 % false positive results. Chapin and co-workers [5] found that SCT diagnosis of platelet dysfunction or clotting factor deficiency correlated well with the results of standard coagulation tests during liver transplantation.

Defects of fibrinolysis have been implicated increasingly as a cause of perioperative bleeding [14, 28]. Sonoclot is not a better test of fibrinolytic activity than routine tests such as measurement of fibrin degradation products, but it may produce results more quickly and prove to be a useful guide to intraoperative fibrinolytic activity. However, TEG is more useful as a monitor of this aspect of coagulation function.

SCT provides dynamic information on the coagulation pathway that is not available from conventional tests and therefore offers a method of rationalizing the management of perioperative bleeding problems.
Sonoclot compared with thrombelastography

TEG was introduced by Hartert in 1948 [11]. Both SCT and TEG measure the viscoelastic properties of a developing clot, and so monitor haemostasis as a dynamic process rather than at isolated end-points as in routine coagulation tests. In both techniques a single blood sample is all that is required to evaluate all phases of coagulation. SCT measures changes in impedance to movement of a vibrating probe in the developing clot, whereas TEG assesses clot formation by measuring the torsional impedance imparted to a fixed piston suspended in a rotating cuvette of coagulating blood. While the characteristic output curves, or “signatures”, produced by these methods are different, they both measure viscoelastic properties of blood, including rate of fibrin formation, clot strength and clot lysis. Both are convenient and easy to perform and have been shown to be of clinical value in the assessment of the haemostatic process during liver transplantation and cardiac surgery [5, 38]. One study has shown that the predictive accuracy of abnormal and normal clinical haemostasis was significantly better using both SCT and TEG compared with routine coagulation studies, but that no significant difference could be shown in overall predictive difficulty, false positive or false negative rates between SCT and TEG [22].

There is a greater opportunity for differences in technique between different operators during TEG compared with SCT, in part because of the need to apply a thin layer of oil over the sample in the TEG cuvette to minimize evaporation. The completed signature takes longer with TEG than with SCT, because TEG relies on the production of a fibrin “bridge” between the cup and the torsion spring while SCT responds as soon as fibrin formation begins. Also, because TEG takes time to produce information on clot lysis, information is available sooner with SCT [5]. However, for information on coagulation, rather than lysis, both techniques are equally fast. One major problem with TEG however, is that the machine must be mounted on a very solid, flat base to produce reliable results.

Sonoclot and cardiac surgery

Postoperative bleeding remains a significant cause of morbidity and mortality after cardiac surgery in which cardiopulmonary bypass has been used, resulting in re-exploration of the chest in approximately 3% of cases [30]. The cause of excessive bleeding may be failure of the surgical technique, haemostatic failure, or a combination of both. Haemostatic failure after cardiopulmonary bypass may be caused by inadequate reversal of heparin with protamine, haemodilution causing a moderate decrease in plasma clotting factors or platelet abnormalities, including a decrease in platelet count and a decrease in platelet aggregation [7, 9]. These changes in coagulation may be induced by oxygenators, roller pumps and cardiotomy suction used during cardiopulmonary bypass. SCT is better than routine clotting studies for predicting post-operative haemorrhage caused by coagulopathy [38]. Shenaq and Saleem [34] concluded that SCT provided predictable information on platelet function after cardiopulmonary bypass. Of 24 patients who bled after operation but had a normal SCT signature, 22 were found to have a surgical cause for the bleeding. In 25 patients with abnormal signatures associated with postoperative bleeding, the bleeding was controlled and the signature returned to normal after platelet transfusion.

Sonoclot and liver surgery

Massive blood loss during liver surgery is a major concern. Before operation, very low concentrations of clotting factors, thrombocytopenia, splenomegaly and malnutrition all contribute to coagulopathy [6]. Another difficulty in the intraoperative management of liver transplantation has been actively monitoring the clotting system and determining the appropriate treatment during dynamic changes in blood volume [16]. Kang and colleagues pioneered the use of TEG to monitor coagulation during orthotopic liver transplantation [15]. Chapin and co-workers compared SCT, TEG and routine clotting studies during orthotopic liver transplantation and found significant correlations between SCT and platelet counts as indicators of platelet function, and similar agreement between SCT and PT and APTT as indicators of coagulation factor status. They concluded that there was substantial agreement between TEG and SCT in diagnosing platelet dysfunction, clotting factor deficiency and defective fibrinolysis during liver transplantation. They also concluded that SCT and TEG diagnoses of platelet dysfunction or clotting factor deficiency correlated well with standard coagulation tests reflecting those two disorders [5].

Sonoclot in hypercoagulable states

A proportion of patients with liver disease have hypercoagulability and one of the most serious complications of liver transplantation is vascular thrombosis [36]. Deficiencies of antithrombin III and protein C may create a prothrombotic state after liver transplantation and contribute to the risk of intravascular thrombosis [10]. Early detection of this hypercoagulable state is important in the prevention of thrombotic complications. In 1979 Peck evaluated viscoelastic measurements for detection of hypercoagulable states and compared SCT with other laboratory tests, including PT; thrombin generation test (TGT) and APTT. He reported a sensitivity of 57–100% detection for TGT compared with 64–67% using SCT. If both tests were used a sensitivity of 79–100% was achieved. From this he concluded that TGT and SCT were practical, rapid and useful for the detection and monitoring of the hypercoagulable state [26].

Platelet dysfunction and aspirin therapy

The value of low-dose aspirin in the prevention of myocardial infarction and stroke has been demonstrated conclusively, and this has resulted in increasing numbers of patients presenting for surgery
while receiving aspirin [2–4, 20]. Samra and colleagues studied the effect of aspirin on platelet function and the ability of SCT to identify those patients who develop significant prolongation of bleeding time after aspirin ingestion [31]. They found that SCT could not detect the effect of aspirin in normal volunteers whether or not they had marked prolongation of bleeding time. Even in patients with prolonged bleeding time but normal platelet counts, a normal SCT signature was observed. They concluded that SCT should be used in a larger study of patients with abnormal platelet function and normal platelet counts before the instrument could be assessed fully. Stern and colleagues found that clot retraction, measured by the down slope on the SCT signature, decreased significantly in patients re-ceiving aspirin, compared with those not receiving aspirin therapy, after cardiopulmonary bypass. However, the values for both groups remained in the normal range and the altered platelet function detection by SCT was not clinically significant [37].

**Other uses of Sonoclot**

Blifield, Courtney and Grass [1] studied platelet function in neonates and found that normal neonates have shorter SonACT times and steeper slopes than those of the normal adult. Blood samples obtained from sick neonates suggested that this group of patients have diminished coagulation and platelet function. They concluded that SCT provided more meaningful results in the assessment of platelet function than conventional coagulation tests. However, LaForce and co-workers [19] concluded that the coefficients of variability for R1, R2 and R3 were so great that SCT could not be recommended for quantitative evaluation of platelet activity in a neonatal population. SCT has also been used as a preoperative coagulation screening test; to assess the efficacy of treatment of factor VIII deficiency; in cases of altered blood viscosity, for example in polycythaemia; and in treating dysfibrinogenemias [8, 32, 33].

**Conclusion**

Assessment of perioperative bleeding disorders, especially those related to platelet dysfunction, remains a clinical challenge. The management of the bleeding patient in the operating theatre or on the postoperative ward is often empirical with little scientific basis. Much of the reason for this is that conventional cloting studies are not immediately available and there is a perceived urgency, particularly among trainee doctors, to treat bleeding disorders without first establishing the exact nature of the coagulopathy.

SCT provides useful information on platelet function, particularly in patients after cardiopulmonary bypass, and has enabled practitioners to rationalize the management of bleeding disorders and not expose their patients to the risks of unnecessary transfusion of blood products. Undoubtedly further studies are required before this instrument can be used reliably in the clinical setting but it may prove to be a useful addition to the available techniques for monitoring perioperative bleeding disorders.

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**References**


