Perioperative thromboelastography and sonoclot analysis in morbidly obese patients

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Purpose: To investigate perioperative coagulation in morbidly obese (MO) patients with the thromboelastograph (TEG) and Sonoclot analyzer.

Methods: Twenty-six consecutive morbidly obese and 26 consecutive lean patients presenting for elective surgery were enrolled in this prospective, observational study. Blood was sampled for TEG and Sonoclot analysis immediately after anaesthetic induction and at the end of surgery in the MO group, and immediately after anaesthetic induction in the lean group. The R and K times, alpha angle, maximum amplitude and percentage fibrinolysis at 30 and 60 min were recorded from the TEG. The Sonoclot ACT, initial clot rate, peak amplitude and time to peak amplitude were recorded from the Sonoclot.

Results: The TEG in the MO group demonstrated decreased R and K times (8.6 ± 4.8 *vs* 11.7 ± 3.9 mm, and 2.8 ± 1.2 *vs* 3.5 ± 0.9 mm respectively ($P < 0.05$)), and increased alpha angle (73.7 ± 6.0 *vs* 66.7 ± 6.0°, $P < 0.05$) and maximum amplitude (72.0 ± 5.4 *vs* 67.9 ± 4.4 mm, $P < 0.05$), without change in fibrinolysis. Sonoclot variables in the MO group included increased clot rate (37.5 ± 11.5 *vs* 23.9 ± 7.7%, $P < 0.05$) and decreased time to peak impedance (11.7 ± 5.0 *vs* 17.5 ± 7.2 min, $P < 0.05$), without change in Sonoclot ACT or peak signature impedance.

Conclusion: The MO group demonstrated accelerated fibrin formation, fibrinogen-platelet interaction, and platelet function compared with lean controls but no difference in fibrinolysis. Viscoelastic measures of coagulation may be useful in MO patients, who are at increased risk of thromboembolic events.

Objectif : Examiner le bilan hémostatique de patients pathologiquement obèses par thromboélastographie (TÉG) et analyse Sonoclot.

Méthodes : Consécutivement, 26 sujets obèses pathologiques (OP) et 26 sujets maigres programmés pour une chirurgie élective ont participé à cette étude prospective et observationnelle. Chez les obèses, du sang a été prélevé pour l'analyse par TÉG et par Sonoclot immédiatement après l'induction de l'anesthésie et à la fin de la chirurgie et, chez les sujets maigres, immédiatement après l'induction. Les temps R et K, l'angle alpha, l'amplitude maximale et le pourcentage de fibrinolyse à 30 et 60 min ont été enregistrés par TÉG. L'ACT, la vitesse initiale de formation du caillot, l'amplitude maximale et le temps d'amplitude maximale ont été enregistrés au Sonoclot.

Résultats : Dans le groupe OP, la TÉG a révélé une baisse des temps R et K (respectivement 8,6 ± 4,8 *vs* 11,7 ± 3,9 mm et 2,8 ± 1,2 *vs* 3,5 ± 0,9 mm, $P < 0,05$) et une augmentation de l'angle alpha (73,7 ± 6,0 *vs* 66,7 ± 6,0°, $P < 0,05$) et de l'amplitude maximale (72,0 ± 5,4 *vs* 67,9 ± 4,4 mm, $P < 0,05$) sans changement fibrinolytique. Au Sonoclot, dans le groupe OP, on observait une augmentation de la vitesse de formation du caillot (37,5 ± 11,5 *vs* 23,9 ± 7,7%, $P < 0,05$) et une diminution du temps d'impédance maximale (11,7 ± 0,5 *vs* 17,5 ± 7,2 min, $P < 0,05$) sans changement à l'ACT Sonoclot ou à l'impédance maximale de signature.

Conclusion : Dans groupe OP, la formation de fibrine, l'interaction fibrinogène-plaquettes et la fonction plaquettaire sont accélérées comparativement aux contrôles maigres alors que la fibrinolyse est identique. Les mesures viscoélastiques de la coagulation peuvent être utiles chez les obèses pathologiques qui sont à risque d'accidents thromboemboliques.

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OBESITY may be a risk factor contributing to an increased incidence of post-operative deep vein thrombosis (DVT) and pulmonary embolus (PE) than in non-obese patients.[1] Decreased fibrinolysis and increased fibrinogen concentration have been identified as risk factors for thromboembolic events in obese patients.[2,3] Epidemiological studies have also demonstrated increased plasminogen activator inhibitor (PAI) activity in obese patients.[4]

The thromboelastograph (TEG) and Sonoclot devices are visco-elastic measures of whole blood coagulation and fibrinolysis that have influenced perioperative coagulation monitoring and therapy during cardiopulmonary bypass, orthotopic liver transplantation, and in patients with qualitative platelet dysfunction.[5,6] As there are few data on perioperative coagulation profiles in morbidly obese (MO) patients, our aim was to compare the TEG and the Sonoclot in surgical MO patients with those of lean controls. This investigation of global coagulation with instruments that are accessible to anaesthetists may be more practical for perioperative monitoring than isolated laboratory indices of coagulation and fibrinolysis. Establishment of normal ranges for TEG and Sonoclot variables for the MO population would assist interpretation of traces in patients whose coagulation and fibrinolysis may differ from lean patients.

Methods

After institutional approval by the Committee for the Protection of Human Subjects and informed patient consent, 26 consecutive MO patients presenting for elective surgery (gynaecological, peripheral orthopaedic, or abdominal wall) were enrolled. Patients presenting for cardiac, vascular surgery, or any procedure with a large anticipated blood loss were excluded. Morbid obesity was defined as a body mass index (BMI) > 35 $kg \cdot m^{-2}$. Preoperative haematocrit, prothrombin and partial thromboplastin times and platelet count were recorded. Patients with a coagulation defect or receiving anticoagulant therapy were not included. Twenty-six consecutive lean patients (BMI < 28 $kg \cdot m^{-2}$) were enrolled in the control group.

Immediately after anaesthetic induction, 1.5 ml blood was sampled from an antecubital vein with a two-syringe technique in both groups. Sampling was repeated after completion of surgery before awakening, in the MO group. Blood was subjected to TEG and Sonoclot analysis within two minutes. One ml blood was added to a tube containing celite 1% (Haemoscope Corp., Skokie, IL), mixed by inversion, incubated for two minutes, and 0.36 ml withdrawn for insertion into a plastic thromboelastograph cuvette. The TEG (Haemoscope Corp., Skokie, IL) underwent daily quality control (QC) testing. Recorded indices included R time (mm), K time (mm), alpha angle (degrees), maximum amplitude (MA- mm), and % fibrinolysis at 30 and 60 min.

For Sonoclot analysis (Sienco, Inc., Morrison, CO), 0.36 ml native blood was added to a cuvette, and a plastic probe immersed by lowering the head of the analyzer. Daily QC testing was performed for the duration of the study. Recorded indices included the Sonoclot activated clotting time (SonACT), initial rate of clot formation (%), peak amplitude (mm) and time to peak amplitude (min) of the signature.

Variables were recorded as mean ± standard deviation. Power analysis to predict a 25% increase in coagulability in the MO group, with an alpha error of 0.05 and a beta error of 0.1, predicted a required sample size of 25. The TEG and Sonoclot variables were compared by analysis of variance for between groups and within group differences, and laboratory and demographic data were compared with a two-tailed t test. Significance was assumed with $P < 0.05$.

Results

Both the MO and control groups were comparable with respect to demographic data except for the differences in weight and BMI. There were no differences in preoperative laboratory measures of coagulation (PT, PTT, or platelet count) (Table I).

The TEG data revealed shorter R and K times ($P < 0.05$), and increased alpha angle and maximum amplitude ($P < 0.05$) in the MO group than in the control group. There were no differences in percentage fibrinolysis, and no difference between the 'initial' and 'end' measurements in MO patients (Table II).

TABLE I Patient and laboratory data

	Morbid obese (26)	*Control (26)*
Male/Female	15/11	13/13
Age (yr)	42.9 ± 12.0	38.6 ± 10.4
Height (m)	1.72 ± 0.1	1.73 ± 0.1
Weight (kg)	122.4 ± 22.6*	72.4 ± 10.6
Body mass index ($kg \cdot m^{-2}$)	43.2 ± 5.4*	24.3 ± 2.9
Haematocrit (%)	39.5 ± 4.9	38.9 ± 3.4
Prothrombin time (sec)	12.6 ± 0.8	12.3 ± 0.3
Partial thromboplastin time (sec)	29.5 ± 4.8	30.4 ± 4.9
Platelet count ($10^3 \cdot mm^{-3}$)	266.4 ± 68.9	259.6 ± 80.1

*$P < 0.05$
Mean ± SD

The MO groups had an increased initial rate of clot formation ($P < 0.05$), and a shortened time to peak impedance ($P < 0.05$) of the Sonoclot, compared with the control group. The SonACT and peak amplitude of the signature were not different from the control and there were no differences between the 'initial' and' end' MO groups (Table III).

Discussion

Obese patients have an increased incidence of postoperative DVT and PE.[1] Among the risk factors for the increased thromboembolism may be decreased fibrinolytic activity with increased fibrinogen concentrations.[2] Studies in the nonsurgical obese population have found increased plasminogen activator inhibitor (PAI) activity, possibly from PAI release from the increased mass of adipose tissue.[3,7] As measurements of laboratory indices of fibrinolysis such as PAI activity are impractical in the operating room, we investigated the application of visco-elastic measures of coagulation in this group of patients.

Anaesthetists are making increasing use of the TEG and the Sonoclot analyzer for perioperative coagulation assessment in patients undergoing cardiopulmonary bypass and liver transplantation, where multiple potential causes exist for haemostatic derangement.[5,6] The advantages of these immediately available, *in vitro* measures of whole blood clotting, which reflect initial fibrin formation through fibrinolysis, have been manifested as objective evidence for blood product utilization[8] and has guided appropriate antifibrinolytic therapy in a neurosurgical patient with accelerated fibrinolysis.[9] In addition, the clinical value of the TEG as a monitor of fibrinolysis (and antifibrinolytic therapy) has been confirmed for cardiopulmonary bypass procedures and liver transplant surgery.[10,11]

In this study, we found no differences in routine, discrete laboratory measurements of coagulation (PT, PTT and platelet count) in the MO patients. The Sonoclot ACT, which corresponds to the conventional ACT, was also not different, as would be expected in the presence of the similar PTT. However, there was evidence of accelerated fibrin formation, as assessed by the R time of the TEG and the initial gradient and time to peak of the primary Sonoclot signature. Fibrinogen-platelet interaction was also increased as assessed by the K time and alpha angle of the TEG and there was evidence of increased platelet function, with the increased MA of the TEG. These clinical results support previous laboratory studies documenting increased fibrinogen concentration in MO subjects[2,7] and the clinical appreciation of the increased risks of thromboembolism in this group.[1] The lack of any difference in the percentage fibrinolysis with the TEG in the MO group may suggest an imbalance in the face of the accelerated clot formation. These clinical data support recent laboratory evidence of increased PAI-1 activity and decreased fibrinolysis in obese subjects,[2-4] although in our study, global fibrinolytic activity was not decreased *per se* compared with lean control patients.

TABLE II Measured thromboelastographic variables

	Morbid obese (initial)	*Mordid obese (end)*	*Control*
R time (mm)	8.6 ± 4.8*	8.3 ± 4.2*	11.7 ± 3.9
K time (mm)	2.8 ± 1.2*	2.8 ± 1.3*	3.5 ± 0.9
Alpha angle (°)	73.7 ± 6.0*	72.0 ± 7.2*	66.7 ± 6.0
Maximum amplitude (mm)	72.0 ± 5.4*	72.0 ± 4.8*	67.9 ± 4.4
Fibrinolysis (% -30 min)	1.3 ± 0.9	1.2 ± 0.8	1.5 ± 0.8
Fibrinolysis (% -60 min)	4 ± 0.6	3.5 ± 1.1	4.2 ± 1.5

*$P < 0.05$ for morbid obese group *vs* control. NS difference between morbid obese groups
Mean ± SD

TABLE III Measured Sonoclot variables.

	Morbid obese (initial)	*Morbid obese (end)*	*Control*
SonACT (sec)	127.0 ± 28.2	122.8 ± 22.4	125.4 ± 25.6
Clot rate (%)	37.5 ± 11.5*	37.2 ± 11.1*	23.9 ± 7.7
Peak impedance (mm)	95.1 ± 11.3	97.5 ± 15.9	93.7 ± 22.1
Time to peak (min)	11.7 ± 5.0*	12.4 ± 4.1*	17.5 ± 7.2

*$P < 0.05$ for morbid obese group *vs* control. NS difference between morbid obese groups.
Mean ± SD

Although visco-elastic measures of coagulation do not assess the role of the endotheluim in the clotting process, the interaction of fibrin, fibrinogen, and platelets that is displayed is more reflective of *in vivo* conditions than are routinely performed laboratory tests that assess the time to fibrin formation only. As such, there is accumulating evidence for the clinical application of these monitors of coagulation as a guide to treatment in the perioperative period.[5,8,10,11]

As acceleration of the coagulation process may occur with the stress of major surgery as measured by the ACT[12] and the TEG,[13] our initial sample was taken after anesthetic induction, before surgical incision. Although the stress of anesthetic induction may have affected visco-elastic patterns, sampling was timed similarly in both groups to avoid bias. Previous TEG evidence of increased coagulability has been documented on post-operative days 1–3 in patients undergoing major abdominal aortic surgery,[13] and the ACT has been shown to decrease with the additional stresses of surgical incision and subsequent sternotomy in cardiac surgical patients.[12] Our original protocol did not call for re-evaluation of the TEG or Sonoclot in the control group. While the lack of any difference in the end-surgery values of the MO group was surprising, the absence of postoperative data in the control group, or extension of testing into the postoperative period precludes further discussion of the postoperative course in the MO group. Our results may be a reflection of the smaller magnitude of surgical stress, as we excluded patients presenting for cardiac, vascular or major procedures with a significant anticipated blood loss.

In this initial study of perioperative viscoelastic measurement of coagulation in MO patients, we have demonstrated hypercoagulability compared with lean controls, without an increase in fibrinolysis. This suggests that published values for normal patients may not reflect appropriate coagulation in MO patients, as with viscoelastic parameters in parturients.[14] This application of the TEG and Sonoclot device may be useful for perioperative monitoring and treatment of MO patients with their increased risk of venous thromboembolic complications especially in light of a recent recommendation that thromboembolic prophylaxis be a part of routine anaesthetic preoperative assessment[15]

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