

Alterations in antithrombin III activity and other blood coagulation parameters after retinal detachment surgery

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PURPOSE. *To evaluate perioperative changes in blood coagulation in patients undergoing retinal detachment surgery.*

MATERIALS. *Prospective study of 56 patients, aged from 19 to 82 (mean \pm S.D. 53 \pm 16.8) years, undergoing retinal detachment surgery (encirclement with scleral buckling) under general anesthesia. Excluded were patients with venous or arterial disease and any other factors that could affect the parameters under consideration.*

METHODS. *Blood was sampled from the cubital vein one day before surgery, immediately after induction of anesthesia but before surgery, immediately after completion of the operation but before the termination of anesthesia and on days 1 and 4 after the operation. We measured antithrombin III activity (AT III), platelet count, fibrinogen concentration, activated partial thromboplastin time (aPTT) and prothrombin time (PT).*

RESULTS. *Intraoperative AT III activity and platelet count were significantly lower, aPTT was shortened and PT prolonged, although all values remained within the normal range. These results indicate moderate activation of coagulation during retinal detachment surgery. On the first postoperative day coagulation activity was reduced, with increases in AT III activity, fibrinogen concentration and platelet count and prolongation of aPTT.*

CONCLUSIONS. *During retinal detachment surgery there is moderate activation of coagulation in the systemic circulation. (Eur J Ophthalmol 2000; 10: 318-23)*

KEY WORDS. *Antithrombin III, Platelet count, Activated partial thromboplastin time, Retinal detachment surgery*

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INTRODUCTION

Some studies on serial changes in a number of hemostatic parameters after major abdominal, urological, gynecological and orthopedic surgery have revealed early marked changes in the blood coagulation cascade (1-7). Other studies suggested that patients undergoing minor surgery did not show these changes (8, 9).

Retinal surgery differs from other surgery in many ways. Although it is a minimal surgical intervention,

surgically induced changes within the vast vascular layer of the eye and in the choroidal microcirculation may be associated with many hemodynamic factors. It seems important to obtain information about how the coagulation system responds to the tissue trauma involved in retinal detachment surgery.

To the best of our knowledge, no studies on the hemostatic system after retinal surgery have been published. The purpose of this study was to assess the changes in blood coagulation during and after retinal detachment surgery.

PATIENTS AND METHODS

Patients

Fifty-six patients with rhegmatogenous retinal detachment, scheduled for retinal detachment surgery, were studied. There were 30 males and 26 females aged from 19 to 82 years (mean \pm S.D. 53 ± 16.8 years). The operations, performed by two retinal surgeons, included encircling combined with segmental scleral buckling, cryopexy and subretinal fluid drainage. All were performed under standardized general anesthesia, induced with fentanyl, atropine and succinylcholine and maintained with O₂, NO₂ and vecuronium.

All patients gave their written informed consent before they were included in this study. The study had been approved by the Ethics Committee of the Faculty of Medicine, University School of Medical Sciences of Bydgoszcz.

Exclusion criteria comprised other illness or medical treatment besides the retinal detachment, surgery during the past two years, tobacco smoking, pregnancy during the past two years, menopause with the last menstruation not longer than a year ago, diabetes mellitus, previous or present venous thrombosis in the patient or close relatives. None of the patients had received any medication that could affect the hemostatic mechanisms in the 30 days before entering the study, intraoperatively or in the postoperative period (e.g., aspirin, anticoagulants, steroids, non-steroid anti-inflammatory agents, oral contraceptives, vasoactive drugs, beta or calcium channel blockers). No perioperative thromboembolic prophylaxis was used in the study group.

Blood sampling

Venous blood samples were taken from the cubital vein and placed in sodium citrate solution (9:1) between 09.00 and 10.00 h at the following times: 24 h before operation (day -1), immediately after induction of anesthesia but before surgery (oper -0), immediately after completion of the operation (oper +0), but before the termination of anesthesia, (usually between 11.00 and 12.00 h), than on the 1st (day 1) and 4th postoperative day (day 4). Days when blood was collected are referred to as follows: day -1, oper -0, oper +0, day 1, day 4. All venepunctures were performed

using minimal venostasis following a rest period of 15 min in a recumbent position. Except on the day of the operation, a standard hospital breakfast was given between 1 and 1.5 h before blood was taken.

Laboratory studies

- 1) AT III activity was determined utilizing Berichrom Antithrombin III, produced by Behring Diagnostic GmbH, according to the manufacturer's instructions. The normal reference range was 75-125%.
- 2) Fibrinogen was measured colorimetrically with Folin-Ciocalteau reagents.
- 3) Platelet count was calculated by direct microscopy in a Burker's chamber.
- 4) The activated partial thromboplastin time (aPTT) was determined as described by Proctor (10).
- 5) Prothrombin time was established using Quick's method.

Statistical analysis

Results of normally distributed data are expressed as mean and standard deviation. Parameters with non-Gaussian distribution are presented as median, range and interquartile range. In such cases the Wilcoxon matched sign rank test was used for paired data. A p-value below 0.05 was considered statistically significant.

RESULTS

The operations lasted 39 - 112 min (median 51 min). There were no complications. Patients were discharged from the hospital on the 5th postoperative day.

AT III decreased significantly during retinal surgery (oper -0 vs oper +0, $p = 0.04$), rose on postoperative day 1 and returned to near - normal on the 4th postoperative day (Fig. 1).

The fibrinogen concentration was not greatly affected by retinal detachment surgery. Its concentration decreased insignificantly during surgery and rose significantly on the first postoperative day (oper +0 vs day 1, $p < 0.0001$) (Fig. 2).

The platelet count fell significantly during surgery (oper -0 vs oper +0, $p < 0.005$), and on the first postoperative day (oper +0 vs day 1, $p < 0.002$). On postoperative day 4 platelet count was near-normal and

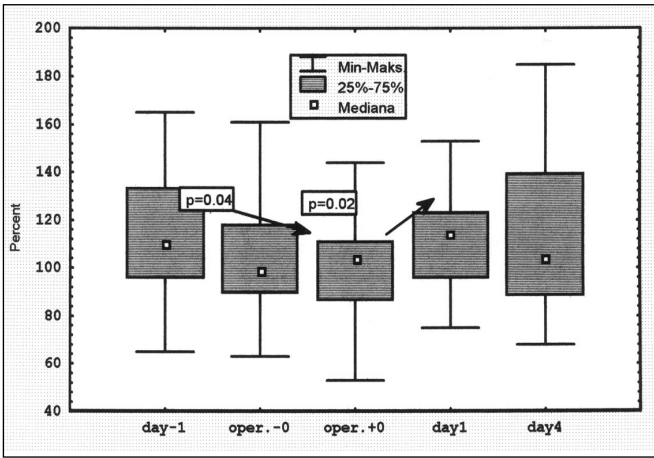


Fig. 1 - Antithrombin III (AT III) activity in patients undergoing retinal detachment surgery.

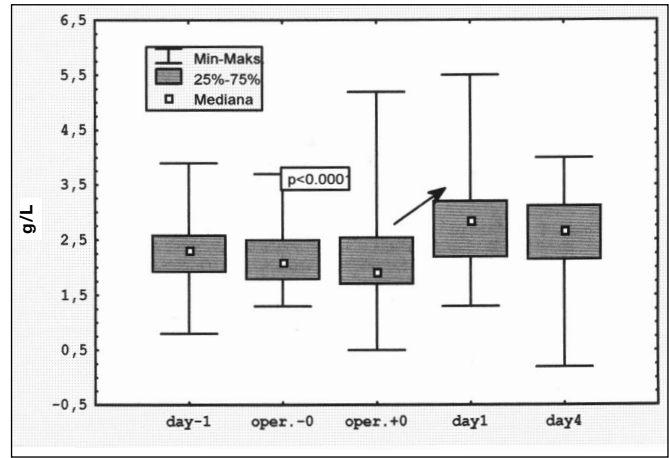


Fig. 2 - Blood fibrinogen concentrations in patients undergoing retinal detachment surgery.

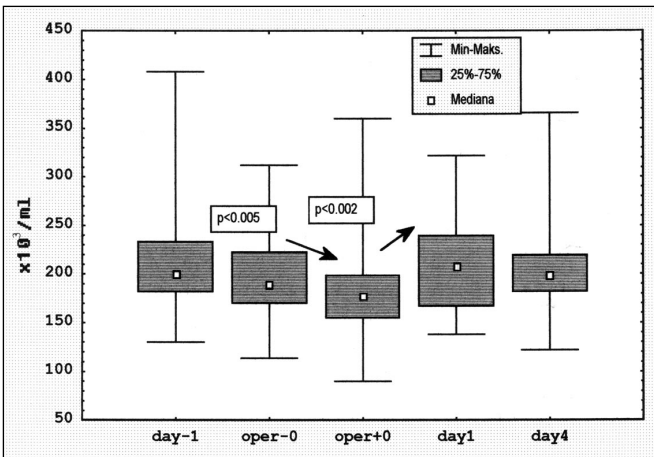


Fig. 3 - Platelet counts in patients undergoing retinal detachment surgery.

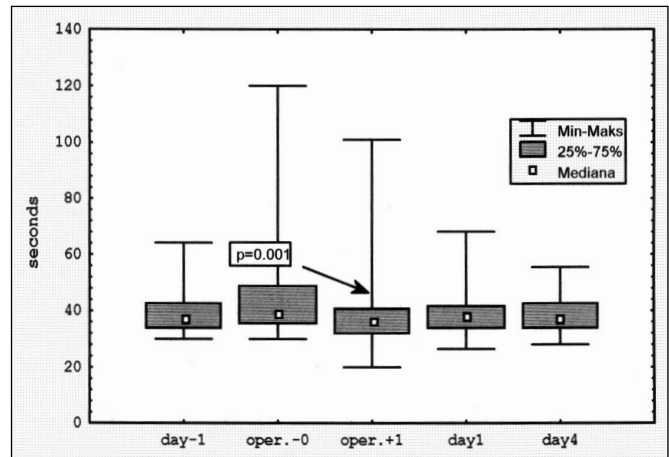


Fig. 4 - Activated partial thromboplastin time (aPTT) in patients undergoing retinal detachment surgery.

was not significantly different from the earlier results (Fig. 3).

After an insignificant prolongation of aPTT immediately after the induction of anesthesia, but before surgery, aPTT became significantly shorter during the operation (oper -0 vs oper +0, $p < 0.001$), but gradually returned to normal after the operation (Fig. 4).

There was a significant prolongation of PT (day -1 vs oper -0, $p < 0.04$) after the induction of anesthesia and it remained prolonged during surgery, compared with the earlier values. Postoperatively, it gradually returned to normal (Fig. 5). Table I summarizes the overall results.

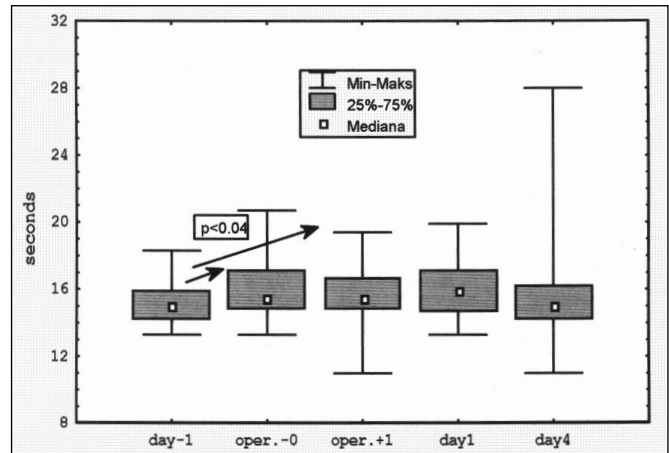


Fig. 5 - Prothrombin time (PT) in patients undergoing retinal detachment surgery.

DISCUSSION

It is well established that during and after major surgical procedures (abdominal, gynecological, urological and orthopedic) there are changes in blood hemostasis (1-7). These changes are induced by many factors e.g. tissue trauma, damage to the vascular wall and retarded blood flow during surgery (11).

The normal intact endothelium is non-thrombogenic and does not activate platelets or blood coagulation factors (12). Activated coagulation factors are serine proteases, whose activity is governed by several naturally occurring protease inhibitors, the most important of which is antithrombin III (13). Antithrombin III (AT III) inhibits thrombin and factor Xa and, to a less marked degree, factors IXa, XIa, XIIa, prekallikrein and plasmin (2, 3). Reduction of AT III levels to about half of normal predisposes to venous thrombosis (12).

In our study, AT III fell significantly during surgery (though remaining within the normal range). It has already been reported that AT III activity falls during major surgical procedures and returns to preoperative values within 7 days (5, 7, 13, 14). The extent of the decrease in AT III is related to, but not necessarily equal to, the amount of thrombin formed. However, the decrease does reflect the amount of thrombin, hence also the extent to which the coagulation sequence is activated.

We also found significant changes in routine labo-

ratory of coagulation parameters (aPTT, PT, platelet count) and a significant postoperative rise in fibrinogen concentration. The pattern of changes in platelet count, fibrinogen, aPTT and PT agrees with previous reports regarding major surgery: intraoperative shortening of aPTT, decrease in platelet count and subsequent prolongation of aPTT, increase in platelet count and fibrinogen and finally a gradual return to normal (1-3, 5, 7). The PT has also been shown to occur in patients undergoing major surgery (5, 7). Previous studies reported an intraoperative decrease in fibrinogen (15). Although the fibrinogen level dropped intraoperatively in our study too, it did not reach statistical significance. However, the postoperative increase in fibrinogen is in agreement with others.

Surgical stress, like other factors such as anesthesia, may influence coagulation activity. Some studies found lumbar epidural analgesia caused a smaller postoperative increase in coagulation factors than general anesthesia (16). Others, however, reported no changes in coagulation, whether general anesthesia was used or not (9, 16, 17). In our study the induction of anesthesia prolonged PT and reduced AT III activity. This is similar to some reports of changes after the induction of anesthesia (general or epidural or cervical block) even before surgery began (16).

It would be difficult to distinguish between the influence of anesthesia and the influence of surgery alone. However, in patients undergoing minor surgery (less

TABLE I - PERIOPERATIVE CHANGES IN COAGULATION VARIABLES IN PATIENTS UNDERGOING RETINAL DETACHMENT SURGERY

	Day -1		Oper -0		Oper +0		Day 1		Day 4	
	Median	Interquartile range	Median	Interquartile range	Median	Interquartile range	Median	Interquartile range	Median	Interquartile range
AT III activity (%)	110.0	37.0	99.0	28	104.0	24.0	113.0	27	103.0	51.0
Fibrinogen (g/L)	2.3	0.7	2.1	0.7	1.9	0.8	2.9	1.0	2.7	0.9
Platelet count (x1000/ml)	210.6	51.0	196.9	53.0	177.7	44.0	209.8	72.0	203.4	38.0
aPTT (sec)	36.9	8.3	39.2	13.8	36.3	8.1	38.1	7.8	37.4	9.0
PT (sec)	15.0	1.7	15.6	2.3	15.4	1.8	15.9	2.4	15.1	1.9

serious than cholecystectomy) under general anesthesia, no changes were seen in hemostasis like those following major surgery (3, 8, 9). Loick et al reported that general anesthesia did not cause activation of the coagulation and fibrinolytic system in 41 patients undergoing elective ophthalmic surgery (8). These observations suggest surgery is the main cause of hemostatic changes. Although ophthalmic surgical procedures seem to cause limited trauma, our results indicate that retinal detachment surgery may facilitate intravascular coagulation.

This study has certain limitations in that it lacks a control group. For ethical reasons we could not form such a group because we do all retinal surgery under general anesthesia. However, our results could be compared with the results of a previous study on the influence of laparoscopic and traditional cholecystectomy on perioperative hemostasis (3). The criteria and the study design were similar to ours (setting, age of patients, exclusion criteria, blood sampling, surgical start times, laboratory studies done in the same laboratory, team of anesthetists and standardized general anesthesia). The present investigation also agrees with other reports in which alterations in coagulation associated with major surgery were identified (1-3, 5, 7, 13-15). It can thus be assumed that

retinal detachment surgery carries a risk comparable to that related to the surgical trauma of a magnitude similar to or greater than traditional cholecystectomy.

In summary, the results presented here indicate that scleral buckling surgery can cause hemostatic sequelae, influencing systemic coagulation. The significance of this is not clear as other factors too may influence coagulation activity at this time e.g., anesthesia. These are therefore preliminary observations. Although we are not certain whether retinal detachment surgery by itself induces blood coagulation, we presume that the changes in blood coagulation might result from the compression of choroidal blood vessels due to buckling procedures (the vast endothelial surface at this level) and vessel wall trauma related to cryopexy. However, on the basis of our laboratory results, it seems that patients undergoing retinal detachment surgery are at some risk of perioperative changes in blood coagulation and this should not be underestimated.

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