·Clinical Research·

# Risk factors of rhegmatogenous retinal detachment associated with choroidal detachment in Chinese patients

*Yong-Hao Gu, Gen-Jie Ke, Lin Wang, Qi-Hong Gu, En-Liang Zhou, Hong-Biao Pan, Shi-Ying Wang*

Department of Ophthalmology, Anhui Provincial Hospital affiliated to Anhui Medical University, Hefei 230001, Anhui Province, China

**Correspondence to:** Yong-Hao Gu. Department of Ophthalmology, Anhui Provincial Hospital affiliated to Anhui Medical University, 7# Road Lujiang, Hefei 230001, Anhui Province, China. aerolplane@hotmail.com

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## Abstract

• **AIM: To comprehensively analyze the risk factors of rhegmatogenous retinal detachment (RRD) associated with choroidal detachment (CD).**

• **METHODS: A total of 265 eyes of 265 consecutive cases of RRD were retrospectively analyzed. All patients had systemic and ophthalmologic examination. CD was diagnosed by indirect ophthalmoscopy, B -scan ultrasonography, and ultrasound biomicroscope (UBM). Each parameter was compared between patients of RRD and rhegmatogenous retinal detachment associated with choroidal detachment (RRDCD). Logistic regression analysis was used to determine the independent risk factors of CD.**

• **RESULTS: There were 52 eyes (19.62%) with CD. Pseudophakia was more commonly seen in RRDCD (21.15% *vs* 6.10%, $P$=0.002). Intraocular pressure (IOP) was lower (8.60±3.62 *vs* 12.96±3.55, $P$<0.001), best-corrected visual acuity was worse [3.00 (2.00 to 3.00) vs 1.92 (1.22 to 3.00), $P$=0.001], and refractive error was more myopic [-4 (-9 to -2) vs -2 (-6 to 0), $P$=0.007] in RRDCD. Eyes with RRDCD had larger extent of retinal detachment ($P$=0.007). In RRDCD, 34.62% of eyes presented with multiple holes ($P$=0.044) and 25.00% with macular holes ($P$=0.012), compared with 20.66% and 14.08% in RRD. High myopia ($P$=0.039), low IOP ($P$=0.017), and larger extent of retinal detachment ($P$<0.001) were significant and independent risk factors for developing CD.**

• **CONCLUSION: For CD in RRD, related factors include BCVA, IOP, lens status, refractive error, extent of retinal detachment, number of holes, and macular hole. Larger extent of retinal detachment, high myopia, and low IOP are significant and independent risk factors.**

• **KEYWORDS:** choroidal detachment; retinal detachment; risk factor

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## INTRODUCTION

The prevalence of choroidal detachment (CD) in rhegmatogenous retinal detachment (RRD) is 2%-4.5% in western countries [1-3]. Most of these eyes have low intraocular pressure (IOP), uveal inflammation, and increased breakdown of the blood-retinal barrier, and always present with rapid progression, poor prognosis, and difficult treatment [4]. It is independently associated with retinal detachment repair failure [5]. Referring to the collection of fluid in the potential space of suprachoroid, the pathogenic mechanism of CD has not yet been clearly delineated [6]. Previous reported risk factors include high myopia, aphakia or psedophakia, old age, and presence of macular hole [1-3,7], but most of these studies have lacked detailed statistical comparison. The aim of this study was to comprehensively analyze the risk factors of combined choroidal and retinal detachment patients in order to improve the understanding and treatment of these conditions.

## SUBJECTS AND METHODS

We conducted a retrospective review of 265 consecutive cases (265 eyes) of primary RRD at Anhui Provincial Hospital in Hefei, China between October 2012 and June 2014. The study was performed in accordance with the tenets of the Declaration of Helsinki and was approved by the Institutional Review Board of Anhui Provincial Hospital affiliated to Anhui Medical University. The informed consent was obtained orally from all patients. Patients were excluded from the study if they had traction-RRD, as seen in diabetes, history of ocular trauma or vitreoretinal surgery, or congenital ocular syndromes with the potential to induce vitreoretinal abnormalities. Cases whose causative breaks were detected intraoperatively were included in the study. CD was diagnosed with indirect ophthalmoscopy, B-scan ultrasonography (CineScan, Quantel Medical, France), and

ultrasound biomicroscope (UBM) (SW3200L, Suoer, China) by two experienced technicians independently.

General information collected included age at presentation, sex, medical and ocular history, duration of the presenting syndrome, and medical history of systemic disease (diabetes mellitus and hypertension). Onset of illness was defined as the time between a sudden blurring of vision or/and partial loss of vision field and apply to the physician. All patients underwent a full ophthalmic evaluation, including best-corrected visual acuity (BCVA), slit-lamp examination, binocular indirect ophthalmoscopy, applanation tonometry, ultrasonography, and UBM. Lens status, refractive error, axial length, involvement of macular hole, extent of retinal detachment, and number of causative retinal breaks were recorded for analysis. Axial length was measured with A-scan ultrasonagraphy (Tomey, AL-100, Japan). Two experienced technicians would modify the data for those with retinal detachment involving posterior pole by differentiating the signal of detached retina and sclera. Because optometry is difficult in patients with retinal detachment, refractive error in these cases was obtained with patients wearing glasses or by accessing their optometry records before the onset of RRD. For patients without optometry results, if previous visual acuity of both eyes was same, refractive error was evaluated by retinoscopy optometry in the other eye. Refractive error of all 24 patients of pseudophakic was evaluated by their wearing glasses or optometry records prior to cataract surgery. Snellen visual acuities were converted to the logarithm of the minimum angle of resolution (logMAR) for statistical analysis. Counting figures, hand movement, and light perception were recorded as logMAR 2, 3, and 4, respectively.

**Statistical Analysis** Statistical analyses were done with SPSS 19.0 software (SPSS Inc, Chicago, Illinois, USA). Quantitative data were checked for normality of distribution by Kolmogorov-Smirnov analysis. The results showed all factors except for IOP did not follow the normal distribution; hence we expressed them in terms of median (quartile1-quartile3) and used the Mann-Whitney $U$ test to assess intergroup differences. IOP was expressed as mean±standard deviation and analyzed by independent-sample $t$- test. Qualitative values were compared by the Fisher exact test or $\chi^2$ test. Finally, stepwise logistic regression was used to determine the independent clinical risk factors of CD. Factors that were significant at the level of $P$<0.4 in the univariate analysis were included in the logistic regression. Significance was defined as $P$<0.05 for all analyses.

## RESULTS

This study included 265 eyes (cases) with RRD. Of these, 52 eyes (19.62% of cases) involved CD. For analysis, we included 213 eyes in a group comprised of rhegmatogenous retinal detachment without choroidal detachment (Group RRD) and 52 eyes in a separate group involving rhegmatogenous retinal detachment with choroidal detachment (Group RRDCD).

Table 1 compares demographic and medical parameters between the two groups. There were no significant differences between the two groups in sex ratio, age, onset of illness, or medical history of hypertension and diabetes.

Eyes in Group RRDCD had larger extent of retinal detachment than eyes in Group RRD ($P$<0.001), and 78.85% eyes in Group RRDCD had nearly total retinal detachment (>3 quadrants) compared with 13.62% eyes in Group RRD. In Group RRDCD, 34.62% of eyes presented with more than three holes and 25.00% with macular holes. In Group RRD, 20.66% of eyes presented with more than three holes and 14.08% with macular holes. There were significant differences between the two groups ($P$=0.044, $P$=0.012, respectively).

Ten related factors were included in stepwise logistic regression analysis. The results showed that high myopia, low IOP, and larger extent of retinal detachment were significant factors for developing CD (Table 2).

## DISCUSSION

In this study, we performed an analysis of the risk factors for RRDCD. A retrospective review of 265 consecutive cases of RRD was performed and 52 cases with CD were found. The incidence of CD in RRD in our report is 19.62%, which is higher than previous reports in Western countries[1-3].

The higher rates of CD in our study might be attributable to the higher prevalence of high myopia in Chinese and the use of UBM. As our results have shown, severe myopia was one of the main risk factors for RRDCD. Chinese people have the higher prevalence of myopia than non-Chinese people, especially for high myopia [8-10]. In the present study, 44.18% of the eyes with CD were high myopia, compared with 25% and 22.7% in Gottlieb's[2] and Seelenfreund *et al*'s[1] reports, respectively. A study [11] on RRDCD in Chinese patients had also shown that 51.52% eyes of RRDCD had high myopia, which was similar to our results.

UBM can detect the detachment of the ciliary body and anterior choroid, which is difficult for indirect ophthalmoscopy and B-type ultrasound[12]. In our study, some patients presented with characteristics of CD, such as hypotony, deeper anterior chamber, or iritis, but no CD was detected on fundus examination and B-type ultrasound. UBM examination found signs of detachment of ciliary body or anterior choroid in some of these patients. Li *et al*[11] showed that UBM was able to detect those RRDCD cases that had been previously missed on three-mirror funduscope or B-type ultrasound; they also demonstrated that UBM examination can reduce the false negative rate of RRDCD.

**Table 1 Comparison between patients with choroidal detachment and patients without choroidal detachment**

| Clinical factors | Group RRD (*n*=213) | Group RRDCD (*n*=52) | *P* |
|---|---|---|---|
| Sex ratio (M/F) | 102/111 | 31/21 | 0.164 |
| Age [a (Q1-Q3) ] | 56 (42-62) | 56.5 (44-64) | 0.326 |
| Onset of illness [d (Q1-Q3) ] | 15 (7-30) | 15 (7-30) | 0.986 |
| Medical history of hypertension (*n*) | 21 | 5 | 0.958 |
| Medical history of diabetes (*n*) | 8 | 3 | 0.456 |
| BCVA [logMAR (Q1-Q3)] | 1.92 (1.22-3.00) | 3.00 (2.00-3.00) | 0.001 |
| IOP (mm Hg) ( $\bar{x} \pm s$ ) | 12.96±3.55 | 8.60±3.62 | <0.001 |
| [a]Refractive error (diopter) [median (Q1-Q3) ] | -2 (-6 to 0) | -4 (-9 to -2) | 0.007 |
| Lens status (*n*) | | | |
| Phakic | 200 | 41 | 0.002 |
| Pseudophakia | 13 | 11 | |
| Axial length (mm) [Median (Q1-Q3) ] | 24.11 (22.88-26.30) | 24.70 (23.39-27.59) | 0.128 |
| Extent of retinal detachment (*n*) | | | |
| 1 quadrant | 36 | 1 | |
| 2 quadrants | 103 | 4 | <0.001 |
| 3 quadrants | 45 | 6 | |
| 4 quadrants | 29 | 41 | |
| No. of retinal holes (*n*) | | | |
| 1-2 | 169 | 34 | 0.044 |
| ≥3 | 44 | 18 | |
| Macular hole (*n*) | 30 | 13 | 0.012 |

IOP was expressed as mean±standard deviation and other quantitative results were expressed as Median (quartile1-quartile3) [median (Q1-Q3)]. Axial length was measured with A-scan ultrasonagraphy. [a]Refractive error data was obtained from 179 cases of RRD and 43 cases of RRDCD.

**Table 2 Relative risks for choroidal detachment** *n* (%)

| Risk factors | Without choroidal detachment (*n*=213) | With choroidal detachment (*n*=52) | Odds ratio (95%CI) | *P* |
|---|---|---|---|---|
| Gender (male) | 102 (47.8) | 31 (59.61) | 0.961 (0.477-1.937) | 0.912 |
| Old age | 80 (37.56) | 23 (44.23) | 1.740 (0.817-3.705) | 0.151 |
| Severe impaired VA | 149 (69.95) | 47 (90.38) | 0.837 (0.355-1.974) | 0.685 |
| Pseudophakia | 13 (6.10) | 11 (21.15) | 1.680 (0.573-4.929) | 0.345 |
| Low IOP | 24 (11.27) | 34 (65.38) | 2.442 (1.173-5.083) | 0.017 |
| [a]High myopia | 53 (29.61) | 19 (44.18) | 3.619 (1.069-12.259) | 0.039 |
| Long AL | 57 (26.76) | 18 (34.62) | 0.508 (0.150-1.721) | 0.277 |
| Extent of retinal detachment (1/2/3/4 quadrants) | 36/103/45/29 | 1/4/6/41 | 0.107 (0.030-0.383) | 0.001 |
| | | | 0.070 (0.028-0.176) | <0.001 |
| | | | 0.141 (0.055-0.358) | <0.001 |
| Multiple holes | 44 (20.66) | 18 (34.62) | 1.028 (0.454-2.327) | 0.948 |
| Macular hole (+) | 30 (14.08) | 13 (25.00) | 0.476 (0.179-1.265) | 0.137 |

Old age: ≥60; Severely impaired VA: VA<0.05 (logMAR>1.30); Low IOP: IOP<10 mm Hg; High myopia: refractive error ≥-6.0 D; Long AL: axial length ≥26.0 mm; Multiple holes: Causative holes ≥3. [a]Refractive error data of high myopia was obtained from 179 cases of RRD and 43 cases of RRDCD.

In our study, we did not find a relationship between choroidal detachment and systemic factors including sex, age, onset of illness, or medical history of hypertension and diabetes. Some reports [1,4,13] have concluded that the majority of RRDCD patients were older, and age is a factor associating with RRDCD. But these studies lacked detailed statistical comparisons. A total of 44.23% cases of RRDCD in our study were older than 60, which agreed with these reports. However, statistical analysis failed to detect a significant relation with CD.

Previous reports [1-5,11,13] have shown that ocular predisposing factors include hypotony, aphakia/pseudophakia, high myopia, and macular hole. According to our study, the BCVA, IOP, lens status, refractive error, extent of retinal detachment, number of holes, and presence of macular hole were related to RRDCD. Low IOP, high myopia, and larger

extent of retinal detachment were significant and independent risk factors for RRDCD.

We found that patients with RRDCD tend to have worse visual acuity, which has not been described by other reports. It might be caused by larger extent of retinal detachment involving macular, macular hole, and amblyopia induced by uncorrected high myopia. Moreover, it also may be due to inherent derangement and retinal pigment epithelial (RPE) cells abnormality from choroidal and retina detachment.

In the present study, no cases of aphakia were involved. Our results showed pseudophakia was related to RRDCD. Cataract surgery could disturb the vitreous and cause its traction and liquefaction, which might induce macular hole, multiple retinal tear, or larger extent of retinal detachment[14], especially when the rupture of posterior capsule occurred[15]. In our cases with pseudophakia, we could not find detailed medical records describing posterior capsule during their previous cataract surgery. Further investigation is needed to understand this relationship.

RRDCD cases tended to have multiple retinal breaks. A previous study [11] also described that 33% of patients with RRDCD have multiple holes and that there was significant difference compared with RRD patients. Our data was similar to it, which suggests that surgeons should carefully search for additional holes when operating on RRDCD patients.

Kang *et al* [16] reported macular hole as a risk factor of RRDCD. These authors concluded that in cases of RRD with macular holes and posterior vitreous detachment, the liquefied vitreous passes through macular hole without inhibition and is absorbed by RPE cells, which results in hypotony and CD[13,16]. Our results are in agreement with that study. Moreover, 11 out of 13 cases of macular hole with RRDCD in our study had high myopia and with posterior staphyloma, which implies that more accurate, myopic macular hole, may be a risk factor of RRDCD. However, this is just speculative as the number of cases was relatively small, which yielded low reliability for statistical analysis.

Hypotony was one of the essential characteristics and independent risk factors of RRDCD in our report. Although hypotony may be a consequence of RRDCD rather than a risk factor, most authors agree that ciliary edema and detachment caused by inflammatory response reduces aqueous secretion, induces hypotony, and the hypotony could favor further exudation of fluid out of vessels into the tissue space and aggravate CD in turn [1-2,13,16]. So hypotony takes part in the pathogenesis of RRDCD to some extent and might be set as a risk factor.

High myopia is defined as having a refractive error of at least -6.0 D or an axial length more than 26.0 mm in the study [17-18]. Our results showed that it is the independent risk factors of RRDCD. Vitreous liquefaction is more prone to take place in eyes with high myopia[19], which predisposing to retinal tear or macular hole formation [20]. Furthermore, eyes with high myopia had much thinner choroid[21], so the drop of IOP in RRDCD may aggravate transudation of fluid and choroidal detachment in these eyes [2]. These pathologic changes might associate with the longer axial length and staphyloma. However, as we showed although refractive error was much more myopic in Group RRDCD than in Group RRD, while cases with high myopia ($\geqslant$-6.0 D) in Group RRDCD were significantly more than that in Group RRD, there is no difference in axial length between two groups. There are three possibilities to explain this. First, there is measurement bias by A-type ultrasound, especially in patients with RRDCD; second, sample size is relatively small. There are 18 cases of RRD with axial length longer than 26.0 mm, which might yield experimental error; finally, high myopes tended to have cataract of higher nuclear density, which might influence the refractive power [22]. So it might be not axial length, but refractive factors such as lens or cornea affecting the refractive error. In our study, cataract type and keratometric values of cases had not been measured and recorded. Thus, further investigation should be taken to elucidate this.

A significantly greater extent of retinal detachment was found in RRDCD patients, a finding that has not been described by any other study as a risk factor. Gottlieb [2] and Seelenfreund *et al* [1] described totally detached retinas in 31/35 (88.57%) and 41/50 (82%) RRDCD eyes, which agrees with our present data. Larger extent of retinal detachment might be more commonly associated with macular detachment. This might partly explain the worse visual acuity in RRDCD patients. Larger extent of RD and multiple holes would expose more retinal pigment epithelium cells to vitreous or subretinal fluid, which could lead to more severe ocular inflammation and more outflow of fluid through the RPE [23-24], which play a role in pathogenesis of hypotony and CD[13].

Clinical treatment of RRDCD remains challenging. The retinal reattachment ratio after the surgery is still lower than that of uncomplicated RRD patients [4]. Our results may be helpful in understanding pathogenesis and treatment of this disease.

There are several other limitations in our study. First, the documented extent of retinal detachment might be masked by CD. A more accurate description could be made after the alleviation of CD. Second, the sample size is limited. Larger samples would provide more accurate analysis and multicenter clinical studies are needed to confirm the findings. Third, this study was undertaken in a Chinese population. Hence there is a population bias and the results and conclusions may not be applicable to the rest of the world population.

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