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L'aspirine n'est pas un facteur de risque de complications hémorragiques pendant et après une première chirurgie de décollement de rétine rhexmatogène

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**L'aspirine n'est pas un facteur de risque de complications
hémorragiques pendant et après une chirurgie de décollement de
rétine rhéomatogène**

THESE

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DIPLOME D'ETAT

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**Aspirin is not a risk factor of bleeding complications
during or after primary rhegmatogenous retinal detachment surgery**

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ABSTRACT

Objective: To evaluate the hemorrhagic risk of treatment by acetylsalicylic acid, during the management of primary rhegmatogenous retinal detachment (RD).

Design: case-control study (according to presence of perioperative bleeding complications).

Participants: 322 patients (322 eyes) from a prospective cohort of 835 patients with primary rhegmatogenous RD operated on between 2004 and 2007.

Methods: After exclusion of patients with RD secondary to trauma, subjects with a history of vitreoretinal surgery, diabetic retinopathy, aphakia or taking clopidogrel and/or a vitamin K antagonist, 74 patients were included in the hemorrhagic group and patients without hemorrhagic complications were randomly selected in order to reach a 1:3 case: control population. Univariate and multivariate analyses were performed to identify risk factors of perioperative bleeding.

Main outcome measures: Occurrence of hemorrhagic complications such as hyphema and intravitreal, subretinal and suprachoroidal hemorrhage. Prognostic factors included final visual acuity (LogMAR) and the single-operation attachment rate.

Results: Univariate analysis showed that the presence of initial vitreous hemorrhage, size of breaks, number of breaks, pars plana vitrectomy (PPV) and the number of cryotherapy impacts were significantly associated with perioperative bleeding. Independent risk factors of perioperative hemorrhage were the number of cryotherapy sessions (odds ratio =1.12 [1.06; 1.20], 95% CI), transscleral drainage (OR =4.22 [1.62; 10.98]), and PPV (OR =3.39 [1.36; 8.47]). The occurrence of

bleeding complications was associated with a lower single-operation anatomical success rate. There was also a trend toward an association between bleeding complications, the total number of RD recurrences, and final visual acuity.

Conclusion: Aspirin was not an independent risk factor of hemorrhagic complications during and after surgery of primary rhegmatogenous RD. The bleeding risk is instead associated with surgical factors such as PPV, cryotherapy, and subretinal fluid drainage.

PRECIS

Treatment with aspirin was not associated with perioperative hemorrhages during or after retinal detachment surgery. Operative factors such as cryotherapy, transscleral drainage, and pars plana vitrectomy were correlated with bleeding complications, leading to a lower single-operation anatomic success rate.

INTRODUCTION

Aspirin is among the most commonly used systemic medications for systemic anticoagulation. In the United States, approximately 36% of the population is treated with antiplatelet agents (APA, 50 million people treated with aspirin).[1]

Aspirin inhibits platelet aggregation by irreversibly binding to platelet cyclo-oxygenase (COX-1), preventing the formation of thromboxane A₂, a potent platelet aggregator and vasoconstrictor. The usual dosage, 50–300 mg/day, is used mainly to prevent thrombosis in the arterial vasculature. Aspirin is prescribed in primary (when the 10-year risk of vascular accidents is greater than 10%) or secondary protection (decreasing myocardial reinfarction by 30% and subsequent stroke by 25%).[2] Acute withdrawal of APA agents could cause a deleterious rebound effect, which induces a prothrombotic phenomenon associated with excessive thromboxane A₂ activity, increased platelet adhesiveness, and decreased fibrinolysis. The clinical consequences are stent thrombosis (1%), arterial thromboembolism (20% of episodes are fatal, 40% resulting in permanent disabilities),[3] and increased mortality by myocardial infarction (30%), especially during the first year following drug-eluting stent placement and during the first 4–6 weeks following bare metal stent placement.[4, 5] Other serious adverse events related to the cessation of APA treatments are stroke and transient ischemic attack with a risk estimated at one event for 1,000 surgeries.[6, 7]

The long-term use of aspirin was shown to be associated with an increased risk of spontaneous intracerebral hemorrhage.[8] Aspirin seems to be associated with a rise in the bleeding rate in specific procedures (2.5–20%), such as tonsillectomy, transurethral prostatectomy, and intracranial surgery.[2, 4, 9, 10]

Large prospective studies on APA agents, rare in the field of ophthalmology, were mainly focused on cataract surgery.[10, 11] The use of APA agents is common, especially among elderly patients eligible for eye surgery, the number of which has risen to 24% in recent studies.[6, 12] Topical anesthesia,[13] nonvascularized clear corneal incision, and phacoemulsification[14] allow for cataract surgery without

stopping the treatment during the preoperative period, at the cost of minor side effects without impacting visual acuity,[7] such as subconjunctival hemorrhage,[15, 16] or a small hyphema.[17] Studies on vitreoretinal surgery have focused mainly on bleeding complications,[18, 19] with very little concern for patients taking aspirin [20, 21] or anticoagulants.[1, 22, 23] Only one prospective study examined the potential effect of aspirin,[24] while also including patients treated with warfarin. It is also the only study that refers to a substantial cohort of 325 patients who underwent retinal detachment (RD). Precise data on the clinical features of RD and surgical techniques unfortunately were not reported.

The context of RD surgery is characterized by the urgency of the surgical indication (duration of macular detachment),[10, 25, 26] and the risks of bleeding secondary to the surgical procedure.[1, 20, 27]

While bleeding is not life-threatening as such in ophthalmology, abnormal bleeding may be responsible for serious complications, such as choroidal, intravitreous, or subretinal hemorrhage.[18] Overall, the clinician should balance the risk and the potential severity of increased perioperative bleeding for a given patient's risk profile, the type of the surgery to be performed, and the frequency and consequences of arterial thromboembolism, as described above.

Thus the objective of this case–control study of 322 patients from a prospective cohort of 835 patients who underwent RD surgery was to identify the risk factors for bleeding during and after operation, most particularly including the role of aspirin before surgery, and define the anatomical and functional severity of hemorrhagic complications.

METHODS

This case–control study included 322 patients (322 eyes) from a prospective cohort of 835 patients with primary rhegmatogenous RD, operated on between 2004 and 2007 (three surgeons: CC, FR, KP, in two university hospitals). This study followed

the Declaration of Helsinki guidelines for research involving human subjects and was approved by the local Institutional Review Board (#5891). All patients enrolled in this study provided signed informed consent before the intervention.

Selection of the population

The inclusion criteria were: primary rhegmatogenous RD, patients over 18 years old, and written consent. The exclusion criteria were: RD secondary to trauma, subjects with a history of vitreoretinal surgery, diabetic retinopathy, or aphakia, and those taking clopidogrel and/or vitamin K antagonist (VKA) treatment not relayed by heparin and/or international normalized ratio (INR) greater than 1.5 in case of relay heparin, and transconjunctival surgery (25 or 23 G).[28] Only one eye per patient was included in this study (the first eye affected by the RD). Finally, seven patients on clopidogrel, two patients receiving VKA-free substitute with heparin, and two patients lost to follow-up were not retained.

Of the 855 patients in the cohort study, 109 patients were excluded and 726 patients were considered for the selection of the hemorrhagic group ($n=74$) and the non hemorrhagic group (control group: three random cases for one hemorrhagic case, $n=248$).

Clinical data

The pre-, intra-, and postoperative data were recorded on standardized case report forms. Indication for treatment with APA and their dosages (75–300 mg/day) were considered consistent with good clinical practice.[29, 30]

Patients with a period of APA cessation less than or equal to 5 days were classified in the treatment group, while those who had stopped consumption more than 5 days before surgery were classified in the group without APA.

Visual acuity (VA) was converted to a logarithm of the minimum angle of resolution (LogMAR) score for analysis.[31] Pre- and postoperative fundus examinations were performed using both the three-mirror (Goldmann) lens and

indirect ophthalmoscopy. Axial length measurements and visualization of the posterior segment in case of intravitreal hemorrhage were obtained from ultrasound imaging (Cinescan™, Quantel, Clermont-Ferrand, France).

The inferior location of a break was defined by the presence of this break strictly below the 3 o'clock or 9 o'clock meridian. The proliferative vitreoretinopathy (PVR) grade was determined in accordance with the Retina Society classification.[32]

Surgical technique

All patients were operated on under general anesthesia. The indication for surgery was selected by surgeons according to the characteristics of RD (location and size of retinal breaks, PVR, vitreous hemorrhage), the lens status and/or the level of myopia. Retinopexy was performed with cryotherapy or laser endophotocoagulation. The numbers of cryotherapy impacts (ErboKryo AE, Erbe™, Limonest, France) on normal retina or retinal breaks were noted. Circumferential or radial scleral buckling was performed depending on the location of dehiscence, size, and/or association with PVR.

The scleral buckling procedure, performed using the three-mirror glass,[33, 34] consisted in (1) conjunctival disinsertion over 360°, establishing tractor thread on the four rectus muscles, (2) checking scleral status and location of scleral vortex veins, (3) cryotherapy of retinal breaks and suspicious retinal areas, (4) scleral location of retinal breaks and scleral buckling, (5) external drainage of subretinal fluid (SRF, with a needle and Vicryl 7.0 suture), and/or intravitreal injection of SF6 or C2F6 expansive gas.

In cases of pars plana vitrectomy (PPV) with the 20-G transscleral system, the Accurus vitrectomy system (Alcon™ Laboratories, Rueil-Malmaison, France) was used with a cutting rate of 1500 cpm/min and a suction rate ranging between 120 and 400 ml/min. A contact wide-angle viewing system combined with an image inverter (SDI Oculus IIe, Wetzlar, Germany) and plane-concave lenses (FCI™, ref. S5.7010, Paris, France) were used for fundus visualization. All eyes underwent complete PPV

with induction of the posterior vitreous detachment (PVD) if necessary, peripheral vitreous dissection under scleral depression, retinopexy (cryotherapy and/or endolaser, limited to areas of retinal breaks, suspected zones, or predisposing lesions), then a fluid/gas exchange using 20% sulfur hexafluoride (SF6) or 16% hexafluoroethane (C2F6) associated with *ab interno* drainage in most cases (Table 2). Perfluorocarbon liquid (PFCL, FCI™, ref. S5.8150, Paris, France) was used, if needed, in selected cases of bullous peripheral RD and/or PVR to flatten the posterior retina and help peripheral vitrectomy.

Definition of peri- and intraoperative bleeding complications

Bleeding complications such as vitreous hemorrhage, suprachoroidal hemorrhage, subretinal hemorrhage, and hyphema were considered. Minor complications involved vitreous hemorrhage less than or equal to 50% of the vitreous cavity (retina visible), subretinal hemorrhage out of the macula, and single peripheral choroidal hemorrhage. Major complications included vitreous hemorrhage involving more than 50% of the vitreous cavity, macular subretinal hemorrhage, and multiple choroidal hemorrhages. Suprachoroidal hemorrhages were classified into three categories [18] with class I: most posterior extent anterior to equator, class II: extension posterior to equator but not involving macula and class III: extension into macula.

Postoperative follow-up

All patients maintained postoperative head positioning defined by the break location for a duration ranging from 3 to 10 days, depending on the type of gas used. Postoperatively, a complete ocular examination was performed on the 1st day and subsequently at 1 and 6 months. An additional examination was completed in cases of recurrent RD to ensure a 6-month follow-up after the last surgery (including removal of silicone if necessary). The definition of hypotony was IOP 5 mmHg or less.[27]

Statistical analysis

Patients were divided into two groups according to the occurrence or nonoccurrence of intra- and/or postoperative bleeding complications. The main factor aspirin was evaluated. Secondary factors such as initial VA, high myopia, the maximum value of intraoperative mean arterial blood pressure, duration of surgery, subretinal fluid drainage, scleral bucking, PPV, and cryotherapy were also evaluated. Data were expressed as mean \pm standard deviation (SD) for quantitative data and in terms of size and frequency for categorical data. The two groups were compared using the Student *t*-test or the Mann-Whitney test (for non-Gaussian assumptions) for continuous data. Independence between qualitative parameters was assessed using either the chi² test or with Fisher's exact test. Multivariate analysis was performed using the stepwise forward logistic regression model. The statistical analysis was performed using the Statistical Package for the Social Sciences program (SPSS 17.0 for Windows, Chicago, IL, USA). Statistical significance was defined as a two-tailed *p*-value less than 0.05.

RESULTS

Preoperative characteristics:

Among the 322 patients with a mean age of 59.5 ± 14.3 years and a 1.8 sex ratio, 29.2% suffered from hypertension, 8.4% from diabetes (Table 1).

Of 40 patients (12.4%) treated with aspirin, a majority ($n=28$) stopped aspirin less than 5 days before surgery ($n=19$) or continued their treatment ($n=9$). The average duration of aspirin cessation was 3.4 days. For 12 patients (3.7%), aspirin was otherwise interrupted more than 5 days. Sixteen patients (5%) were on heparin, including patients previously treated with AVK ($n=7$, 2.2%), stopped for a mean 4.1 days; their INR at the time of surgery was less than 1.5.

The RD was usually associated with a superior break (63.4%), macula-off (63%), and intravitreal hemorrhage in 14.6% of the cases. High myopia was noted in 26% of cases.

The univariate analysis showed that clinical factors associated with a bleeding complication (Table 1) were the presence of initial vitreous hemorrhage, size of breaks, and number of breaks. High myopia, the severity of RD (extension, type of break, PVR) and aspirin treatment were not associated with risk of bleeding. The preoperative vitreous hemorrhage showed no significant correlation with aspirin ($p=0.5$). Aspirin was not a risk factor significantly associated with bleeding complications ($p=0.8$). The occurrence of bleeding complications was not associated with time no taking aspirin (Table2).

Description of complications (Table 2):

In the cohort of 726 patients, the incidence of bleeding complications was 20.2%. In this case–control study, bleeding complications were considered minor in 67.4% of the cases (15.5% of 322 eyes) or major in 36.6% (7.5% of 322 eyes). Taking into account the type of perioperative hemorrhage, aspirin was significantly associated with an increased risk of hyphema ($p=0.03$) and was not associated with other complications.

During surgery, all bleeding complications ($n=16$, 5.1%) occurred within the patient group without aspirin. Only one patient had more than one intraoperative complication (vitreous hemorrhage and suprachoroidal hemorrhage).

Postoperatively, the most common bleeding complications (Table 2) were: vitreous hemorrhage (15.2%, severe in 5.6%), subretinal hemorrhage (7.1%, submacular in 1.6%), and suprachoroidal hemorrhage (5.6%, class III in 0.3%).

Intraoperative data (Table 3):

Using univariate analysis, the surgical factors associated with bleeding complications were PPV and the number of cryotherapy impacts (Figure 1). The number of breaks

(3.3 ± 3.3 vs 2.5 ± 2.1 , $p=0.01$) and the number of cryotherapy impacts (6.7 ± 4.7 vs 5.6 ± 3.05 , $p=0.03$) were higher in the group treated with PPV. The “retinotomy” factor was not studied given the small number of patients in each group ($n=4$).

Postoperative data and final result (Table 4):

The occurrence of bleeding complications was associated with a lower single-operation anatomical success rate. There was also a trend toward an association between bleeding complications, the total number of RD recurrences, and final VA. A final retinal reattachment was achieved in 310 cases (96.3%).

Multivariate analysis

The following factors were considered for multivariate analysis: high myopia, duration of aspirin cessation less than 5 days, number of cryotherapy impacts, transscleral drainage, scleral buckling, PPV, duration of surgery, pupillary dilation, intraocular pressure, hypertension, and systolic and diastolic blood pressure. The following parameters were associated independently with bleeding complications: number of cryotherapy impacts (odds ratio =1.12 [1.06; 1.20], 95% CI), transscleral drainage (OR =4.22 [1.62; 10.98]), and PPV (OR =3.39 [1.36; 8.47]) after adjusting the model to pupillary dilation (OR = 0.89 [0.74; 1.07]), and aspirin (OR =0.76 [0.28; 2.03]). In both univariate and multivariate analyses, aspirin was not associated with bleeding complications.

DISCUSSION

This prospective study shows that aspirin treatment does not increase the risk of bleeding complications during and after rhegmatogenous RD surgery. Onset of ocular hemorrhage was promoted by surgical factors such as the number of cryotherapy impacts, transscleral drainage and/or posterior vitrectomy. The onset of

ocular hemorrhage tended to lead to failure of the first RD surgery and to be associated with less good postoperative visual acuity recovery.

The percentage of patients in this prospective cohort initially treated with aspirin was low (12%). Cessation of aspirin for 5 days, as retained in this study, was chosen since it corresponds to 50% recuperation of the blood platelet pool (10% per day).[4, 35, 36] Using a point-of-care test, Cahill et al. reported a significant recovery of antiplatelet aggregation less than 48 h after the cessation of aspirin, with a return to baseline values by the 5th day.[37]

The decision to interrupt or continue aspirin depended on the balance between hemorrhagic risk and the risk of thrombosis at treatment cessation, demonstrating the importance of studies specific to ophthalmology in assessing the risk of ocular hemorrhage. Approximately 100 million adults undergo noncardiac surgery worldwide every year and up to 40% of these patients have coronary artery disease or are at risk for it.[38] Oscarson's randomized study [39] demonstrated in high-cardiovascular-risk patients that low-dose aspirin in the intra- and postoperative period (abdominal, urological, orthopaedic, and gynecological surgery) reduces by 7.2% the absolute risk of adverse cardiac events such as death from cardiac or cerebral damage, without necessarily increasing the risk of bleeding complications. In the retrospective study of 1911 patients with drug-eluting stent implantation, stent thrombosis occurred in 0.8% of patients during long-term follow-up [40] and was associated with premature antiplatelet therapy interruption. The meta-analysis by Burger and al. revealed that aspirin withdrawal precedes up to 10.2% of acute cases of cardiovascular syndrome.[10] The results of a randomized control trial comparing maintenance of aspirin versus 10 days preoperative withdrawal for noncardiac surgery excluding patients with drug-eluting stents will be available soon

(STRATAGEM, <http://www.clinicaltrials.org>, NCT00190307). With no randomized studies in patients undergoing vitreoretinal surgery, the risk/benefit ratio is not known at this time. Guidelines for the perioperative management of APA are based on small observational studies [1, 41] case reports, case series, and expert opinion.[9, 42-44] A recent study among vitreoretinal surgeons[45] also showed that 32% of these surgeons discontinued APAs before surgery, thus reflecting individual preferences rather than a nonexistent consensual attitude.

Surgical bleeding risk associated with the risk of APA has been poorly evaluated in the field of vitreoretinal surgery.[24] The risk of bleeding should be studied, in terms of frequency and severity. Our study focused on RD demonstrated a low rate of complications related to aspirin, in agreement with the data reported by Narendran on 60 patients treated with aspirin.[24] We found no association between aspirin use and initial intravitreal hemorrhage, like Chandra et al. [23] Another study [21] showed a low rate of vitreous hemorrhage in the group treated with Plavix + aspirin, but this group only included 15% eyes operated for RD. Moreover, it is difficult to compare our results with this study because the patients were operated on using the 25-G transconjunctival approach, with a variety of indications (diabetes, macular hole, and retinal detachment), most often locoregional anesthesia, with one group treated with VKA (warfarin) or clopidogrel (with aspirin associated in 75% of the cases). Other prospective studies will be necessary to more specifically investigate the bleeding risks associated with VKA + AAP treatment [21, 24] or the association of two AAPs.[46]

This prospective study showed the role played by three independent hemorrhagic risk factors: cryotherapy, transscleral drainage of subretinal fluid, and PPV. The role of aspirin does not appear to be significant in multivariate analysis. We

found that the amount of cryotherapy was significantly correlated with bleeding risk and associated with congested choroidal vasculature. As a qualitative factor (presence or absence), this treatment was also found to be associated with suprachoroidal hemorrhage during pars plana vitrectomy.[20] We usually performed cryotherapy before drainage, since this surgical sequence has not been reported to increase the risk of intraocular hemorrhage (3–4%).[47] It should be noted that in the present series, both drainage and cryotherapy were independent factors, with no effect of cryotherapy on the hemorrhage drainage rate. The hemorrhagic risk of drainage using a needle is associated with choroidal vessel lesions, and the consequences are more serious in macula-off RD, with the risk of displacement of blood beneath the macula. In our experience, drainage was preferentially used in eyes with bullous RD, inferior retinal breaks, and/or chronic RD. Using a needle or a suture needle, the hemorrhagic complication rate varies from 1 to 28% in eyes investigated in previous prospective studies.[48-53] Choroidal hemorrhage could be influenced by hypotony, more frequently observed during the procedure in bullous RD. We usually perform SRF drainage using needle suture (spatulated 7.0 needle), as described previously,[53] avoiding reduction of IOP by either tightening the scleral buckle or indenting the sclera using a cotton swab. A rare situation involves inadvertent scleral perforation,[54, 55] which can also result in choroidal hemorrhage in 16–23% (one case in our series, with subsequent subretinal hemorrhage).

Pars plana vitrectomy is the third factor associated with perioperative hemorrhages, with a frequency of 27% (29.4% with PPV alone and 24.7% with PPV + scleral buckling; $p=0.4$), mainly minor hemorrhages. The rates of subretinal hemorrhage and choroidal hemorrhage, reported in 6.4% and 4.8% of our series (calculated on the cohort of 726 patients), respectively, is comparable to recent

studies of pseudophakic patients: the incidence of severe hemorrhage is rare, 4% for submacular hemorrhage,[56] and 0.3–5.6% for suprachoroidal hemorrhage.[18, 48, 57, 58] The mechanism underlying ocular hemorrhages during or after PPV may include transitory hypotony during the procedure, lesions at the sclerotomy site, or internal drainage with or without retinotomy. The effect of aspirin in these populations was not analyzed in these earlier studies. RD is recognized as a surgical risk factor for choroidal hemorrhage during PPV.[18, 20, 59]

We did not find high myopia to be an independent risk factor of hemorrhagic complications. Myopia has been associated with an increased risk of bleeding complications during PPV.[20] Recent published studies showed an incidence of 2–11.3% for choroidal hemorrhage [60, 61] and 4% for subretinal hemorrhage in this population. [62] One study suggested that drainage-related complications were not related to the degree of myopia.[62]

Systemic arterial pressure (intraoperative hypertension) during surgery in patients with suprachoroidal hemorrhage during PPV has previously been suggested as a possible cause of bleeding complications.[20] Whereas a moderate rise in arterial pressure has little or no influence on choroidal blood flow due to efficient autoregulation,[63], a rapid and substantial increase in ocular perfusion pressure (> 140%) can raise choroidal blood flow and intraocular pressure.[64] Arterial pressure may act more as an aggravating factor than as a triggering factor of choroidal hemorrhage.

We found no harmful role played by scleral buckling, contrary to Tabandeh.[20] It is possible that several biases explain this lack of an impact: very low incidence or perforating points in our study ($n=1/322$) and placement of narrow

indentations (5 mm in most cases, therefore with little risk of compression of vortex veins).[65]

The bleeding complications described in the present study were considered to be serious in 8.1% of the cases, including subretinal hemorrhages and/or choroidal hematomas with macular involvement or large-volume hematomas and/or vitreous hemorrhages involving more than 50% of the vitreal cavity. Intra- or postoperative subretinal hematoma (6.4% in this series) may be serious because of the toxicity of blood for photoreceptors, notably in the macular region.[66, 67] In this latter case, the surgeon can drain the hematoma during surgery in cases of vitrectomy or request the patient to keep a head-down position postoperatively to displace the hematoma (which was done in this study). All the patients had final VA greater than 20/200 (82% > 20/160) and an attached retina at the last visit. These results are consistent with previous studies showing that subretinal hemorrhage after drainage did not influence the anatomical success of the procedure [49, 54] nor visual recovery.[49]

Vitreous hemorrhage that was not present at the end of surgery may be due to an intra- or postoperative choroidal hemorrhage that dissects into the vitreous cavity or to persistent traction of retinal vessels.[65] Vitreous hemorrhage is significantly associated with a recurrence of RD (31% vs 15%; $p=0.01$), which could be explained by the fact that vitreous hemorrhage is usually associated with a severe choroidal hematoma (grade II or III, 50%).

Choroidal hematomas are rarely serious: in the present series only one patient presented a choroidal hematoma with macular involvement (this patient had undergone several surgeries for recurrent RD with PVR). Two eyes with intra- or postoperative choroidal hematomas had a detached retina at the final visit. The high incidence of visual loss (< 5/200) was not higher after choroidal hematoma onset.[18]

In our study, six eyes out of 25 with choroidal hematomas achieved VA less than or equal to counting fingers at the last visit.

Finally, the onset of an intra- or postoperative bleeding complication was associated with a higher probability of failure of the first surgery, as has already been suggested for pseudophakic eyes.[68] Intraocular hemorrhage is known to be a risk factor for developing PVR.[69, 70] Finally, the onset of intraocular hemorrhage in the perioperative period is also a source of an increase in the length of the hospital stay (notably because of postoperative high IOP).

This study presents a number of strong points such as its prospective framework, the minimum follow-up of 6 months, the homogeneity of the techniques used by the three surgeons (trained identically), and the number of patients included. There was very little bias related to the patients lost to follow-up ($n=2$). This study focused on RD surgery, whose characteristics differ from vitreoretinal surgery (e.g., macular or diabetic retinal surgery).[18, 21-23] In addition, the patients taking clopidogrel and/or VKA treatment were excluded from the analysis so that no confounding factors would be introduced.

One of this study's limitations is related to the limited number of patients taking aspirin in the population operated on for RD (12% initially and 8.7% at the time of surgery) and the low frequency of ocular hemorrhage onset after scleral buckling or PPV.[57, 71, 72] In the population treated for cataract surgery, the incidence of aspirin treatment was estimated at 24% [6] and could vary depending on the selection bias of the participating centers and associated confounding factors (cardiovascular factors, age, population base). The incidence in the population with RD estimated in this study was 12% (40/322). The a posteriori calculation of

statistical power showed that assuming 8.9% of controls exposed, 74 cases and 248 controls included in this study detected a 3.5 increase in the odds ratio (25.5% of cases exposed) with a 90% power and a two-sided alpha level of 5%. Conducting a randomized study in ophthalmology should be debated, given the cost, the number of patients to include, and the already known systemic risks of APA in certain populations.[3-5]

In conclusion, the main risk factors of perioperative ocular hemorrhage are related to surgical technique (cryotherapy, scleral drainage, vitrectomy). These complications should, however, be prevented given their association with a more limited anatomical and visual prognosis. Aspirin is not a major intra- and postoperative risk factor for bleeding; therefore, there is no indication to interrupt APAs before RD surgery.

TABLE 1: Demographics and baseline clinical and treatment characteristics

	All patients (n=322)	No hemorrhagic complication (n=248)	Hemorrhagic complication (n=74)	P-value
Gender (male)	207 (64.3%)	164 (66.1%)	43 (58.1%)	0.2
Right eye	151 (46.9%)	121 (48.8%)	30 (40.5%)	0.13
Age (years)	59.5 ± 14.3	59.5 ± 14.3	59.6 ± 14.2	0.9
Diabetes	27 (8.4%)	22 (8.9%)	5 (6.8%)	0.5
High blood pressure	94 (29.2%)	75 (30.2%)	19 (25.7%)	0.4
Aspirin				
>5 days	12 (3.7%)	11 (4.4%)	1 (1.4%)	0.4
<5 days	28 (8.7%)	22 (8.9%)	6 (8.1%)	0.8
Preop cessation(days)	3.4± 2.7	3.7± 2.7	2± 1.9	0.1
VKA interruption	7 (2.2%)	4 (1.6%)	3 (4.1%)	0.2
Preop cessation (days)	4.1±1.3	4.5±1.3	3.7±1.5	0.5
Heparin (bridging aspirin n=9 or VKA n=7)	16 (5%)	13 (5.2%)	3 (4.1%)	0.7
Visual acuity (LogMAR)	1.21 ± 0.91	1.19 ± 0.91	1.24 ± 0.92	0.7
Visual acuity				
20/20–20/40	80 (24.9%)	63 (25.5%)	17 (23%)	0.6
20/50–20/160	72 (22.4%)	52 (21.1%)	20 (27%)	0.2
20/200–20/400	32 (10%)	25 (10.1%)	7 (9.5%)	0.8
Shand motions	137 (42.7%)	107 (43.3%)	30 (40.5%)	0.6

Intraocular pressure (mmHg)	13.5 ± 4.3 n=312	13.5 ± 4.2 n=240	13.3 ± 4.6 n=72	0.7
Axial length (mm)	24.9 ± 2.4 n=295	24.8 ± 2.4 n=225	25.1 ± 2.6 n=70	0.3
High myopia (≥ 26 mm)	83 (25.9%)	62 (25.2%)	21 (28.4%)	0.5
Pseudophakic status	114 (35.4%)	92 (37.1%)	22 (29.7%)	0.2
Size of retinal detachment (degrees)	197.1 ± 89.2	197.4 ± 88.85	196.2 ± 91.31	0.7
Macula-off	203 (63%)	160 (64.5%)	43 (58.1%)	0.3
Giant tears	16 (5%)	12 (4.8%)	4 (5.4%)	0.7
Proliferation vitreoretinopathy (PVR)				0.3
≤ stage A	264 (82%)	203 (81.8%)	61 (82.4%)	
≥ stage B	58 (18.8%)	45 (18.1%)	13 (17.6%)	
Tears				0.5
Superior	203 (63.4%)	157 (63.6%)	46 (63%)	
Inferior	40 (12.5%)	33 (13.4%)	7 (9.6%)	
Superior and inferior	77 (24.1%)	57 (23.1%)	20 (27.4%)	
Size of retinal detachment	197 ± 89 n=322	197 ± 89 n=248	196 ± 91 n=74	0.7
Size of tear	8.3 ± 20.9	5.9 ± 16.1	16 ± 30	0.0001

Number of tears >1 disc diameter	0.25 ±0.65	0.2 ± 0.5	0.5 ± 0.8	0.01
Number of tears	3.2 ±3	2.7 ± 2.4	3.7 ± 3.9	0.002
Vitreous hemorrhage	47 (14.6%)	21 (8.5%)	26 (35.1%)	≤0.001
Choroidal detachment	6 (1.9%)	5 (2%)	1 (1.4%)	0.99

VKA: Vitamin K antagonists

TABLE 2: Intra- and postoperative hemorrhagic complications according to the treatment with aspirin

	Overall population	No aspirin	Aspirin n=28
Intraoperative			
Intravitreal hemorrhage	5 (1.6%)	5 (1.7%)	0 (0%)
Subretinal hemorrhage	5 (1.6%)	5 (1.7%)	0 (0%)
Choroidal hemorrhage	6 (1.9%)	6 (2%)	0 (0%)
Postoperative			
HypHEMA	9 (2.8%)	6 (2%)	3 (10.7%)
Intravitreal hemorrhage	49 (15.2%)	44 (15%)	5 (17.9%)
Severe	18 (5.6%)	16 (5.4%)	2 (7.1%)
Hemorrhage under retina	23 (7.1%)	20 (6.8%)	3 (10.7%)
Severe/under macula	5 (1.6%)	4 (1.4%)	1 (3.6%)
Choroidal hemorrhage	18 (5.6%)	16 (5.4%)	2 (7.2%)
Class II	7 (2.2%)	6 (2%)	1 (3.6%)
Class III	1 (0.3%)	1 (0.3%)	0

TABLE 3: Intraoperative data of the 322 patients with retinal detachment

	All patients (n=322)	No hemorrhagic complication (n=248)	Hemorrhagic complication (n=74)	P-value
Duration of surgery	87.5 ±34.3	88.5 ±33.7	91.1 ±36.2	0.3
Scleral buckling	235 (73%)	187 (75.4%)	48 (64.9%)	0.07
Size of scleral buckling (degree)	176 ± 110 n=234	176 ± 111 n=186	174 ± 106 n=48	0.99
Endolaser	30 (10.2%)	20 (9%)	10 (14.1%)	0.2
Number of endolaser spots	759 ± 585 n=28	693 ± 574 n=19	899 ± 620 N=9	0.4
Cryotherapy	318 (98.8%)	248 (98.8%)	74 (98.7%)	0.99
Number of cryotherapies	8± 4.9	6.8 ± 4.1	9.2 ± 5.7	0.0001
Pars plana vitrectomy	171 (53.3%)	124 (50.2%)	47 (63.5%)	0.04
Epiretinal membrane peeling	19 (11.1%)	15 (12.1%)	4 (8.3%)	0.8
Tamponade Nothing Gas Silicone oil	50 (15.5%) 255 (79.2%) 17 (5.3%)	40 (16.1%) 196 (79%) 12 (4.8%)	10 (13.5%) 59 (79.7%) 5 (6.8%)	0.7
Transscleral drainage	79 (24.5%)	57 (23%)	22 (29.7%)	0.2
Combined cataract surgery	10 (3.2%)	8 (3.3%)	2 (2.7%)	0.99
Systolic arterial pressure (mmHg)	127.6 ± 64.4	127.9 ± 72.7	126.7 ± 19.4	0.2

Diastolic arterial pressure (mmHg)	72.7 ± 12.4	72.1 ± 12.3	74.4 ± 12.6	0.4
Pupillary dilation (mm)	8.3 ± 1.7	8.5 ± 1.7	8.1 ± 1.7	0.2

TABLE 4: Postoperative data of the 322 patients with retinal detachment

	All patients (n=322)	No Hemorrhagic complication (n=248)	Hemorrhagic complication (n=74)	P-value
Final visual acuity (LogMAR)	0.6 ± 0.7	0.5 ± 0.6	0.7 ± 0.7	0.09
Final visual acuity 20/20–20/40	155 (49.1%)	128 (52.9%)	27 (36.5%)	0.09
20/50–20/160	95 (30.1%)	68 (28.1%)	27 (36.5%)	
20/200–20/400	25 (7.9%)	18 (7.4%)	7 (9.5%)	
≤hand motions	41 (13%)	28 (11.6%)	13 (17.6%)	
Single-operation success rate	264 (82.2%)	210 (84.7%)	54 (74%)	0.03
Number of recurrences	0.26 ± 0.57	0.19 ± 0.5	0.34 ± 0.65	0.06
Final retinal attachment rate	310 (96.3%)	240 (96.8%)	70 (94.6%)	0.4

Figure 1

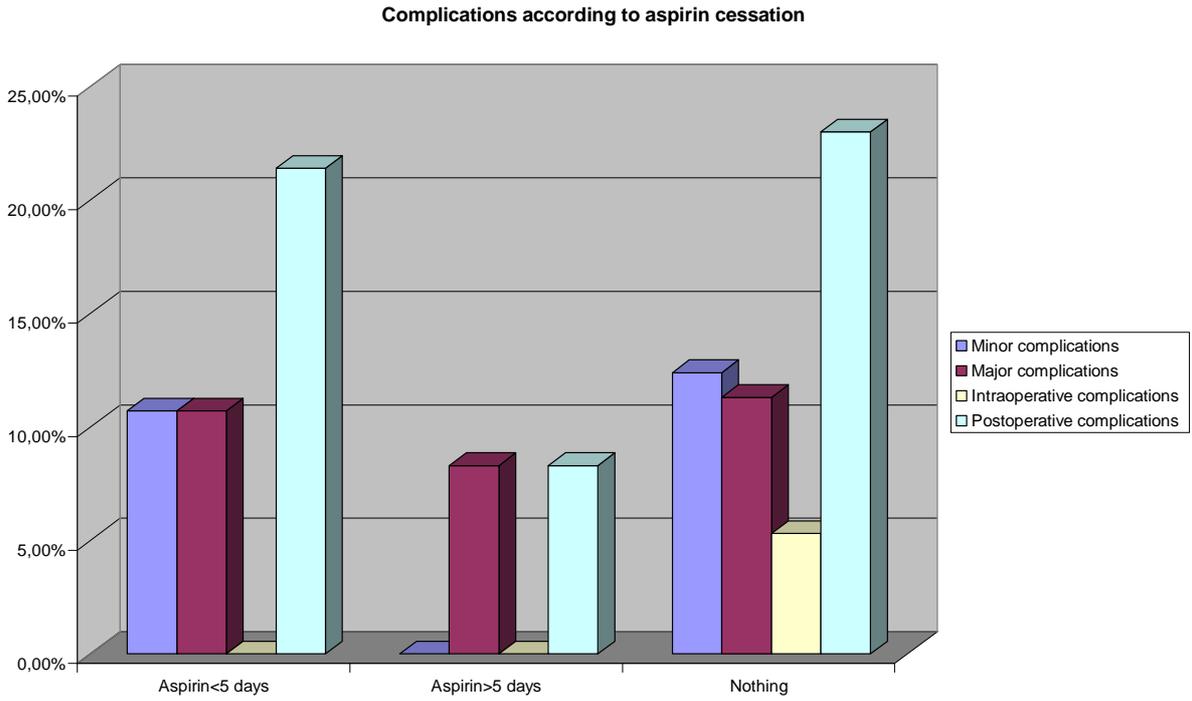
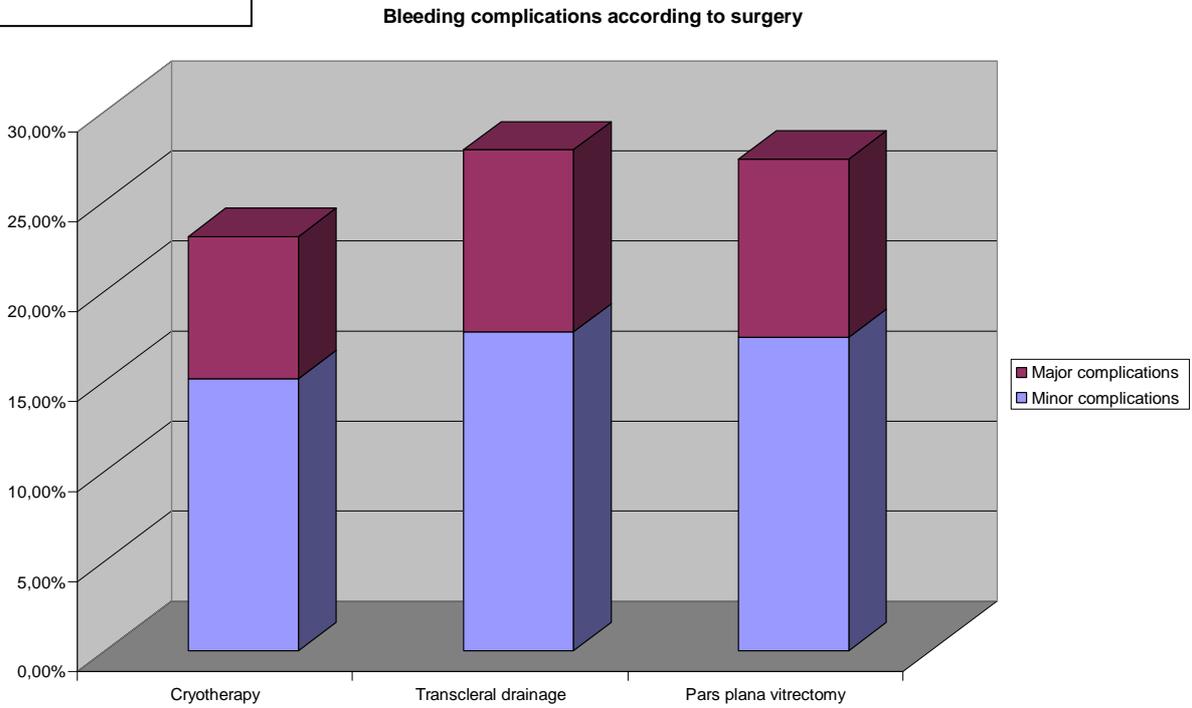


Figure 2



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THESE SOUTENUE PAR: ZARATZIAN BRILLAT EVA

Aspirin is not a risk factor of haemorrhagic complications during or after surgery of primary rhegmatogenous retinal detachment

In conclusion, this prospective study which included 322 patients showed that aspirin was not an independent risk factor for hemorrhagic complications during and after surgery of primary rhegmatogenous RD (8.1% vs 8.9%). It is then not necessary to stop aspirin before surgery of RD.

Multivariate analysis demonstrated that an amount of cryotherapy, pars plana vitrectomy and subretinal fluid drainage were independent risks factors of perioperative intraocular hemorrhages.

Prevention during surgery remains the best way to prevent major bleeding complications source of post-operative visual loss (0.7 ± 0.7 logMar vs 0.5 ± 0.6 logMar at the final visit).

Vu et permis d'imprimer

Grenoble le 15 Avril 2011

Le doyen

B.Sele



Le président de thèse

Pr Romanet JP



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HIPPOCRATES. 9.



Qui diu memorem laudes, repetamque fideles
Ingenij dotes, Hippocratisque decus.
Democriti auditor Phocæba, ô, Côt propago,
Certius an quis te tradidit artis opes?

SERMENT D'HIPPOCRATE

En présence des Maîtres de cette Faculté, de mes chers condisciples et devant l'effigie d'HIPPOCRATE,
je promets et je jure d'être fidèle aux lois de l'honneur et de la probité dans l'exercice de la Médecine.

Je donnerai mes soins gratuitement à l'indigent et n'exigerai jamais un salaire au dessus de mon travail. Je ne participerai à aucun partage clandestin d'honoraires.

Admis dans l'intimité des maisons, mes yeux n'y verront pas ce qui s'y passe ; ma langue taira les secrets qui me seront confiés et mon état ne servira pas à corrompre les mœurs, ni à favoriser le crime.

Je ne permettrai pas que des considérations de religion, de nation, de race, de parti ou de classe sociale viennent s'interposer entre mon devoir et mon patient.

Je garderai le respect absolu de la vie humaine.

Même sous la menace, je n'admettrai pas de faire usage de mes connaissances médicales contre les lois de l'humanité.

Respectueux et reconnaissant envers mes Maîtres, je rendrai à leurs enfants l'instruction que j'ai reçue de leurs pères.

Que les hommes m'accordent leur estime si je suis fidèle à mes promesses.

Que je sois couvert d'opprobre et méprisé de mes confrères si j'y manque.

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