Coagulopathies in Patients After Transurethral Resection of the Prostate: Spinal Versus General Anesthesia

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This prospective, randomized study evaluated the effects of spinal versus general anesthetic technique on perioperative blood loss and the development of postoperative coagulopathies in 50 patients undergoing transurethral resection of the prostate (TURP). Preoperative hematologic measurements included hemoglobin, platelet count, electrolytes, prothrombin time, partial thromboplastin time, fibrinogen, factor V, plasminogen, antithrombin III, and fibrinogen degradation product (FDP) levels. All hematologic blood samples were repeated postoperatively at 1, 6, and 24 h. Intraoperative blood loss was not significantly different between the spinal and general anesthesia groups. The total blood loss after TURP was significantly correlated ($r = 0.76$; $P < 0.0001$) with the prostatic tissue weight. When the tissue weight resected exceeded 35 g, blood loss was in excess of the linear correlation shown with the weight of resected prostatic tissue. Platelet count decreased and prothrombin time increased in the spinal group at all postoperative time intervals compared to preoperative value ($P < 0.05$). There was no significant difference in measured coagulation variables (fibrinogen, factor V, plasminogen, antithrombin III, and FDP) between the spinal and general anesthesia groups, but there were significant decreases in postoperative fibrinogen and Factor V levels compared to preoperative values in both spinal and general anesthesia groups. Three patients (6%) had increased FDP levels 1 h postoperatively. The prostatic tissue weight and the surgical duration was significantly higher in these patients. We conclude that perioperative blood loss in TURP patients is not affected by the anesthetic technique. However, 6% of TURP patients developed subclinical intravascular coagulopathies which correlated with mass of resected prostate tissue.

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Surgeons performing a transurethral prostatectomy use a modified cystoscope to remove tissue and coagulate bleeding vessels (1). Significant bleeding frequently occurs after transurethral resection of the prostate (TURP). Although when compared to general anesthesia, epidural and spinal anesthesia reduce the incidence of postoperative thromboembolism (2–4) and blood loss (5) after lower limb surgery, the influence of these anesthetic techniques on blood loss during and after TURP remains controversial (6,7).

The etiology of perioperative bleeding in TURP may result from proteolytic enzymes released from prostatic tissue (8,9). Visual estimation of blood loss during TURP is grossly inaccurate (10). There is also controversy concerning the relationship between the anesthetic technique and blood loss in TURP surgery. Some authors have reported less bleeding under epidural anesthesia (7,11), whereas others found no difference in blood loss between epidural and general anesthesia (6,12,13). There has been no prospective randomized study evaluating the influence of anesthetic technique on perioperative coagulopathies in TURP patients. The aim of this prospective, randomized clinical study is to evaluate the effect of spinal and general anesthesia on perioperative blood loss and postoperative coagulopathy in patients undergoing TURP.

Methods

After institutional ethics committee approval and informed consent, 50 patients undergoing TURP were prospectively randomized by computer-generated numbers to receive either spinal or general anesthesia. All patients were ASA classification I or II and over the age of 60 yr. Exclusion criteria included previous prostate surgery, contraindications to spinal anesthesia, existing coagulopathy, anemia, and on antiplatelet or anticoagulation therapy within 7 days of surgery. None of the patients had indwelling bladder catheters inserted before their surgery.

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On arrival to the operating room, all patients were monitored as per standard anesthetic practice for electrocardiogram, blood pressure, and oxygen saturation. General anesthesia was performed using fentanyl, thiopental, vecuronium, and isoflurane with positive pressure ventilation. Spinal anesthesia was performed aseptically using a 25-gauge Quincke spinal needle and 50–75 mg of hyperbaric lidocaine. Preoperative hematologic measurements included hemoglobin, platelet count, electrolytes, blood urea nitrogen, creatinine, prothrombin time (PT), and partial thromboplastin time (PTT). Coagulation studies included fibrinogen, factor V, plasminogen, antithrombin III, and fibrinogen degradation product (FDP) levels. All hematologic and coagulation blood samples were repeated postoperatively at 1 h, 6 h, and 24 h.

A Stern-McCarthy 24-F resectoscope, suprapubic trocar, and a continuous irrigation system with glycine 1.5% were used. Resection to the prostatic capsule was attempted. For each patient the resected prostatic tissue weight and surgical duration were recorded. Surgical time was recorded from the introduction of the cystoscope to the insertion of the Foley catheter at the end of the operation.

Perioperative blood loss was calculated from spectrophotometrically measured urinary free hemoglobin using the technique described earlier by Desmond (8). All effluent irrigation fluid was collected intraoperatively and 1, 6, and 24 h postoperatively in buckets containing sodium citric acid to prevent coagulation of the blood. Exact blood loss was calculated from the urinary hemoglobin, blood hemoglobin, and the volume of the irrigant at each of the time intervals. The calculated blood loss was standardized for differences in surgical time and resected prostatic tissue weight by dividing the blood loss by the duration of surgery and resected prostatic tissue ($mL \cdot g^{-1} \cdot h^{-1}$). This allows for the fact that some operations took considerably longer than others and also the amount of prostate resected varied. All values are expressed as mean ± SD. Differences between groups (spinal versus general anesthesia) were determined using unpaired Student's *t*-tests for demographic and baseline variables. Spearman's rank correlation test was used to determine the predictive variable for blood loss after TURP. Differences within each group were determined using analysis of variance with repeated measures. The Pearson correlation coefficient test was used to detect significance for blood loss. All differences were considered significant if $P < 0.05$.

Results

There were no significant differences between the two groups in age, weight, surgical duration, prostate tissue resected weight, and pathology (Table 1). There was no significant difference in the measured blood loss ($mL \cdot g^{-1} \cdot h^{-1}$) between the two groups during any of the perioperative intervals (Fig. 1). Likewise, there was no significant difference in blood loss in patients with benign or malignant tumors (14.3 ± 9 vs 13.9 ± 12 $mL \cdot g^{-1} \cdot h^{-1}$, respectively). There was a significant correlation between the prostatic tissue resected with the intraoperative blood loss ($r = 0.75$; $P < 0.05$), and the 24-h total blood loss ($r = 0.76$; $P < 0.0001$) (Fig. 2). There was no significant correlation between the prostatic tissue resected and the surgical duration ($r = 0.63$). However, when the resected tissue exceeded 35 g, the blood loss and tissue weight were not linearly related.

Table 1. Patient Characteristics

	Anesthesia	
	General (n = 25)	Spinal (n = 25)
Age (yr)	70.2 ± 6	73.9 ± 9
Resected tissue weight (g)[a]	22.5 ± 18	19.8 ± 14
Surgical duration (min)	50.4 ± 23	47.8 ± 25
Malignant tumors	5 (25.0%)	6 (31.6%)

Values are mean ± SD. There was no significant difference between the groups.
[a] Resected tissue weight is the prostatic tissue removed during surgery.

Hematologic results (Table 2) showed a significant reduction in hemoglobin for both groups in all perioperative periods compared to preoperative values. At 24 h postoperatively, the percent reduction in hemoglobin was more pronounced in the general than in the spinal anesthetic group (−13.8% vs −9.2%). There was also a significant reduction in platelets and increased PT in the spinal group at all postoperative time intervals. At 24 h, platelets were reduced by 11.4% (general) and 16.0% (spinal); however, for both groups the absolute platelet count remained within the normal accepted range. The reduction in platelets cannot be explained by a dilutional effect as serum sodium did not change significantly during the same time periods (−2.2% general and −1.8% spinal, preoperatively to 24 h postoperatively). There were no changes in PTT for either group in any postoperative period.

Most measured coagulation variables showed significant reductions ($P < 0.05$) in both groups during the postoperative period (Table 3). By 24 h, however, levels of fibrinogen and factor V returned to preoperative levels. Postoperative levels of plasminogen and antithrombin III remain reduced 24 h postoperative. Despite the changes in the coagulation factors, all measured variables in each group were within the clinical normal range.

Three patients had FDP > 20 $\mu g/mL$ at 1 h postoperatively. All resected prostatic tissue from these patients was benign and two of these patients received general and one spinal anesthesia. In the FDP positive

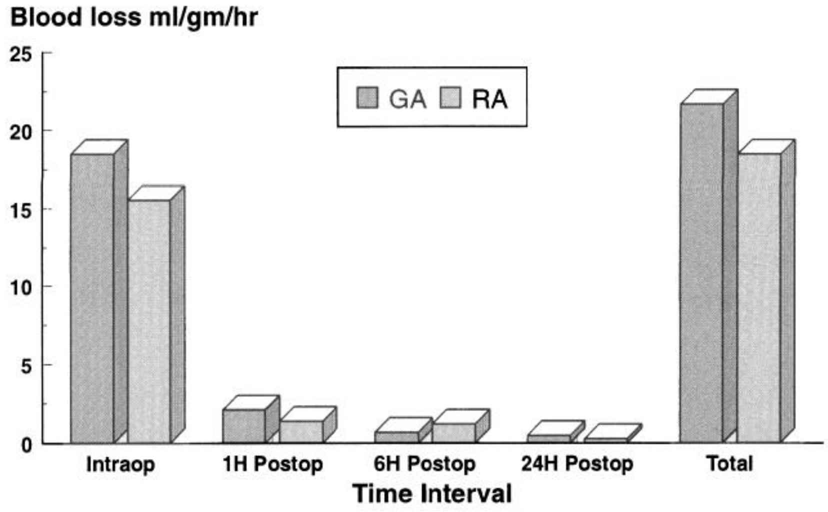

Figure 1. Perioperative blood loss for groups receiving regional anesthesia (RA) or general anesthesia (GA). Blood loss expressed as milliliters per gram per hour. Blood loss was assessed during the intraoperative (intraop) period and 1, 6, and 24 h postoperatively (Postop). The total blood loss included is the summation of the four measurements. Results are mean ± SD.

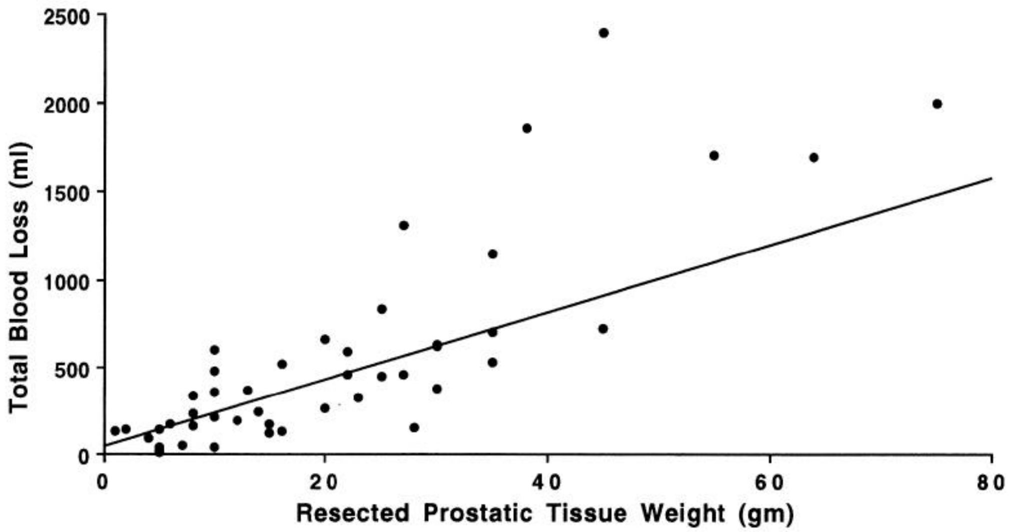

Figure 2. Perioperative blood loss for both groups of anesthesia versus prostatic resected tissue weight. The total blood loss included is the summation of the four variables. The correlation is $r = 0.76$ with the equation $y = 19.2x + 41.3$ (where y = blood loss and x = resected prostatic tissue weight).

versus the FDP negative groups, resected tissue weight was 54.7 ± 9 and 18.9 ± 14 g, and surgical duration was 95.0 ± 25 min and 45.5 ± 20 min, respectively. Intraoperative blood loss was also greater in these three patients (1291.2 ± 713 mL vs 270.3 ± 320 mL). These three patients also had a measured reduction of 28.9% in fibrinogen (g/L) from preoperative to 1 h postoperative (Table 4). One of these patients required postoperative transfusion of 2 U of packed red cells.

Discussion

The total blood loss after TURP was significantly correlated with the prostatic tissue weight and when the tissue weight exceeded 35 g, blood loss was out of proportion to the resected tissue weight. Six percent of patients had increased FDP levels at 1 h postoperatively and the prostatic tissue weight resected and the surgical duration was significantly higher in these patients.

The relationship between anesthetic technique and intraoperative blood loss remains controversial. In agreement with our data, Neilsen et al. (14) reported no significant difference in operative blood loss between epidural and general anesthesia groups undergoing TURP. The study by Neilsen et al. (14) did not evaluate changes in coagulation variables during TURP nor did they take detailed postoperative blood loss measurements. The authors also indicated a possible type II error due to the sample size. There were however, significant correlation's between operative blood loss, tissue weight, and surgical duration. Abrams et al. (7) reported greater blood loss in patients receiving general anesthesia compared to epidural for TURP. McGowan and Smith (6) showed that when ventilation was controlled, blood loss

Table 2. Hematologic data

Variable	Anesthesia	Preoperatively	Postoperatively 1 h	Postoperatively 6 h	Postoperatively 24 h
Hb (g/L)	General	138.3 ± 18	130.8 ± 18*	126.1 ± 17*	119.1 ± 19*†
	Spinal	142.6 ± 8	135.8 ± 15*	131.6 ± 16*	129.8 ± 15*
Platelets (× 10^9/mL)	General	244.7 ± 88	229.1 ± 67	232.0 ± 64	216.3 ± 60*
	Spinal	287.7 ± 78	257.5 ± 71*	268.6 ± 69*	241.7 ± 69*
PT (s)	General	10.6 ± 1	11.2 ± 1*	10.8 ± 1*	11.2 ± 1*
	Spinal	10.2 ± 1	11.0 ± 1*	11.0 ± 1*	10.7 ± 1*
PTT (s)	General	27.4 ± 2	27.3 ± 3	27.3 ± 3	27.1 ± 2
	Spinal	27.4 ± 3	28.1 ± 4	28.1 ± 3	28.2 ± 3

Values are mean ± SD.
Hb = hemoglobin; Platelets = platelet count; PT = prothrombin time; PTT = partial thromboplastin time.
* $P < 0.05$ compared to preoperatively.
† $P < 0.05$ between groups.

Table 3. Coagulation data

Variable	Normal value	Anesthesia	Preoperatively	Postoperatively 1 h	Postoperatively 6 h	Postoperatively 24 h
Factor V (μ/mL)	0.7–1.2	General	0.9 ± 0.2	0.8 ± 0.3*	0.7 ± 0.3*	0.9 ± 0.3
		Spinal	0.8 ± 0.3	0.8 ± 0.2	0.7 ± 0.2	0.8 ± 0.2
Fibrinogen (g/L)	1.5–3.5	General	3.1 ± 0.8	2.9 ± 0.8*	2.8 ± 0.8*	3.1 ± 0.8
		Spinal	3.2 ± 0.8	2.9 ± 0.7	2.8 ± 0.6*	3.2 ± 0.7
Plasminogen activity (μ/mL)	0.8–1.2	General	1.0 ± 0.2	0.9 ± 0.2*	0.8 ± 0.2*	0.9 ± 0.2*
		Spinal	1.0 ± 0.2	0.9 ± 0.2*	0.9 ± 0.2*	0.9 ± 0.2*
Plasminogen antigen (g/L)	0.06–0.2	General	0.11 ± .01	0.11 ± .01*	0.09 ± .01*	0.08 ± .01*
		Spinal	0.12 ± .01	0.09 ± .01*	0.10 ± .01*	0.09 ± .01*
Antithrombin III activity (μ/mL)	0.8–1.2	General	1.12 ± 0.2	1.00 ± .17*	0.99 ± .16*	0.96 ± .17*
		Spinal	1.10 ± 0.2	1.07 ± 0.3	0.99 ± 0.2	0.99 ± 0.2
Antithrombin III antigen (g/L)	0.22–0.39	General	0.30 ± 0.1	0.27 ± 0.1*	0.28 ± 0.1*	0.27 ± 0.1*
		Spinal	0.29 ± 0.1	0.28 ± 0.1*	0.27 ± 0.1*	0.27 ± 0.1*

Values are mean ± SD.
* $P < 0.05$ compared to preoperative.

was more than in spontaneously ventilated patients (0.27 $mL \cdot g^{-1} \cdot h^{-1}$, controlled; 0.24 $mL \cdot g^{-1} \cdot h^{-1}$, spontaneously ventilated), although, not statistically significant. Our (standardized) measurements of intraoperative blood loss for the two groups (18.5 $mL \cdot g^{-1} \cdot h^{-1}$ and 15.5 $mL \cdot g^{-1} \cdot h^{-1}$ for general and spinal anesthesia, respectively) are consistent with the findings by McGowen and Smith (6). Although not statistically significant, intraoperative and total blood loss tended to be higher in patients receiving general anesthesia.

The initial premise that regional anesthesia decreases venous pressure and reduces operative blood loss has not been a consistent finding (7,11). Decreasing venous pressure may be expected to increase postoperative blood loss as the reduced venous hydrostatic pressure would promote uptake of resected prostatic tissue into the open venous sinuses, providing the stimulus for fibrinolysis. Our results did not show higher blood loss in the postoperative period after spinal anesthesia and there were no significant differences in the measured coagulation variables between the two groups. Although there may have been more uptake of prostatic tissue, the quantity or the intrinsic fibrinolytic properties were insufficient to elicit defects in the coagulation pathways. There were small but significant reductions in coagulation variables in the postoperative period which were not explained by a dilutional effect. In both groups there was a significant increase in PT which is a measure of the extrinsic pathway of the coagulation cascade. There was a significant reduction in the plasminogen, factor V, and fibrinogen, which is measure of the common pathway of the coagulation cascade, but PTT remained unchanged. However, it is unlikely that these changes contributed to any residual bleeding as all levels remained within the normal accepted range. Betkurer et al. (15) measured various coagulation factors pre- and 24 h post-TURP and reported small but significant reductions in most of the measured variables.

Table 4. Fibrinogen Degradation Product (FDP) Positive and Negative Results

	FDP negative (n = 47)			FDP positive (n = 3)		
Coagulation variables	Preoperatively	1 h postoperatively	% Change	Preoperatively	1 h postoperatively	% Change
Platelets (× 10^9/mL)	262 ± 91	241 ± 74	−8.0	259 ± 81	224 ± 56	−13.5
PT (s)	10.1 ± 1	11.0 ± 1	6.0	10.2 ± 1	11.8 ± 1	16.0
PTT (s)	27.4 ± 3	27.5 ± 3	0.3	26.4 ± 3	33.1 ± 6	25.2
Factor V (μ/mL)	0.86 ± 0.3	0.81 ± 0.3	−5.4	0.91 ± 0.1	0.62 ± 0.2	−32.0
Fibrinogen (g/L)	3.2 ± 1	2.9 ± 1	−7.0	3.2 ± 0.9	2.3 ± 0.6	−28.9
Plasminogen (g/L)	0.11 ± 0.1	0.10 ± 0.1	−12.2	0.11 ± 0.1	0.07 ± 0.1	−38.9
Antithrombin III (μ/mL)	1.1 ± 0.2	1.1 ± 0.2	−2.6	0.9 ± 0.2	0.9 ± 0.1	−3.2

Values are mean ± SD. Negative values indicate a decrease in the coagulation factors whereas positive values indicate a prolongation of the coagulation factors and time.
Platelets = platelet count; PT = prothrombin time; PTT = partial thromboplastin time.

Our results indicate that there is a significant correlation between the prostatic tissue resected and the total blood loss. Similar results of positive correlation between the prostatic tissue and perioperative blood loss have been reported (16). In a large study of 417 cases, multiple regression analysis confirmed that bleeding was more closely related to prostate weight than to operating time and that operating time appears to be an iatrogenic factor in blood loss during TURP (17). Our results showed that when the resected prostate tissue exceeded 35 g, the total blood loss was in excess of the liner correlation shown with the weight of resected prostatic tissue. A study by Levin et al. (18) reached a similar conclusion that when the estimated weight of the prostate to be resected is less than 30 g, preoperative cross-matching should not be required but, if the predicted weight of the gland is greater than 30 g, 2–4 U of blood will probably be required for transfusion. In our study population, patients who had more than 35 g resected also had a tendency for developing disseminated intravascular coagulopathy (DIC).

Defects in the clotting mechanism involving the fibrinolytic system have been observed more often in patients undergoing surgery of the prostate than in patients subjected to other types of surgery (19). An imbalance of the delicate equilibrium between the active enzyme plasmin and its antagonist antiplasmin appears to be the cause. Plasmin, the enzyme that digests fibrinogen and fibrin, is found in the globulin fraction of blood as its inactive precursor, plasminogen. Antiplasmin, on the other hand, is contained in the albumin fraction. The transformation of plasminogen to plasmin can be affected in a restricted area by a local tissue activator, or, in a general manner by the entry into the circulation of several agents such as prostatic or pancreatic tissue. Activation of this anticoagulant system may also occur as a result of destruction or dilution of the circulating antiplasmin. Thus, reversal of the albumin/globulin ratio may upset the normal plasmin-antiplasmin ratio (19).

Changes in fibrinogen and FDP indicated the potential development of DIC. In our study, three patients (two general, one spinal) showed a clinical picture of coagulopathy. Patients that were FDP positive had a larger increase in PT and PTT compared to FDP negative patients. In addition, there were larger reductions in factor V, fibrinogen, and plasminogen whereas the platelet and antithrombin III levels did not differ from FDP negative patients. The hematologic changes due to primary fibrinolysis include a normal platelet count, antithrombin III with prolonged fibrinogen, factors V and VIII, and plasminogen (20). There are two ways by which intravascular consumption of clotting factors may be induced: DIC with or without secondary fibrinolysis, and primary fibrinolysis, which is a very rare event. In TURP, primary fibrinolysis is a possibility for induction of a coagulopathy syndrome because of the high content of proteolytic enzymes in the prostate. All resected tissue from the three patients showed benign hypertrophy. Duration of surgery was prolonged in these cases and the mean resected tissue weight was greater than the remainder of the study group.

The presence of prostatic cancer was not a significant factor in higher levels of perioperative blood loss. These findings are supported by retrospective analysis (21) of over 1600 patients with prostatic cancer and in a prospective study of 417 cases (19). It is known that there is a greater lytic activity in malignant tumors compared to benign prostatic tissue, but a prospective study by Betkurer et al. (15) demonstrated no difference in coagulation variables between the patients with benign or malignant tumors.

We conclude that perioperative blood loss in TURP patients is not affected by the regional or general anesthetic technique. The type of anesthetic, therefore, appears to be a matter of personal choice. However, the anesthesiologist should be aware that a small percent (6%) of TURP patients develop subclinical intravascular coagulopathy which is related to the mass of prostate tissue resected, and is more likely to occur if the resection is greater than 35 g.

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