The Risk Factors of the Progression of Rhegmatogenous Retinal Detachment on Patients with the Fourteen-day Quarantine in the Early Period of COVID-19 Outbreak

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Research Article

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Abstract

Backgrounds: The COVID-19 pandemic has great impact on hospitals and patients. The fourteen-day quarantine caused surgery of RRD postponed. To explore the risk factors of rhegmatogenous retinal detachment (RRD) progression in a group of patients whose surgery was postponed during the top-level emergency response of COVID-19.

Methods: Retrospective case series study. The information on RRD patients who received surgeries in Beijing Tongren Hospital's retina service from February 16, 2020, to April 30, 2020 has been collected retrospectively. The history, manifestation on presentation and admission, and progression of RRD were recorded. RRD progression was defined as the presence of either choroidal detachment (CD) or proliferative vitreoretinopathy (PVR) progression during the quarantine period. Risk factors were analyzed using the Cox proportional hazards model, survival analysis, and logistic regression.

Results: There were 79 cases enrolled in this study. The median time from the patients' presentation at the clinic to admission for surgery was 14 days (3–61 days). There were 70 cases (88.6%) who did not present to the hospital within one week of the onset of visual symptoms. There were 69 (87.3%) macular-off cases at the presentation. There were 27 (34.2%) cases combined with choroidal detachment. There were 49 (62.0%) cases with PVR B, 22 (27.8%) cases with PVR C, 4 (5.1%) cases with PVR D, and 4 (5.1%) cases with PVR A. After the 14-day quarantine, 21 (26.6%) cases showed RRD progression, and 9 cases showed RD regression at the time of surgery. Neither the time of onset of the visual symptom (p=0.46) nor the time between presentation and admission (p=0.31) was significantly different between the patients with RRD progression and patients without RRD progression. The combination of CD (3.61, 1.86-6.99, p=0.001) and retinal breaks located posterior to the equator (3.78, 1.25-11.45, p=0.02) were factors related to the progression of RRD.

Conclusions: In the cases enrolled in our study during the COVID-19 outbreak period, the RRD progression risk factors included a combination of CD and retinal breaks posterior to the equator. Ophthalmologists should schedule the surgeries for RRD patients with these signs as soon as possible.

Background

Rhegmatogenous retinal detachment (RRD) is a sight-threatening ocular disease requiring surgical intervention[1]; it has a prevalence of 6.3–17.9/100 thousand people [2]. It can lead to the development of choroidal detachment (CD) [3, 4], the progression of proliferative vitreoretinopathy (PVR) [5, 6], and irreversible visual damage [7] if it is not treated in time. It has been reported that the poor visual acuity outcome is related to the delay of surgery in RRD patients[8, 9], and it is recommended to perform surgery within three days of the onset of symptoms to achieve a better visual outcome[8, 10–12]. The outcome of long-standing RRD is not well addressed.

The outbreak of the highly contagious coronavirus disease (COVID-19) has a significant impact on health services worldwide. In China, Beijing upgraded its emergency response to top-level three days after ten

COVID-19 cases were first confirmed in February 2020. A 14-day self-quarantine for all patients who were going to be admitted was announced later. In response to the pandemic, most elective surgeries were postponed except for urgent surgeries [1, 13, 14]. RRD surgeries were carried out in patients who had a negative screening result for COVID-19. Since there was no laboratory test of the COVID-19 virus in the early days of the pandemic, the COVID-19 screening in our center included a 14-day self-quarantine with daily self-reported normal body temperature, as well as a normal blood cell count and pulmonary CT scan before admission. During the period, the RRD patients could only visit the emergency room for diagnosis and had to wait at least14 days to be operated on in the ward.

We have tried to investigate the progression of RRD after a 14-day quarantine. We looked for the risk factors related to the progression of RRD.

Methods

We retrospectively reviewed the RRD cases who underwent surgery from February 16, 2020, to April 30, 2020, in Beijing Tongren Eye center. This study was approved by the Ethics Committee of Beijing Tongren Hospital and adhered to the tenets of the Declaration of Helsinki.

All patients were registered as soon as they were diagnosed at the outpatient clinics. They were asked to report their daily temperature and quarantine in Beijing. After the quarantine, patients were informed to go to the hospital to screen for the COVID-19, take laboratory tests, and receive ocular examinations for surgery. We collected the preoperative characteristics of the patients. These characteristics included age, gender, presurgery waiting times (from visual symptom to surgery), quarantine time (from being diagnosed to surgery), history of previous eye trauma, previous surgical history, preoperative visual acuity (VA), lens status, the extent of retinal detachment, location of retina breaks, proliferative vitreoretinopathy (PVR), choroidal detachment (CD) and congenital vitreoretinal diseases (coloboma, familial exudative vitreoretinopathy et al.). The changes of RD at admission compared to the record of the first time at the outpatient clinic were recorded. The focus was placed on the development and progression of CD and PVR. PVR progression was defined as the growth of membranes on both surfaces of the detached retina and on the posterior surface of the detached vitreous gel[5]. CD was defined as presenting with low intraocular pressure, anterior chamber inflammation, choroidal detachment were found by either indirect ophthalmoscopy or B scan[4]. RD progression was recorded as at least one of the following conditions developed at the time of admission compared to the initial presentation: 1) development of CD; 2) progression of PVR; 3) the extent of RRD progressed to 3/4 quadrants of 4 quadrants RRD.

Statistical analysis was performed using R version 3.20 (http://www. R-project.org). Patient characteristics were retrieved from their medical charts and recorded in Epidata Entry Clientversion2.0.3.15 (http://epidata.dk). Mean and standard deviation (SD) were calculated for continuous variables with a normal distribution. Median with quartiles was calculated for continuous variables with a non-normal distribution. T-test or Mann-Whitney U test was carried out for continuous variables. Chi-square test or Fisher's exact test was carried out for discrete data. The Cox proportional-

hazards model was used to investigate the association between patients' quarantine time and several characteristics that may be related to RD progression. The survival analysis, Kaplan-Meier curve, and log-rank test were performed on the related factors. The binary backward stepwise logistic regression model was carried out to explore the potential risk factors at the initial presentation. One variable was included or excluded from the model each time by comparing the Akaike information criterion (AIC) value, and the model with the lowest AIC was chosen.

Results

Seventy-nine patients were enrolled in this study, with a majority of male patients (70.9%). The average age was 49.8 ± 15.7 (12–74) years old. The median quarantine time was 14 days (3–61, IQR 12). The median time between the onset of symptoms and operation was 28 days (7– 336, IQR 35). There were 70 (88.6%) patients who failed to present to the hospital within one week after the onset of their visual symptoms.

1. Basic characteristics at presentation

There were 45 (57.0%) patients with primary RRD, 27 (34.2%) patients with RRD-CD, five patients (6.3%) with recurrent RRD (one previously had scleral buckling, and four had pars plana vitrectomy (PPV) and silicone oil tamponade), and two patients (2.5%) with combined coloboma.

The percentage of pseudophakic eyes and PM was 18 (22.8%), 36.7%(29/79), respectively. Six patients had a history of PPV, while five patients had a history of scleral buckling. There were 44 (55.7%) patients whose preoperative VA was less than 0.02, 28 (35.5%) patients whose preoperative VA was between 0.02 and 0.4, and seven (8.9%) patients whose preoperative VA was equal to or greater than 0.5.

There were 42(53.2%)patients with four quadrants RD. There were 68（86.1%）patients with a macular-off RD.

There were 49 (62.0%) patients with PVR B, 22 (27.8%) patients with PVR C, four (5.1%) patients with PVR D, and four (5.1%) patients with APVR. The prevalence of PVR C-D and APVR was higher in patients with RRD-CD than patients with RRD (44.1%, 31.1%, $p = 0.01$).

Thirty-seven (46.8%) patients' retinal breaks were located anterior to the equator, 38 (48.1%) patients' retinal breaks were located posterior to the equator, and four (5.1%) patients had a macular hole (one of them combined with tear which was posterior to the equator). RRD-CD prevalence was higher in patients with retinal breaks located posterior to the equator than patients with retinal breaks located anterior to the equator (55.9%, 22.2%, $p = 0.01$).

2. Changes of RRD at admission

Twenty-one (26.6%) patients had a progression of RD after quarantine. Among them, 16 RRD-CD patients had a progression of PVR (4 patients from C1 to D2, 6 patients from C1 to C3, and 2 recurrent patients with anterior PVR), and 5 RRD patients developed CD (1 patient had a simultaneous progression of PVR). Nine (11.4%) patients had a regression of RD, while 49 (70.6%) patients had no significant RD progression, including 11 RRD-CD patients.

Fifty-seven patients received PPV, while 22 patients received scleral buckling. Among the patients who received PPV, ten patients had preoperative posterior vitreous detachment, 25 patients whose PVD was easily induced during vitrectomy, and 28 patients had sticky vitreous, which was hard to peal during vitrectomy.

3. Factors that may be related to the progression of RD (Table 1)

We divided the patients into two groups based on whether RD progressed at admission. There was a significant difference between the two groups in terms of the following factors:: gender ($p = 0.04$), the combination of CD ($p < 0.001$), previous history of vitrectomy ($p = 0.04$), location of retinal breaks ($p < 0.001$), macular hole ($p = 0.03$), macular detachment ($p = 0.05$), sticky vitreous during vitrectomy ($p < 0.001$),and VA distribution ($p = 0.04$). There was not a significant difference in quarantine time ($p = 0.46$) or the time between the onset of symptoms and presentation ($p = 0.31$) in the two groups (Table 1).

Table 1
Initial characteristics of RRD patients enrolled

	Patients with RD progression (21)	Patients without RD progression(58)	*p* value
Age (mean ± SB)	51.1 ± 12.2	49.3 ± 16.9	0.62
Gender (male, n, %)	19, 90.5%	37, 63.8%	0.04
Time between diagnosis and surgery (median, range,day)	18 (3–61)	13(11–75)	0.46
Time between onset of symptom and surgery (median, range,day)	28 (7–84)	28 (7-336)	0.31
Diagnosis			< 0.001*
RRD (n,%)	2, 9.5%	42,72.4%	
RRD-CD(n,%)	14, 66.7%	14,24.1%	
Recurrent RRD(n,%)	3,14.2%	2, 1.7%	
Combined coloboma(n,%)	2,9.5%	0	
pseudophakic(n,%)	7,33.3%	11,19.0%	0.22*
PM (n,%)	8,38.1%	21,36.2%	1*
Previous PPV(n,%)	4,19.0%	2,3.4%	0.04 *
Previous SB(n,%)	1,4.8%	4,6.9%	1 *
Location of retinal break			0.03
Anterior to equator (n,%)	1,4.8%	36,62.1%	< 0.001
Posterior to equator (n,%)	17,81.0%	21,36.2%	
Macular hole(n,%)	3,14.3%	1,1.7%	0.05
PVR			0.35
B(n,%)	12,57.1%	37,63.8%	
C(n,%)	5,23.8%	17,29.3%	
D(n,%)	2,9.5%	2,3.4%	
APVR(n,%)	2,9.5%	2,3.4%	
Macular-off(n,%)	21,100%	48,82.8%	0.05
PVD			< 0.001*
Presurgery VA			0.04

	Patients with RD progression (21)	Patients without RD progression(58)	*p* value
Less than 0.02(n,%)	14,66.7%	21,36.2%	
[0.02–0.1) (n,%)	7,33.3%	30,51.7	
>=0.5(n,%)	0	7,12.1%	

The Cox proportional-hazards model showed that, patients with RRD-CD at presentation were 3.61 times more likely to have RD progression (1.86–6.99, p = 0.001) than patients without CD; patients with retinal breaks located posterior to the equator were 3.78 times more likely to have RD progression (1.25–11.45, $p = 0.02$) compared to patients with retinal breaks located anterior to the equator (Wald test F = 27.64, $p < 0.001$, LogRank test F = 46.47, $p < 0.001$). The median survival time for RD progression was 61 days after the onset of symptoms (Fig. 1–2). The log-rank test in survival analysis showed that the median survival time for RD progression was 13.5 days in patients with macular hole, 22 days in patients with retinal breaks located posterior to the equator, 14 days in patients with giant tears, 18.5 days in patients with unattached retina after surgery, 22 days in RRD-CD patients, and 18 days in patients with sticky vitreous.

The logistic regression analysis showed that female (25, 2.04–1000, $p = 0.03$), combination with CD (5.22, 2.18–17.66, $p = 0.001$), and retinal breaks located posterior to the equator (17.91, 3.44–224.56, $p = 0.004$) were factors that may be related to RD progression (AIC = 52.23, AUC = 0.918).

Discussion

The 14-day quarantine during the early period of the COVID-19 pandemic provided us the chance to observe the short natural course of RRD when the surgery had to be delayed. We found that 26.6% of patients had RD progression, while 11.4% of patients had RD regression, 70.6% of patients had no significant RD progression after the quarantine. We further investigated the initial characteristics that may be related to the RD progression.

Previous reports focusing on RD progression find that prolonged presurgery waiting time is related to the development of macular-off RD[12], irreversible macular damage[15–17], PVR progression[18], and development of CD[19]. We chose PVR progression, the progression of RD's extent, and CD's development as the signs for RD progression. Since the prevalence of macular detachment (86.1%) in our group of patients was much higher than what was reported in previous studies [10, 20], which focused on RD's progression from macular-on to macular-off, we could not use the development of macular-off as a sign for RD progression.

CD is related to retinal detachment surgery failure[21], and its prevalence is 8.6%[22] – 18.79[23]% in Chinese RRD patients. We had a much higher prevalence of RRD-CD in our group of patients at 34.2%. The prevalence of PVR C-D is higher in RRD-CD patients at 28[24]-66.9%[25] compared to RRD patients in previous reports. PVR progression was found in 16 RRD-CD patients. We found a similar result of PVR C-D at 44.1% in RRD-CD patients and 33.1% in RRD patients. We found a retinal break located posterior to

the equator was related to the RRD-CD development, similar to previously reported[22]. Our result showed RRD-CD patients were much more likely to experience RD progression shortly after diagnosis. The median time for RD progression in RRD-CD patients was 22 days after the onset of the symptom. Our result suggested that patients with RRD-CD should be operated on without delay in case of fast progression of RD.

PVR is the most common cause of RRD surgery failure [5, 21]. The progression of PVR is reported to be related to the following conditions: a giant tear, a long course of RRD, vitreous hemorrhage, pseudophakic eye, the combination of CD, gas tamponade, and cryotherapy[6, 26]. The chance of developing PVR B-C has been reported to be higher in patients whose presurgery waiting times are longer than 40 days[18]. The prevalence of PVR C-D and APVR in our study was 38.0%. It was similar to what was previously reported at 12.9–21.6%[27] in patients with scleral buckling and 26.9–41.6%[18, 27, 28] in patients with PPV. The initial presentation of PVR in our group of patients was not related to RD progression. The reasons may be related to the fact that the presurgery waiting time was too short to observe PVR progression. In other words, except for patients with CD, the presence of PVR was not related to short-time RD progression.

In addition to the presence of CD and the location of a retinal break, the survival analysis found that the median survival time for RD progression was short in the following conditions in survival analysis: macular hole (13.5 days), giant tear (14 days), combining with coloboma (6 days), and recurrent RD (18.5 days). We failed to show the relationship between the factors mentioned above to RD progression due to the small sample size. We still need to pay extra attention to RRD patients with the conditions mentioned above in the case of RD progression.

The limitation of the study was due to the retrospective character and the limited case number. During the COVID-19 pandemic, we gained the chance to observe the natural course of RRD. The prolonged presurgery waiting time may lead to a high prevalence of CD, PVR C-D, and macular-off. Since there was a high prevalence of 4 quadrants RD in our group of patients, the presence of more challenging cases at the initial presentation makes it impossible to progress to a more severe condition in a short follow-up time. More cases with newly developed RRD with short presurgery waiting time should be involved to see the risk factors for RD progression. Also, we did not report the outcomes of surgeries. We can not show the impact of prolonged presurgery waiting time on the prognosis of RRD.

Conclusion

We have reported a group of RRD patients with a high prevalence of PVR C-D, CD, and macular-off who underwent surgery during the COVID-19 pandemic. After the quarantine, some of the patients had RD progression. Ophthalmologists should pay more attention to RRD patients with CD or retinal breaks located posterior to the equator in case of RD progression shortly after the diagnosis.

List Of Abbreviations

Akaike information criterion AIC

choroidal detachment CD

coronavirus disease COVID-19

visual acuity BCVA

intraocular pressure IOP

intraocular lens IOL

macular hole MH

pathological myopia PM

posterior vitreous detachment PVD

proliferative vitreoretinopathy PVR

receiver operating characteristic curve ROC curve

rhegmatogenous retinal detachment RRD

retinal detachment RD

standard deviation SD

Declarations

Ethics declarations

Ethics approval and consent to participate:

This study was conducted in accordance with the Declaration of Helsinki and approved by the medical ethics committee of Beijing Tongren Hospital. The reference number is TRECKY 2020-071. The need for written informed consent was waived because of the retrospective design and use of deidentified patients data. This was also approved by the medical ethics committee of Beijing Tongren Hospital

Consent for publication:

Not applicable.

Availability of data and material

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

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

All authors read and approved the final manuscript. M Zhao collected and analyzed the data, she was the one major contributor in writing the manuscript. HC She interpreted the data she was one major contributor in writing and reviewing the manuscript. JP Li collected the data and reviewed the manuscript. NPL reviewed the manuscript and contribute in writing the manuscript.

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Figures

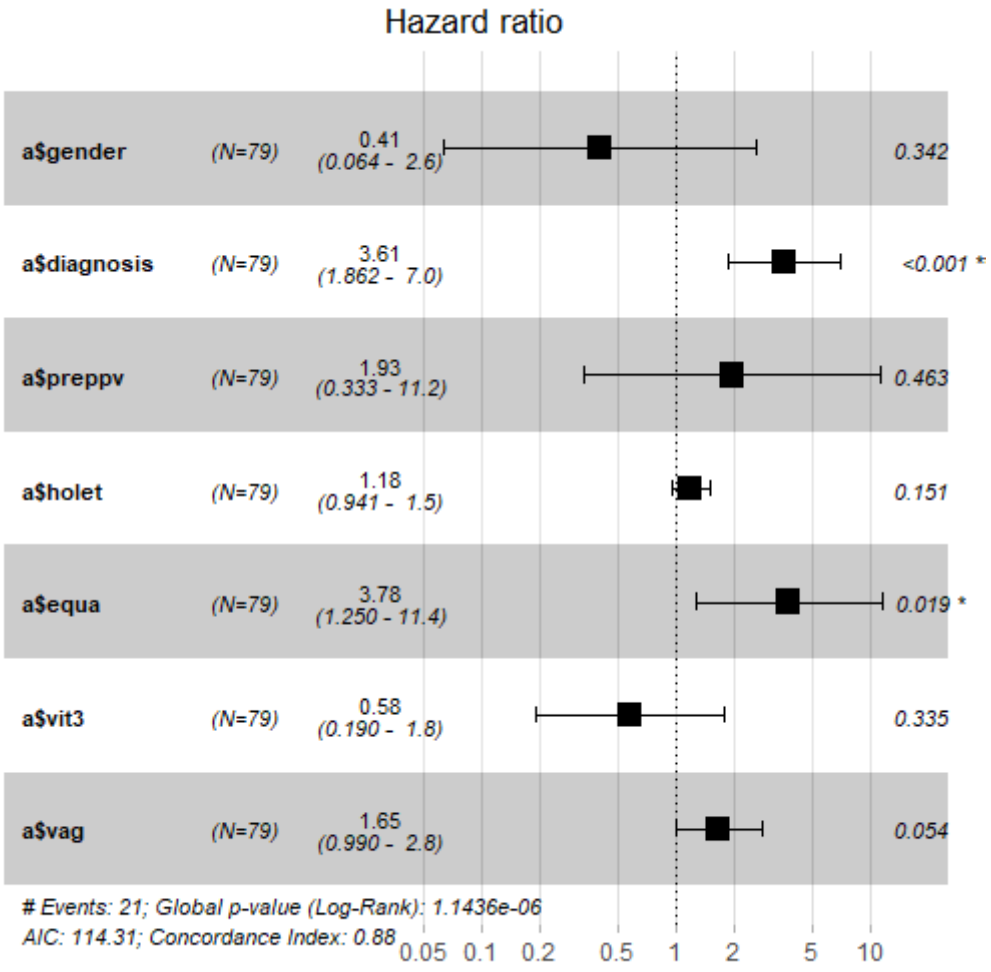

Figure 1

The tree-plot of Cox proportional-hazards model for RD progression The patients with RRD-CD at presentation were 3.61 times more likely to have RD progression (1.86-6.99, p=0.001) than patients without CD; patients with retinal breaks located posterior to the equator were 3.78 times more likely to have RD progression (1.25–11.45, p=0.02) compared to patients with retinal breaks located anterior to the equator (Wald test F=27.64, p<0.001, LogRank test F=46.47, p<0.001)

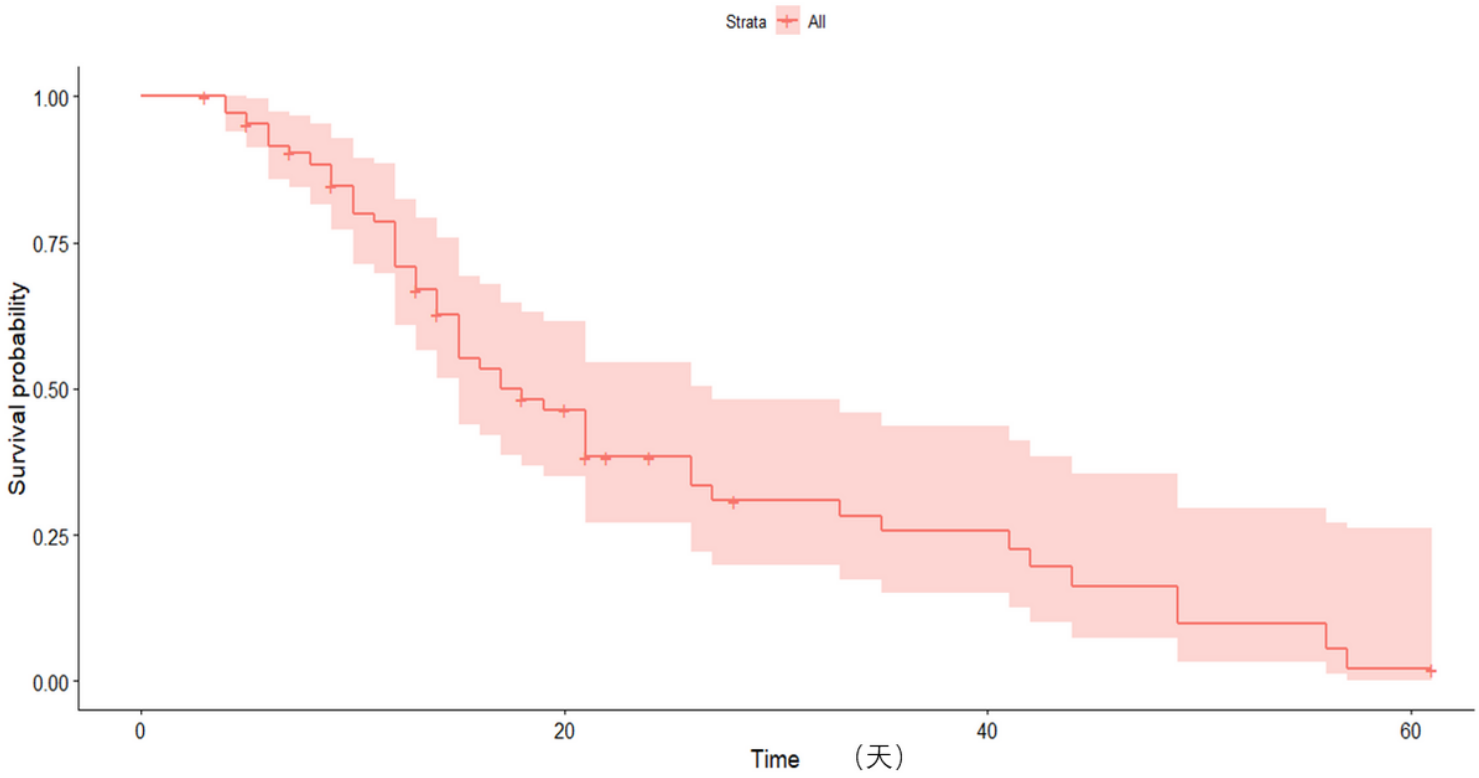

Figure 2

Kaplan-Meier survival analysis curve for the RD progression The median survival time for RD progression was 61 days after the onset of symptoms.