

# The Effect of Anesthetic Techniques on Blood Coagulability in Parturients as Measured by Thromboelastography

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Anesthetic techniques may affect blood coagulability and the subsequent incidence of thromboembolic events. The purpose of this study was to evaluate the effect of spinal and general anesthesia on blood coagulability in normal pregnant women undergoing cesarean section, using thromboelastography. In the spinal anesthesia group ( $n = 15$ ), thromboelastography was performed after crystalloid preloading and during the immediate postanesthesia course. In the general anesthesia group ( $n = 15$ ), thromboelastography was performed before induction and during the immediate postanesthesia course. Values for all thromboelastographic variables (reaction time [r], clot formation time [K], coagulation time [rK], maximum amplitude [MA], elastic shear modulus [G], clot formation rate [ $\alpha$  angle],

and coagulation index [CI]) in the preanesthesia period were similar in both the spinal and general anesthesia groups. However, in the postanesthesia period, r and K significantly decreased ( $P < 0.05$ ), and  $\alpha$  angle ( $P < 0.05$ ) and CI significantly increased ( $P < 0.01$ ) in the general anesthesia group when compared with the spinal anesthesia group. In the postanesthesia period, MA and G were similar in both groups. In the spinal anesthesia group, thromboelastographic variables did not change significantly in the postanesthesia compared with the preanesthesia period. We conclude that the use of general anesthesia for cesarean section is associated with accelerated coagulability when compared with spinal anesthesia.

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**T**hromboelastography (TEG) provides an effective and convenient means of monitoring whole blood coagulation. It has been used to assess changes in blood coagulation during liver transplantation, cardiac bypass surgery, and obstetric hemorrhage (1-4). It evaluates the elastic properties of whole blood and provides information concerning hypocoagulability (1-5) as well as hypercoagulability (6-8).

Pregnancy, a hypercoagulable state, is associated with a high risk of thromboembolic complications that is further increased by cesarean delivery. Anesthetic techniques and anesthetic-related events may also have an effect on blood coagulability and the subsequent incidence of thromboembolic events in the postanesthesia period (9-11). Stress produced by tracheal intubation during general anesthesia has been associated with the release of catecholamines (12,13), which, in turn, have a stimulatory effect on platelet aggregation and hence may accelerate blood coagulation (14).

On the other hand, the use of regional anesthesia has been associated with a decreased incidence of deep vein thrombosis (9-11). The purpose of this study was to evaluate the effect of spinal and general anesthesia on blood coagulability in normal pregnant women undergoing cesarean section using TEG.

## Methods

After institutional approval, informed consent to collect blood samples for TEG analysis was obtained from 30 healthy women presenting for elective cesarean delivery under either general or spinal anesthesia. Women who had a history of coagulation disorders, who had preeclampsia, who were receiving magnesium therapy, or who were receiving aspirin or heparin therapy were excluded from the study. All patients received premedication with sodium citrate 30 mL *per os* and metaclopramide 10 mg intravenously (IV).

After 3 min of preoxygenation, women requesting general anesthesia ( $n = 15$ ) underwent rapid sequence induction with thiopental 5 mg/kg IV and tracheal intubation after muscle paralysis with succinylcholine 1.5 mg/kg IV. Anesthesia was maintained using isoflurane 1% in combination with N<sub>2</sub>O 50% in O<sub>2</sub> and a fresh gas flow of 6 L/min. After delivery, fresh gas

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flow was reduced to 3 L/min (N<sub>2</sub>O 2 L:O<sub>2</sub> 1 L), and isoflurane was maintained at 0.5% throughout the operation. Intraoperative analgesia was provided using fentanyl 2-3 µg/kg IV and morphine 0.15-0.2 mg/kg. Muscle relaxation was maintained using atracurium 10-20 mg IV as required, and residual neuromuscular block was reversed after closure of the facial layers, using neostigmine 0.02-0.04 mg/kg IV and glycopyrolate 0.01 mg/kg. When the patient was able to follow simple commands, the trachea was extubated. The patient was then transferred to the post-anesthesia care unit (PACU). Analgesia in the immediate postoperative period was provided according to the patient's requirement using bolus doses of morphine sulphate 5 mg IV.

In parturients requesting spinal anesthesia ( $n = 15$ ), after an IV infusion of 1000 mL of lactated Ringer's solution, a 25-gauge Whitacre spinal needle was inserted at the L2-3 or L3-4 interspace in the sitting position, and 1.5 mL of 0.75% bupivacaine in 8.25% dextrose with 10 µg of fentanyl was injected into the subarachnoid space. After intrathecal injection, the patient was placed in a supine position with left uterine displacement. Maternal hypotension was treated with bolus doses of ephedrine 5-10 mg IV.

TEG was performed using a computerized Thromboelastograph® (Haemoscope Corp., Skokie, IL) using disposable plastic cups and pins and native whole blood. In the spinal anesthesia group, TEG was performed after crystalloid preloading and in the PACU in the immediate postanesthesia period. In the general anesthesia group, TEG was performed before induction and in the PACU in the immediate postanesthesia period. Blood was collected from a peripheral vein via an 18-gauge needle using a two-syringe technique. The first sample was discarded to avoid tissue contamination of blood, while the second sample was used for TEG measurements and other laboratory tests. Three hundred sixty microliters of whole blood was pipetted into a disposable plastic cup within 4 min of blood sampling and then placed in a prewarmed (37°C) thromboelastograph, which was allowed to run until maximum amplitude of the TEG tracing (MA) could be determined.

TEG variables collected from the computer screen included  $r$  (reaction time),  $K$  (clot formation time),  $rK$  (coagulation time),  $MA$ ,  $\alpha$  angle (clot formation rate), and a TEG coagulation index (CI). A TEG CI is derived from a simple linear equation that combines all the TEG variables (native whole blood  $CI = -(0.1227)r + (0.0092)K + (0.1655)MA - (0.041)\alpha - 5.0220$ , normal range for nonpregnant women +2 to -2) (7,8). The elastic shear modulus ( $G$ ) in dynes per centimeter squared was derived from  $MA (5000 \cdot MA / 100 - MA)$  (15). Other laboratory tests performed in all women included a preanesthesia and postanesthesia hematocrit,

**Table 1.** Demographic Characteristics and Intraoperative Data

	Spinal anesthesia ( $n = 15$ )	General anesthesia ( $n = 15$ )
Age (yr)	24 ± 4	25 ± 3
Weight (lb)	166 ± 40	170 ± 46
Height (in.)	62 ± 3	64 ± 2
Gestational age (wk)	39 ± 1	38 ± 2
Surgical time (min)	58.4 ± 13.5	61 ± 18.6
IV fluid (mL)	2230 ± 250	2260 ± 30

Data are expressed as mean ± SD.  
IV = intravenous.

a platelet count, prothrombin time, activated partial thromboplastin time, and fibrinogen concentration.

All data were expressed as mean ± SD. Statistical analyses were performed using the SAS (SAS Institute, Cary, NC) statistical package. Student's  $t$ -test was used for the comparison of demographic data between the two groups. The TEG and laboratory data were analysed using Wilcoxon rank sum test or Wilcoxon signed rank test as indicated. All tests were two-sided, and a  $P$  value ≤ 0.05 was considered significant.

## Results

Demographic characteristics (age, weight, height, and gestational age) were similar in the spinal anesthesia and general anesthesia groups (Table 1). There was no difference in the duration of surgery and the amount of maintenance fluid received during the surgical period between the two groups (Table 1). The amount of blood loss was within the normal range (750-1000 mL) in all patients.

The values for all TEG variables ( $r$ ,  $K$ ,  $rK$ ,  $MA$ ,  $G$ ,  $\alpha$  angle, and  $CI$ ) were similar in the preanesthesia period in the two study groups. However, in the postanesthesia period, the values for  $r$  and  $K$  significantly decreased ( $P < 0.05$ ), and the values for  $\alpha$  angle ( $P < 0.05$ ) and  $CI$  ( $P < 0.01$ ) significantly increased in the general anesthesia group when compared with the spinal anesthesia group (Table 2, Figure 1). The values for  $MA$  and  $G$  in the postanesthesia period were similar in both groups. Comparison within the groups also showed a significant decrease in the values for  $r$  and  $K$  ( $P < 0.01$ ) and a significant increase in the values for  $\alpha$  angle ( $P < 0.01$ ) and  $CI$  ( $P < 0.01$ ) in the postanesthesia period compared with the preanesthesia period in the general anesthesia group (Table 2, Figure 1). In the spinal anesthesia group, the values for TEG variables did not change significantly in the postanesthesia period compared with the preanesthesia period. The mean coagulation time (i.e.,  $rK$  time) was significantly reduced from 20 min in the preanesthesia period to 13.7 min ( $P < 0.01$ ) in the postanesthesia period in the general anesthesia group, compared

Table 2. Thromboelastographic Variables

	Spinal anesthesia (n = 15)			General anesthesia (n = 15)		
	Preanesthesia	Postanesthesia	P value	Preanesthesia	Postanesthesia	P value
r (mm) <sup>a</sup>	26.6 ± 5.4	26.3 ± 5.8	0.71	28.6 ± 5	20.6 ± 6*	<0.01
K (mm) <sup>a</sup>	10.9 ± 2.6	9.2 ± 2.8	0.16	11.5 ± 3.2	6.9 ± 2.1*	<0.01
rK (min) <sup>a</sup>	18.7 ± 3.1	17.6 ± 3.2	0.26	20 ± 3	13.7 ± 3.6*	<0.01
MA (mm)	66.3 ± 6.1	64.8 ± 6.6	0.35	67.1 ± 7.5	67.2 ± 4.3	0.86
G (1000·dyn <sup>-1</sup> ·cm <sup>-2</sup> )	10.4 ± 3.1	9.7 ± 3.0	0.27	11.0 ± 4.1	10.5 ± 2.2	0.48
α angle (°)	40.3 ± 6.4	43.3 ± 5.8	0.41	39.5 ± 7.6	50.8 ± 12.1	<0.01

Values are mean ± sd.

r = reaction time, K = clot formation time, rK = r + K time, G = shear elastic modulus in dyn per centimeters squared (5000·MA/100-MA), angle = clot formation rate, MA = maximum amplitude.

<sup>a</sup> All measurements are recorded at 2 mm/min speed and can be converted to minutes by multiplying the value in millimeters by 0.5.

\* P < 0.05 compared with postanesthesia in the spinal anesthesia group.

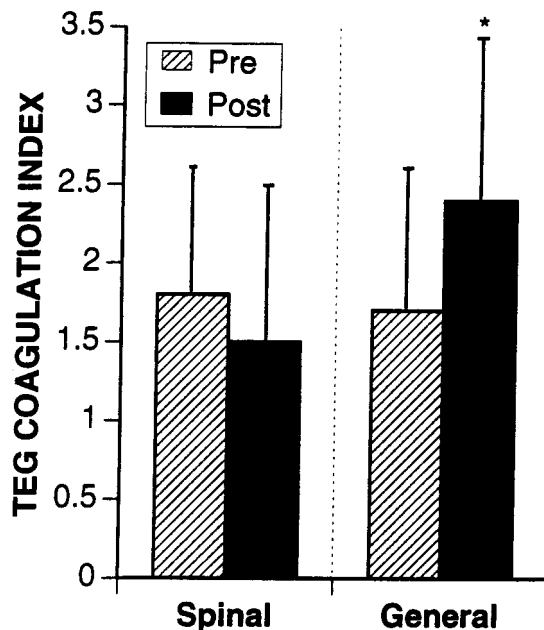


Figure 1. Changes in the computerized thromboelastographic (TEG) coagulation index in women undergoing cesarean section. Values are expressed as mean ± sd. Spinal anesthesia P = 0.43, general anesthesia \*P < 0.01, preanesthesia (pre) versus postanesthesia (post) period.

with 18.7 min to 17.6 min (P = 0.26) in the spinal anesthesia group (Table 2).

The hematocrit and platelet counts were significantly decreased in the postanesthesia period compared with the preanesthesia period in both groups (P ≤ 0.01) (Table 3). There were no significant differences in the prothrombin time, partial thromboplastin time, and fibrinogen concentrations in the preanesthesia and postanesthesia periods between the study groups (Table 3).

### Discussion

TEG has been used to assess hypocoagulability as well as hypercoagulability of whole blood (1-8). The prin-

ciple and interpretation of TEG is well described in the literature (15,16). Individual TEG variables from a thromboelastogram (a graphic display of the stages in the formation of a whole blood clot) include r, which indicates clotting factor activity, K, MA, which reflects clot strength; and α angle, which indicates platelet and fibrinogen activity. G is related to MA and indicates clot strength in dynes per centimeter squared (15). To reflect all activities of the clotting factors, platelets, and fibrinogen that contribute to whole blood coagulation in a composite fashion, a computerized TEG CI can be derived from r, K, MA, and α angle using a simple linear equation to combine all the TEG variables. Since it combines all the variables from a thromboelastogram, a CI reflects the overall coagulability of blood (7,8). This index might represent a valuable way of reporting and applying TEG data, if it is validated before it is applied clinically. Normal values for CI in nonpregnant women for native whole blood, using disposable cups and pins, range from +2 to -2 (8). Outside this range, a more positive value would reflect greater hypercoagulability, while a more negative value would reflect greater hypocoagulability.

Using TEG, our study shows that general anesthesia is associated with a decrease in coagulation time by 30%, an increase in the speed of clot formation by 25%, and no change in clot strength. This was reflected in the postanesthesia period in the general anesthesia group by the following: a decrease in r and K time, reflecting increased clotting factor and platelet activity, an increase in α angle, reflecting an increased speed in clot formation, and no change in MA and G, reflecting no change in clot strength. This reflects accelerated blood coagulability with no change in final clot strength. This implies that general anesthesia might cause blood to clot more readily without having any effect on the strength of the final clot that is formed.

Clinical (17) and animal (18) studies have demonstrated that blood is hypercoagulable during stress. This is due to the release of catecholamines during

Table 3. Laboratory Data

	Spinal anesthesia (n = 15)		General anesthesia (n = 15)	
	Preanesthesia	Postanesthesia	Preanesthesia	Postanesthesia
Hematocrit (%)	37.0 ± 3.8	32.8 ± 3.6*	34.5 ± 3.7	31.1 ± 4.2*
PC (10 <sup>3</sup> /mm <sup>3</sup> )	232 ± 62	205 ± 53*	234 ± 21	212 ± 27*
aPTT (s)	30 ± 2.9	31.4 ± 4.2	29.6 ± 3.4	31.8 ± 3.2
PT (s)	11.1 ± 0.8	11.3 ± 0.6	11.2 ± 1.1	11.5 ± 0.8
Fibrinogen (mg%) <sup>a</sup>	422 ± 66	397 ± 53	408 ± 40	393 ± 43

Values are mean ± SD.

PC = platelet count (normal range 140–450 × 10<sup>3</sup>/mm<sup>3</sup>), aPTT = activated partial thromboplastin time (normal range 25–38 s), PT = prothrombin time (normal range 11–13 s).

<sup>a</sup> Normal range 148–400 mg%.

\* P < 0.01 postanesthesia versus preanesthesia.

stress, which have a stimulatory effect on platelet aggregation, which, in turn, contributes to accelerated coagulability (14). Tracheal intubation during general anesthesia in normal and high-risk parturients has been associated with significant stress and release of catecholamines (12,13). This can have a stimulatory effect on platelet aggregation, which, in turn, may contribute to accelerated coagulability, as demonstrated in our study. Increased stress is likely during extubation, as well as in the immediate postoperative period, due to pain.

Studies have shown that the use of inhaled anesthetics during general anesthesia is associated with a suppressive effect on platelet aggregation, which, in turn, may impair coagulation (19). In our study, however, it is likely that the degree of stress and associated elevation in serum catecholamine levels during general anesthesia offset any hypocoagulable tendency resulting from the use of inhaled anesthetics during general anesthesia. Tuman et al. (5) demonstrated a decrease in coagulation activity in nonpregnant patients immediately after the induction of general anesthesia. However, their use of opioids with induction of general anesthesia in their patients may have contributed to reduced stress and lower catecholamine levels during intubation and subsequent hypocoagulability. In our study, we did not use opioids during rapid-sequence induction of general anesthesia. It is possible that the use of lidocaine or  $\beta$ -blockers before intubation, a practice not routinely employed might have reduced the accelerated coagulation response.

Regional anesthesia has been associated with a reduced incidence of thromboembolic events (9–11). This beneficial effect may be attributed to reduced intraoperative catecholamine release during regional anesthesia and better pain relief during the immediate postoperative period due to the residual spinal anesthetic blockade. Local anesthetics have been shown to have an inhibitory action on platelet aggregation (20). However, the amount of local anesthetic used for intrathecal injection is too small to affect blood coagulation. *In*

*vivo* and (5) *in vitro* (21) studies of hemodilution with crystalloid have demonstrated hypercoagulability. For these reasons, in the spinal anesthesia group, TEG was performed after crystalloid preloading so as to eliminate the effects of a crystalloid preload. However, in our study, there was no difference in the preanesthesia TEG variables between the spinal and general anesthesia group, which suggests that hemodilution with 1000 mL of crystalloid solution prior to spinal anesthesia does not increase coagulation activity in parturients.

In contrast to the accelerated coagulability reflected by TEG variables in the general anesthesia group, there was no difference in the results of the coagulation profile between the pre- and postanesthesia periods in the general anesthesia group. This lack of similarity between TEG results and results of a coagulation profile can be explained by the fact that TEG variables are interrelated and collectively reflect activities of clotting factors, platelets, and fibrinogen, and their interaction (22,23), while a coagulation profile monitors an isolated portion of the coagulation cascade and does not reflect the interaction among clotting factors, platelets, and fibrinogen. Therefore, a coagulation profile does not reliably monitor hypercoagulability, whereas TEG is sensitive in detecting such changes (23).

In conclusion, this study suggests that the use of general anesthesia for cesarean section, when compared with spinal anesthesia, accelerates blood coagulability in the immediate postoperative period but has no effect on the final clot strength. Pregnancy itself is a hypercoagulable state that results in a fivefold to sixfold increase in the relative risk of thromboembolism compared with nonpregnant women (24). Cesarean delivery further increases the risk of thromboembolism (25). Therefore, further investigations are warranted to determine whether this acceleration of coagulation in women undergoing cesarean section under general anesthesia has any clinical implication in terms of increased frequency of postoperative thromboembolic complications.

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