Risk factors of tractional retinal detachment in non-silicone oil tamponade eyes after vitrectomy for proliferative diabetic retinopathy

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Abstract

Background

Traction retinal detachment is one of the serious complications of proliferative diabetic retinopathy (PDR) and poses a serious threat to the visual acuity of patients.The purpose of this paper is to investigated the risk factors of tractional retinal detachment (TRD) in non-silicone oil tamponade eyes after vitrectomy for PDR.

Methods

We performed a retrospective review of patients with postoperative TRD who underwent vitrectomy with non -silicone oil tamponade (C3F8, sterilized air or BSS) for PDR. The clinical information, including laboratory tests and the history of ocular treatment, was determined and compared to the control group to analyze their significance.

Results

The control group consisted of 28 patients who underwent vitrectomy with non-silicone oil tamponade for PDR immediately one proceeding and one following the surgery of each of the 14 patients (TRD group) with postoperative TRD. The history of photocoagulation, serum albumin, blood urea nitrogen and serum creatinine were significantly associated with TRD. The logistic regression analysis indicated that lower serum albumin concentration was the major systemic risk factor for the occurrence of TRD (P = 0.027).

Conclusion

The main systemic risk factor related to TRD was serum albumin in patients with PDR who underwent vitrectomy with non-silicone oil tamponade. Preoperative albumin supplementation may reduce the risk of postoperative TRD.

Background

Tractional retinal detachment (TRD),as one of the most severe complications of vitreoretinopathy,is more common in proliferative diabetic retinopathy (PDR), central retinal vein occlusion (CRVO), retinal reattachment surgery and so on. The basic pathological process of TRD is the proliferation of cells and the formation of preretinal membrane. The contraction of the proliferating membrane leads to the separation of (RPE) between the inner nerve sensory retinal and the external retinal pigment epithelial, which leads to retinal detachment[1, 2].

TRD is a significant cause of vision loss or even blindness in PDR patients. Although it is relatively rare as a postoperative complication after vitrectomy in patients with PDR who underwent complete removal of fibrous tissue and panretinal photocoagulation (PRP), TRD may be a distressing event for patients with more surgery and worse visual prognosis. In general, postoperative recurrent TRD is thought to be

primarily related to the severity of retinopathy and vitreoretinal surgery. But more and more studies recognized that systemic conditions can have a huge impact on the effectiveness of retinal surger[3],4. Recent evidence indicates that the best corrected visual acuity(BCVA) were strongly associated with systemic factors after vitrectomy, for example, BCVA was significantly lower in patients with a higher preoperative glycosylated hemoglobin[3]. Another study has reported that PDR patients with poor glycemic control were more likely to develop NVG after vitrectomy[4].

Compared with the silicone oil tamponade eye, postoperative recurrent TRD is more common in PDR patients who underwent vitrectomy without silicone oil tamponade (C3F8, sterilized air or BSS) because lacking long-term adequate support for retina. However, to the best of our knowledge, its specific mechanisms are not reported, and the current related research is also very limited. In order to better understand this rare problem, this paper retrospectively investigated the risk factors which are associated with TRD in non-silicone oil tamponade eyes after vitrectomy for PDR. The data may be useful for perioperative management and reducing the incidence of TRD.

Methods

Study population

A retrospective review of patients with postoperative TRD who underwent vitrectomy with non-silicone oil tamponade (C3F8, sterilized air or BSS) for PDR during 4 year from January 2015 to December 2018 at the Affiliated Hospital of Qingdao University was performed.

The control group consisted of 28 patients who underwent vitrectomy with non-silicone oil tamponade for PDR immediately one preceding and one following the surgery of each of the 14 patients (TRD group) with postoperative traction retinal detachment. Patients with eligible eyes were allowed to participate, but only one eye was allowed to enroll in the study.

The following were the exclusion criteria for the study eye(ie. they may have been existed in the non-study eye):

1. Patients with a history of previous vitreoretinal surgery.
2. Patients with ocular diseases including endophthalmitis,tumor, ocular trauma or congenital ocular disorders.
3. Patients who had residual retinal tears without laser closure after surgery.
4. Patients with retinal detachment less than 1 month from surgery.
5. Systemic disease such as immune diseases,lymphoma,hematological or cardiocerebrovascular disease.

Surgeries performed by one vitreoretinal surgeon in all patients. The protocol was approved by the Ethics Committee, Affiliated Hospital of Qingdao University and complied with the tenets of the Declaration of

Helsinki.

Data collection

For all patients, anterior segment examination and dilated ophthalmoscopy were performed before surgery to conduct a preliminary assessment of diabetic retinopathy. Besides, to ensure the effect of vitrectomy surgery, B-ultrasound was also performed, especially for those who have a glimpse of the fundus because of the vitreous lesion or severe cataract to further rule out other retinopathy or choroidal lesions. The routine blood, urine and coagulation routine were in the normal range, and there was no obvious abnormal liver function and renal function. Moreover, the following clinical data were collected and analyzed as risk factors for TRD: admission blood glucose; serum total protein concentration; serum albumin concentration; serum creatinine; blood urea nitrogen; glycated albumin; uric acid; the history of cataract surgery or retinal laser photocoagulation and the use of anti-vascular endothelial growth factor (VEGF) drugs before vitrectomy. No statistical analysis was performed on long-term blood glucose levels due to limited long-term follow-ups..

Surgical technique

A 3-port 23-G PPV was performed with the Stellaris PC platform (Bausch & Lomb, Rochester, NY, USA) at a speed of 5000 cuts per minute under local anesthesia for all patients. All patients underwent removal of the vitreous and fibrovascular membranes. Flattening the retina with perfluorocarbon liquid.Endophotocoagulation was carried out on the edges of the retinal tears, with at least three rows of laser marks. Complete PRP was followed by a 360°inspection of the retina in order to rule out residual retinal tears. C3F8, sterile air or BSS was used for internal tamponade.Phacoemulsification with intraocular lens implantation was performed for those who had a visually significant cataract before the PPV. Patients were instructed to remain face down for 10 to 30 days according to different intraocular tamponade conditions to press the retina effectively after vitrectomy. Not required, if the intraocular tamponade is BSS.After operation,topical eye drops were prescribed: topical antibiotic (levoflfloxacin) drops,4 times daily for 2 weeks and steroid (prednisolone) drops,4 times daily for 3 weeks and tapered off slowly. No complications related to surgery were found during or after surgery.

Statistical analysis

All findings were evaluated using GraphPad Prism 5 software. In the case of a normal distribution, the Chi-squared test and the independent sample t-test were used to compare data between patients with or without TRD. Binary logistic regression was used to analyze the relationship between different influencing factors of TRD patients, and to further explore the risk factors of TRD. $P<0.05$ was considered statistically significant.

Results

Except for 6 patients with missing partial data (glycated albumin), all patients' clinical features, admission blood glucose, serum total protein, serum albumin, serum creatinine, blood urea nitrogen, glycated albumin, and uric acid were all within the range required for vitrectomy. Data were compared between the two groups of patients, and statistical analyses were performed.

Clinical features

The clinical features of all cases are summarized in Table 1.There were 14 eyes in the study group and 28 eyes in the control group.Among patients, the Chi-squared results showed that no difference was found in gender(p=1.000), duration of DM(p=0.451), treatment regimen for DM(p=0.406), extent of fibrovascular proliferation(p1=0.841,p2=0.845,p3=0.632) and systemic hypertension(p=0.326) between the two groups. The ages of the two groups were compared by t-test□no statistical significance(p=0.093) (Table 1). The above can be seen that patient characteristics were not significantly different in the two groups. Grading of the extent of fibrovascular proliferation was defined as follows[5]: Grade 1, focal adhesions only; Grade 2, broad adhesion≥1 sites or vitreous-retinal adhesion at disk, macula or arcade; Grade 3, vitreous-retinal attachment extending to the periphery.

Univariate analysis

The Chi-squared results showed that the history of phacoemulsification combined with intraocular lens implantation (*P*=1.000) and the use of anti-VEGF drugs before vitrectomy(*P*=0.383) were not different signifificantly between TRD group and control group (Table 2). However, the patients with a history of retinal laser photocoagulation were less likely to have TRD (*P* = 0.015).

In the TRD group,the independent sample t-test revealed a significantly lower serum albumin concentration(P = 0.001), and significantly higher serum creatinine (P=0.001) and blood urea nitrogen (P=0.049). However, there were no significant differences between TRD group and control group regarding blood glucose (*P* = 0.278), serum total protein (*P* = 0.053), glycated albumin (*P* = 0.445), and uric acid (*P* = 0.468)(Table 2).

Multivariate analysis

Binary logistic regression was applied to analyze the relationship between different influencing factors of TRD patients and to determine the relatively independent hazards (Table 3). On logistic regression analysis, lower serum albumin concentration was the significant risk factor for TRD (*P* = 0.027)(Table 3). Compared with the control group,fewer patients underwent retinal laser photocoagulation in the TRD group before surgery, but the difference was no statistically significant(p=0.067).

Discussion

The results of the current study showed that serum albumin concentration was the major systemic risk factor for the occurrence of TRD in the patients with PDR who underwent vitrectomy with non-silicone oil

tamponade.

Albumin, which is the most abundant plasma protein in mammals, playing a decisive role in the maintenance of homeostasis and making a balance between intravascular hydrostatic and colloid osmotic pressure. Serum albumin also has binding substances, anti-inflammatory, antioxidant and other physiological functions[6]. Studies have shown that a decrease in serum albumin concentration enhances vascular endothelial cell permeability possibly by decreasing plasma colloid osmotic pressure and inducing oxidative stress and endothelial inflammatory injury, leading to tissue edema[7, 8].

Increasing the permeability of albumin is a typical feature of diabetic microvasculature, and diabetic retinopathy is one of the diabetic microvascular complications. Some studies have demonstrated that hyperglycemia can increases albumin permeability through a-calpain-dependent mechanism[9].Coupled with the increase of endothelial cell permeability and the breakdown of the blood-retinal barrier lead to albumin and macromolecule exudation, which lead to vitreous cavity haze and intraretinal exudate formation[10, 11].On the one hand, cell damage or death can lead to exudative fluid accumulation in the subretinal space, which can lead to exudative retinal detachment[12].On the other hand, this exudate may be an excellent culture medium for proliferating cells, which can form preretinal membrane due to continuous exudation, and its contraction provided mechanical strength for TRD[10, 13] .

Retinal homeostasis disorder can activate Müller cells, lead to cell proliferation, cellular shape change, produce stress fibers, which provided traction for the process of tractive retinal detachment. In addition to Müller cells, astrocytes and microglia are also contribute to retinal fibrosis[13, 14].Hypoosmotic gradients across glial membranes are present in the neural tissues of the retina under conditions associated with ischemia hypoxia and some pathological processes (such as hypoalbuminemia). Under this hypotonic condition, serum albumin can cause the swelling of the glia cells[8].In order to prevent such osmotic swelling under pathological conditions, retinal glial cells induce the continuous release of purines (in particular, ATP and adenosine)by activating a glutamatergic purinergic receptor[8, 15].In addition, purinergic signals can stimulate the proliferation of retinal progenitor cells and Müller cells, leading to the formation of epiretinal membranes. Furthermore, the traction produced by membrane contraction can further induce Müller cells to release ATP, to aggravate the disease and eventually lead to TRD[15].

In addition to albumin, there were also differences between the TRD group and the control group in blood urea nitrogen, serum creatinine and PRP before operation. The association between PRP and TRD has been controversial. The PRP could inhibit the expression of some cytokines to reduce neovascularization and retinal vascular leakage[12, 16]. However, a sufficient amount of PRP during the operation would also destroy endothelial cells and aggravate the inflammatory response[12]. Serum creatinine and blood urea nitrogen are markers of vascular pathology and inflammation[17]. Previous studies proved that high blood urea nitrogen and high serum creatine could aggravate the progress of DR[18]. Furthermore, studies have shown that blood glucose and glycated albumin may be associated with postoperative complications of PDR[19, 20]. The consistently elevated blood glucose in retina could destroy the integrity of retinal blood vessels and increase the vascular permeability through oxidative stress and the secretion

of pro-inflammatory cytokines, which could lead to the formation of retinal neovascularization, continuous exudation, and epiretinal membranes[19, 20]. However, there was no significant difference in blood glucose and glycated albumin between the two groups in our study, which may be due to the fact that all patients received the same control criteria for preoperative blood glucose levels before the operation.

Conclusion

In summary, our findings suggest that the main systemic risk factor related to TRD was the serum albumin in the patients with PDR who underwent vitrectomy with non-silicone oil tamponade. Preoperative albumin supplementation may reduce the risk of postoperative TRD. It is necessary to carry out a larger sample of research to confirm the conclusion.

Abbreviations

TRD: traction retinal detachment

PDR: proliferative diabetic retinopathy

CRVO: central retinal vein occlusion

BCVA: the best corrected visual acuity

VEGF: vascular endothelial growth factor

RPE: retinal pigment epithelium

PRP: panretinal photocoagulation

Declarations

Ethics approval and consent to participate

This study followed the tenets of the Declaration of Helsinki and was approved by the Ethics Committee, Affiliated Hospital of Qingdao University. All patients provided written consent to participate in the study.

Consent for publication

Not applicable.

Availability of data and material

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

ZDD designed this study. WYW carried out the surgeries. QLC performed the data analysis and drafted the manuscript. All authors participated in the collection of data and approved the final manuscript for submission.

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Tables

Table 1. Baseline features of TRD group and control group

Characteristics	TRD group (n=14)	control group (n=28)	*P*
Age (years)(mean±SD)	60.07±9.20	54.54±10.12	0.093
Gender			1.000
Male	6	13	
Female	8	15	
Duration of DM (n)			0.451
<10 years	2	8	
>10 years	12	20	
Treatment regimen for DM (n)			0.406
No insulin	10	24	
Insulin	4	4	
Extent of fibrovascular proliferation (n)			
Grade 1	4	9	0.841
Grade 2	7	15	0.845
Grade 3	3	4	0.632
Systemic hypertension (n)	9	12	0.326

P<0.05 was considered statistically significant.

SD, standard deviation; DM, diabetes mellitus.

Table 2 Risk factors of TRD in non-silicone oil tamponade eyes after vitrectomy for proliferative diabetic retinopathy

	TRD group (n=14)	Control group (n=28)	*P*
History of ocular treatment			
Anti-VEGF drugs (n)			0.383
Yes	3	3	
No	11	25	
PRP (n)			0.015
Yes	1	13	
No	13	15	
Phacoemulsification (n)			1.000
Yes	2	4	
No	12	24	
Laboratory tests (mean±SD)			
serum total protein, g/L	67.79	71.59	0.053
serum albumin, g/L	40.14	43.77	0.001
blood urea nitrogen, mmol/L	7.47	6.024	0.049
serum creatinine, umol/L	92.93	66.18	0.001
blood glucose, mmol/L	7.38	6.70	0.278
glycated albumin, %	18.53	17.19	0.445
uric acid, umol/L	293.43	311.57	0.468

P<0.05 was considered statistically significant.

SD, standard deviation; VEGF, vascular endothelial growth factor; PRP, panretinal photocoagulation.

Table 3 Multivariate risk factor for TRD in non-silicone oil tamponade eyes after vitrectomy for proliferative diabetic retinopathy

	B	S.E.	Wals	df	Sig	Exp(B)	EXP (B) 95% CI
Serum albumin	0.394	0.178	4.897	1	0.027	1.483	1.046-2.103
blood urea nitrogen	-0.374	0.243	2.368	1	0.124	0.688	0.428-1.108
serum creatinine	-0.032	0.028	1.355	1	0.244	0.968	0.917-1.022
Retinal laser photocoagulation	-2.758	1.505	3.357	1	0.067	0.063	0.003-1.212
Constant	-8.783	7.287	1.453	1	0.228	0.000	——