RESEARCH ARTICLE

Ocular findings, surgery details and outcomes in proliferative diabetic retinopathy patients with chronic kidney disease

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Abstract

Purpose

We investigated the influence of impaired renal function on fundus characteristics, pars-plana vitrectomy (PPV) details, and outcomes in patients with proliferative diabetic retinopathy (PDR).

Design

A retrospective cohort study

Methods

We investigated a consecutive series of PDR patients who underwent PPV. The diabetic complications, previous photocoagulation, intravitreal injections before PPV, ocular findings during PPV, surgical details, short-term visual outcome and post-PPV complications were recorded and compared between patients with and without impaired renal function.

Results

149 patients had normal renal function (67.7%), and 71 (32.3%) patients had impaired renal function; 85.4% of patients were identified with chronic kidney disease (CKD) during the pre-operative assessment. Impaired renal function was related to hypertension (3.40[1.58–7.29], p = 0.002), incomplete pan-retinal photocoagulation (PRP) (3.18[1.50–6.72], p = 0.002), severe fibrovascular membrane (8.19[3.43–19.54], p<0.001), and extensive retinal vascular closure (3.40[1.54–7.52], p = 0.002). There was a more frequent occurrence of severe intraoperative bleeding (56.3%, 32.2%, p = 0.001) and a higher percentage of intra-ocular subretinal fluid drainage (45.1%, 22.1%, p = 0.008) in patients with impaired renal function. The percentage of patients whose visual acuity (VA) increased was similar between the two groups (42.3%, 54.4%, p = 0.34).

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Conclusions

In PDR patients, screening for CKD was required before PPV. PDR patients with impaired renal function tended to have more severe ischemic retinal conditions. Comparable PPV outcomes could be obtained in patients with and without impaired renal damage.

Introduction

Proliferative diabetic retinopathy (PDR) and chronic kidney disease (CKD) are microvascular complications of diabetes mellitus (DM), with prevalence rates of 30–40% [1] and 18.45% [2], respectively. The two complications often coexist in patients with long-standing DM, and the prevalence of patients with an impaired estimated glomerular filtration rate (eGFR) in patients with diabetic retinopathy (DR) is 21.3–40.9% [3, 4]; conversely, the prevalence of DR in patients with an impaired eGFR is 26.7–38.5% [4, 5].

Fundus photography [6–8] is the standard screening tool for DR severity evaluation but can be of little value when the fundus of a patient is obscured by vitreous hemorrhage (VH) or tractional retinal detachment (tRD). The two conditions are commonly anticipated to be severe complications of PDR. PDR patients with VH or tRD may require pars plana vitrectomy (PPV), which provides the opportunity to investigate obscured fundus characteristics. The previous work on PDR patients who underwent PPV implies that with tolerable postoperative complications, patients with impaired renal function can achieve a similar visual outcome to those with normal renal function [9, 10], but renal failure is the leading cause of mortality in the follow-up [11]. However, there was little information on the fundus characteristics and operation details in previous work on PDR patients with CKD who underwent PPV.

The prevalence of DM in China has increased 17-fold from 0.67% to 11.6% of the population in the past 30 years [12]. The prevalence of CKD in China is also increasing [13]. Dialysis has provided more PDR patients with end-stage renal failure opportunities for PPV [10, 11]. Therefore, ophthalmologists must face the increasing challenge of performing PPV on PDR patients with CKD. Herein, we investigated a group of PDR patients who underwent PPV, and we compared the fundus characteristics, operative details, and PPV outcomes between patients with impaired renal function and patients with normal renal function.

Materials and methods

This study was a retrospective cohort of consecutive hospitalized patients with PDR who underwent PPV at our hospital during 2016.1.1–2017.12.31. The eye with more severe ocular manifestations was selected if there was bilateral involvement. The authors had access to information that could identify individual participants during or after data collection. This study was approved by the Ethics Committee of Beijing Tongren Hospital and adhered to the tenets of the Declaration of Helsinki (No. TRECKY 2021–070, Chairman: Mingzhao Qin, approval date: Apr 1, 2021). The informed content was waved.

Patient enrollment and grouping

Inclusion and exclusion criteria. Inclusion criteria: 1) PDR patients who have been hospitalized for PPV because of a nonclearing VH (persistent or recurrent) or tRD; 2) the high-risk PDR [14] defined by Early Treatment of Diabetic Retinopathy Study (EDTRS) guidelines were confirmed in operation; 3) available history records and laboratory tests; 4) detailed operation records; 5) detailed follow-up records for at least three months; 6) patients under dialysis without systemic contraindication to PPV were not excluded.

The patients with one or more of the following conditions were excluded from the study: 1) vitreous hemorrhage not related to PDR during vitrectomy; 2) eyes with PDR that had PPV for the epiretinal membrane or macular hole; 3) eyes with a history of PPV; 4) a lack of history of DM, or lack of diagnosis information for hypertension (HBP), DM-related cardio cerebral vascular disease (CVD) or CKD; 5) a lack of operation data for further statistical analysis; 6) a lack of 3-month follow-up; or 7) a history of other renal diseases that caused abnormal renal function.

Grouping based on the stage of CKD. CKD was defined as diabetes with albuminuria, impaired eGFR, or both according to the National Kidney Foundation KDOQI (Kidney Disease Outcomes Quality Initiative) classification [19]. We classified CKD into the following ranges by eGFR: stage 1 ($\geq$ 90 ml/min/1.73 m^2); stage 2 (60–89 ml/min/1.73 m^2); stage 3 (30–59 ml/min/1.73 m^2); stage 4 (15–29 ml/min/1.73 m^2); and stage 5 ($<$15 ml/min/1.73 m^2). Impaired renal function was defined as eGFR$<$60 ml/min per 1.73 m^2 (stage 3 or worse than stage 3) [20].

All patients were divided into two groups: patients with normal renal function (CKD stage 1–2) and patients with impaired renal function (CKD stage 3–5).

Baseline investigations.

1) Systemic complication investigation

Baseline data were collected from past history and presurgical anesthesia assessment records. The following information was included: age, sex, DM duration, DM medication, history of diabetes-related complications, including stroke, coronary heart disease (CAD), congenital heart failure (HF), diabetic foot, CKD, HTN. All the patients underwent laboratory tests on blood cell counts, urine analysis, blood coagulation function tests, serum creatinine, and blood urine nitrogen. All patients underwent a preoperative routine 12-lead electrocardiogram.

The long-term use of antiplatelet or anticoagulant medication and adjustment of these medications in the perioperative period were recorded. Aspirin was discontinued for at least one week before surgery in patients with aspirin monotherapy. In patients with CAD treated with dual antiplatelet therapy, clopidogrel was discontinued for at least five days before surgery. In patients with anticoagulant therapy, aspirin was continued, while dabigatran and clopidogrel were discontinued. Warfarin was stopped and bridged with low-weight-molecular heparin (LMWH) three days before the operation. In patients on dialysis, heparin was stopped and bridged with LMWH during the perioperative period. The previous therapy was left unchanged for patients who could not change the antiplatelet or anticoagulant therapy due to systemic abnormalities.

All anticoagulant and antiplatelet therapies were restarted within one week after PPV when the absence of rebleeding in the fundus was confirmed with an indirect ophthalmoscopy examination in each case.

2) The ocular findings

The history of previous pan-retinal photocoagulation (PRP), cataract phacoemulsification extraction, and intravitreal injection (IV) of anti-vascular endothelial growth factor (VEGF) agents was recorded. The course of unresolving VH from the onset of symptoms to the presentation, recurrent or persistent, was recorded.

All patients underwent comprehensive ophthalmological examinations, including corrected visual acuity (VA), which was tested using a decimal VA chart, slit-lamp biomicroscopy, intraocular pressure (IOP) measurement, dilated fundus examination with indirect ophthalmoscopy, color fundus photograph, optical biometry, coherent optic tomography (OCT) and B scan. Corrected bilateral VA, iris neovascular or neovascular glaucoma and dense vitreous hemorrhage in the operated eye were recorded.

Operative ocular findings and management. All patients underwent 23/25 gauge 3-port PPV (Constellation Vision System, Alcon, Fort Worth, Texas, USA) (Stellaris PC, Bausch +LOMB, USA) with 5000 cuts/min vitreous cutting rates. Patients with active fibrovascular epiretinal proliferative membranes (FVPs) or severe VH obscured fundus were treated with intravitreal injection (IV) of ranibizumab within seven days before PPV. Pre-PPV IVR was recorded.

After core vitrectomy to remove opacified vitreous, the extent of the FVP, the presence of macular-involving TRD, photocoagulation scars and the retinal vessel status were recorded.

IV triamcinolone acetonide (TA)-assisted PPV was performed. Anterior-posterior vitreoretinal traction was released as much as possible. Induction of PVD, FVP dissection, segmentation, delamination, endodiathermy and drainage of subretinal fluid, retinectomy and intraocular tamponade were performed as required according to each subject's particular need. Peripheral vitrectomy with scleral indentation and endolaser photocoagulation were performed in each case. IOP elevation, perfluorocarbon liquids and endodiathermy were used to handle the intraoperative bleeding. The severity of intraoperative bleeding was recorded as follows:

grade 0: none;

grade 1: minor bleeding stopping spontaneously or with transient bottle pressure elevation;

grade 2: moderate to severe bleeding requiring endodiathermy or with the formation of broad-sheets of clots [15].

Incomplete scatter photocoagulation was defined as a lack of preexisting photocoagulation in all four quadrants, fewer than 1000 laser spots or the required additional more than 500 laser spots during PPV [16].

The operation time was calculated from making the first PPV trocar incision to removing the eyelid speculum after the PPV. The combined procedures were recorded, including cataract extraction, silicone oil tamponade, photocoagulation, and the use of endodiathermy. The laser points were recorded.

The extension of FVPs was recorded as follows:

grade 0: absence of any adhesion;

grade 1: multiple point adhesions with or without one broad adhesion (broad adhesion was defined as focal adhesion at three sites or more);

grade 2: 1–3 broad adhesions posterior to the equator;

grade 3: 3+ broad adhesions posterior to the equator or two or fewer in quadrants adhesions anterior to the equator;

Grade 4: broad adhesions anterior to the equator in multiple sites [17, 18].

FVPs were classified as predominantly neovascular, mixed neovascular and fibrotic, and predominantly fibrotic [15]. A marked reduction in the caliber of retinal vessels and widespread retinal vessel closure were recorded.

Follow-up. All patients were followed for at least three months monthly. All patients underwent corrected VA, slit-lamp biomicroscopy, IOP measurement, and dilated fundus examination with indirect ophthalmoscopy. The VA result, occurrence of reoperated postoperative vitreous hemorrhage (POVH), retinal detachment, and development of neovascular glaucoma (NVG) were recorded. Optic Coherent Tomography (OCT) evaluation of macular attachment was carried out on patients with silicone oil tamponade just before undergoing silicone oil removal. The status of the macula was recorded as attached or detached.

Statistical analysis

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 Client version 2.0.3.15 (http://epidata.dk). The corrected VA results were converted to logMAR values for statistical analysis. The mean and standard deviation (SD) were calculated for continuous variables with a normal distribution. The median with quartiles was calculated for continuous variables with a nonnormal distribution. The t test or Mann–Whitney U test was carried out for continuous variables. The chi-square test or Fisher's exact test was carried out for discrete data.

To investigate the relationship between impaired renal function and PDR characteristics, the patients were divided into two groups: those with impaired renal function and those with normal renal function. The baseline systemic condition, presurgical findings, and ocular findings during PPV were compared between the two groups. Variables with a p value less than 0.3 were further enrolled in a binary backward stepwise logistic regression model. One variable was included or excluded from the model each time by comparing the Akaike information criterion (AIC) value; the model that had the lowest AIC was chosen.

To investigate the influence of CKD on the PPV and PPV outcomes, the variables of PPV management, VA, retinal attachment rate, and the occurrence of POVH and NVG were compared between the two groups.

To investigate the factors related to final VA, we compared initial VA, completion of PRP, IV-anti-VEGF agents, macular-involved tTD, gender, age, and grade of CKD between patients whose final VA increased for more than two lines and patients whose final VA failed to increase for more than two lines.

Results and discussion

Results

There were 220 patients enrolled in our study with an average age of 51.8±11.8 years. Among them, 126 (57.3%) were males, and 94 (42.7%) were females. There were 5 cases excluded due to failure to follow up, and all of them had stage 1 CKD. The median of HbA1c in the preoperational assessment was 7.7 (6.65, 8.65).

There were 149 patients with stage 1–2 CKD (67.7%) and 71 (32.3%) patients with impaired renal function and stage 3–5 CKD (Fig 1).

There were 20 (9.1%) patients who had gone through urine examination or renal function test before the onset of ocular symptoms, 12 (5.5%) patients under dialysis, and 188 patients (85.4%) who did not have CKD screening before the preoperative assessment. In addition to the 12 patients undergoing dialysis, four received medical treatment to protect renal function.

Impaired renal function-related systemic and ocular findings.

1. Univariable relationship between impaired renal function and systemic and ocular findings

The association of the medical history and preoperative and intraoperative factors with impaired renal function was listed in Table 1. The univariable analysis showed that compared to patients with normal renal function, patients with impaired renal function had a higher percentage of males (70.4%, 51.0%, $p<0.001$), a higher percentage of coexistent HTN (69.0%, 42.3%, $p<0.001$), more patients with stroke (9,7, $p = 0.04$), a higher percentage of patients who

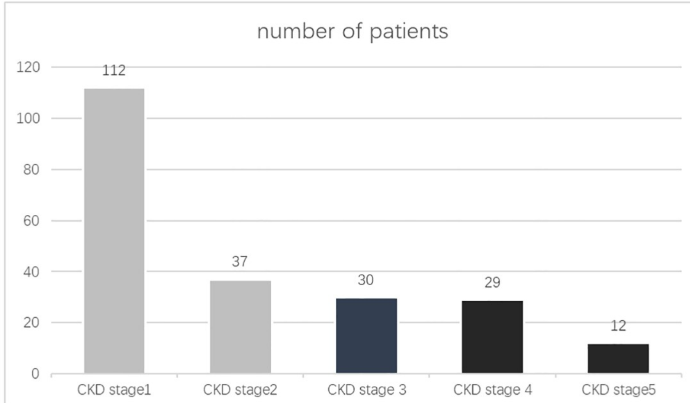

Fig 1. The prevalence of CKD in the investigated PDR patients.

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had incomplete PRP (64.8%, 42.3%, p<0.001), a higher percentage of patients who presented with predominantly fibrotic FVP (43.7%, 25.5%, p = 0.01), a higher percentage of patients who presented with board FVP (> = stage 3) (77.5%, 28.9%, p<0.001), a higher percentage of patients with macula-involved tRD (46.5%, 24.1%, p<0.001), and a higher percentage of patients with extensive retinal vessel closure (63.3%, 13.4%, p<0.001).

2. Multiple variables logistics regression

Logistic regression showed that factors related to impaired renal function were the presence of HTN (3.40[1.58–7.29], p = 0.002), preoperative incomplete PRP (3.18[1.50–6.72], p = 0.002), presence of grade 3 FVP (8.19[3.43–19.54], p<0.001), and presence of extensive retinal vascular closure (3.40[1.54–7.52], p = 0.002) (AIC = 203.4, AUC = 0.854).

The influence of impaired renal function on PPV. There was no significant difference in the operation time, percentage of patients who received a preoperative IV anti-VEGF agent injection, rate of patients who underwent combined phacoemulsification cataract extraction, number of laser points during the surgery, or percentage of silicone oil tamponade between the two groups (Table 2). There was a more frequent occurrence of grade 2 intraoperative bleeding (56.3%, 32.2%, p = 0.001), a higher percentage of intraocular subretinal fluid drainage (45.1%, 22.1%, p = 0.008), and a higher percentage of perfluorocarbon liquids (46.5%, 30.9%, p = 0.035) in patients with impaired renal function than in patients with normal renal function.

The occurrence of severe intraocular bleeding was not different in patients under antiplatelet or anticoagulant agent and patients did not use those medications (33/70,55/150, p = 0.18). The occurrence of severe intraocular bleeding was not different in patients who continued or adjusted antiplatelet or anticoagulant therapy and patients who discontinued antiplatelet or anticoagulant therapy (12/34, 10/36, p = 0.61).

Influence of impaired renal function on PPV outcomes. There was no significant difference in the preoperative VA or VA at the three-month follow-up between the two groups (p = 0.72) (Fig 2, Table 3).

During a median follow-up of 29 weeks, ranging from 24 to 40 weeks, 46.5% (33/71) of patients with impaired renal function had VA increased for more than two lines at their 3-month follow-up, similar to the 54.4%(81/149) of patients with normal renal function (p = 0.34); 42.3% (30/71) of patients with impaired renal function had stable (VA changes

Table 1. The baseline and intraoperative characteristics of PDR patients by the presence of impaired renal function.

	Patients with impaired renal function (71)	Patients with normal renal function (149)	P
age (mean±SD, y)	51.0±13.3	52.1±11.1	0.55
gender (male, n, %)	50, 70.4%	76, 51.0%	<0.001
duration of DM (median, IQR, m)	120[66,180]	120[60,208]	0.27
HbA1c	7.8 (6.8, 9.3)	7.7 (6.7, 8.9)	0.66
combined systemic abnormalities			
combined HTN (n, %)	49,69.0%	63,42.3%	<0.001
combined coronary heart disease (n, %)	20, 28.2%	47, 31.5%	0.32
combined stroke (n, %)	9, 12.7%	7, 4.7%	0.04
long-term use of antiplatelet or anticoagulant medications			
aspirin monotherapy (n)	21, 29.6%	24, 16.1%	0.03
anticoagulant (n)	4, 5.6%	1, 0.2%	0.04
dual antiplatelet (n)	2, 2.8%	3, 2.0%	0.66
combined antiplatelet and anticoagulant (n)	12,16.9%	3, 2.0%	0.003
adjustments of antiplatelet or anticoagulant therapy during PPV			
continue therapy during PPV(n)	9, 12.7%	13, 8.7%	0.06
switching to LMWH (n)	5, 7.0%	7, 4.7%	
discontinued therapy	25, 35.2%	11,7.4%	
presurgery ocular findings and ocular medical history			
recurrent or persistent VH (n, %)	53,74.6%	50,33.6%	<0.001
IVR after VH (n, %)	3, 6.5%	5,7.5%	0.72
previous history of PRP			
incomplete PRP (n, %)	46, 64.8%	63, 42.3%	<0.001
VH occurred before the initiation of PRP (n, %)	35, 76.1%	35, 55.6%	0.045
VH occurred after the initiation of PRP (n, %)	11, 23.9%	28, 44.4%	
without PRP (n, %)	22, 31.0%	82, 55.0%	0.001
complete PRP (n)	3, 4.2%	3, 2.0%	0.68
VA >0.5 (n, %)	2, 2.8%	2, 1.3%	0.61
0.01<VA< = 0.5 (n, %)	29, 40.8%	60, 40.3%	
VA< = 0.01(n, %)	40, 56.3%	87, 19.4%	
surgical characteristics (n, %)			
presence of predominantly fibrotic FVP	31, 43.7%	38, 25.5%	0.01
grade of extension of FVP (n, %)			
< = grade2	16, 22.5%	106, 71.1%	<0.001
> = grade3	55, 77.5%	43, 28.9%	
macula-involved TRD (n, %)	33, 46.5%	36, 24.1%	<0.001
extensive retinal vessel closure (n, %)	45, 63.3%	30,13.4%	<0.001
combined retinal tear (n, %)	26, 32.9%	56, 39.7%	0.99

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were less than two lines) 3-month follow-up VA, similar to the 39.6% (59/149) patients with normal renal function (p = 0.77).

There was no significant difference in gender (p = 0.30), age (p = 0.25), grade of CKD (p = 0.19), presence of previous PRP (p = 0.20), previous IV-anti-VEGF (p = 0.75), baseline VA (p = 0.37) in patients whose final VA increased for more than two lines and patients whose final VA increased for less than two lines.

In 74 patients with silicone oil tamponade, macular reattachment was found in all patients at silicone oil removal. Four patients with impaired renal function and three patients with normal renal function had persistent macular edema. In 220 patients, two patients with impaired

Table 2. The surgical characteristics of PDR patients by the presence of impaired renal function.

	Patients with impaired renal function (71)	Patients with normal renal function (149)	P
IV-anti VEGF before surgery (n, %)	58, 81.7%	132, 88.6%	0.23
operative time (median, IQR, min)	95.0[60,120]	100[60,120],	0.24
combined cataract extraction (n)	6	7	0.46
combined subretinal fluid drainage (n, %)	32, 45.1%	33, 22.1%	0.008
severe intraoperative bleeding (grade 2, n, %)	40, 56.3%	48, 32.2%	0.001
use of perfluorocarbon liquids (n, %)	33, 46.5%	46, 30.9%	0.035
laser points (median, IQR, n)	980[696,1306]	1092[669,1595]	0.12
silicone oil tamponade (n, %)	24, 33.8%	50, 33.5%	0.99

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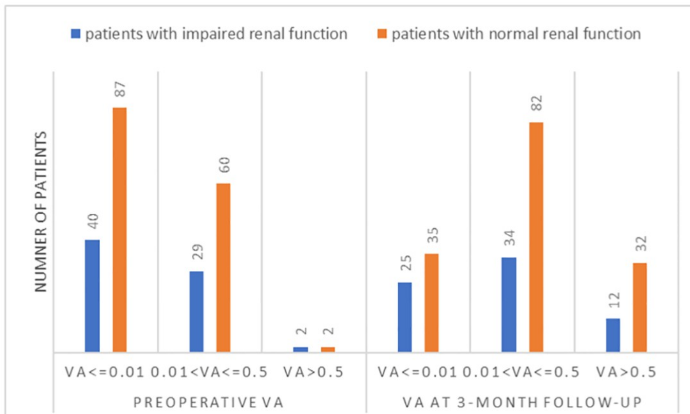

Fig 2. The preoperative and final follow-up visual acuity between PDR patients with and without impaired renal function.

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Table 3. VA changes in patients with and without impaired renal function.

	patients with impaired renal function (71)	patients with normal renal function (149)	P
VA increased for more than two lines (n, %)	33, 46.5%	81, 54.4%	0.31
VA changed for less than two lines (n, %)	30, 42.3%	59, 39.6%	0.77
VA decreased for more than two lines (n, %)	8, 11.2%	9, 6.0%	0.19

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renal function and one with normal renal function had secondary PPV for recurrent retinal detachment; the retinal attachment rates were 97.2% and 99.3%, respectively (p = 0.24).

Four patients with impaired renal function and eight with normal renal function had POVH (p = 0.99). POVH occurred after restarting antiplatelet therapy.

No patient in our study developed NVG during the follow-up period.

Discussion

Previous investigations on the relationship between DR and CKD were carried out in DM patients with transparent optic media. These studies often excluded PDR patients with VH due to failure to obtain a clear fundus photograph. We enrolled PDR patients with VH who underwent PPV and investigated the fundus characteristics of PDR patients after removing the VH by PPV. We divided the patients into two groups: a group with normal renal function (including patients with stage 1–2 CKD) and a group with impaired renal function (including patients with stage 3–5 CKD). We found that PDR patients with impaired renal function had specific FVP and retinal vascular characteristics. Correspondingly, specific operative details were different between the two groups. Finally, after proper operative management, we found that PDR patients with or without impaired renal function could achieve comparable operative outcomes

Low awareness of CKD and poor compliance in PDR patients who underwent PPV. The prevalence of CKD and impaired renal function in our PDR patients was 49.1% and 32.8%, respectively, far beyond the hospital-based CKD prevalence of 10.7% [19] and the population-based CKD prevalence of 11.98–29.60% [20, 21] in China. Previous studies showed that the five-year survival rate of PDR patients who underwent PPV was 81–86% [28, 29], and renal failure was the leading cause of mortality in PDR patients who underwent PPV [14, 28, 29]. The high prevalence of patients with impaired renal function in our study indicated that the patients enrolled were a group of patients with a risk of post-PPV mortality if the renal condition was left untreated.

It is well known that poor control of DM and patients' non-cooperative behavior are related to the progression of PDR and the deterioration of renal function. However, poor compliance can confound the role of CKD in the progression of PDR. We further investigated the compliance of our patients by their history of CKD screening and preoperative HbA1c results. Among the 220 patients, 85.4% did not know they had CKD, and only 1.8% were under treatment in addition to patients undergoing dialysis. The low awareness rate and treatment rate of CKD in our group of patients were similar to the results of previous population-based investigations in China, with an awareness rate of CKD of 8.7–9.5% and a treatment rate of 4.9% [22–24]. We also found that both groups had abnormal HbA1c results, and there was no difference between the two groups. The low screening rate for CKD and abnormal HbA1c results in both groups implied that the patient's poor compliance was comparable between the two groups. Thus, we could rule out the role of variation of compliance between patients with and without impaired renal function on the progression of DR. In addition, most patients with CKD are asymptomatic, and our results suggested that ophthalmologists should pay extra attention to the screening and treatment of CKD when dealing with fundus abnormalities in PDR patients who underwent PPV.

The impaired renal function-related fundus characteristics of PDR. The 4-grade classification system of FVPs based on the severity of vitreoretinal adhesion is related to PPV visual prognosis [17, 18]. It also reflects the difficulty in dealing with FVPs, for example, combined retinal tears are often found in patients with grade 3 or more severe FVPs [18], and retinectomy is often required in patients with grade 4 FVPs [17, 18].

The progression of PDR is related to the diabetic course [25] and the combination of CKD [26, 27]. There was no significant difference in the duration of the diabetes course between the two groups (120, 120 months). For a similar duration of diabetes, we found that PDR patients with impaired renal function had a higher percentage of patients with severe FVP (grade 3 or more severe) (77.5%, 28.9%), macular-involved tRD (46.5%, 24.1%), extensive retinal vessel closure (63.3%, 13.4%), predominantly fibrotic FVP (43.7%, 25.5%), and incomplete PRP (64.8%,42.3%) than PDR patients with normal renal function. Previous research in patients with clear optic media shows that large nonperfusion areas in DM patients are related to CKD progression [8], while the combination of CKD is related to DR progression [26, 27]. We extended the relationship of CKD and DR to patients who underwent PPV with unclear optic media, and our results showed that impaired renal function was related to more severe ischemic retinal changes, including retinal vessel closure and board FVP. It suggests that more aggressive treatment for CKD in patients with DR should be applied, and more attention should be given to DR progression in CKD patients.

Impacts of CKD on PPV and outcomes. The current study reported a comparable percentage of patients who had VA improvement after PPV in both groups (46.4–54.3%), similar to previous work on PDR patients (49–75%) [28] and PDR patients under dialysis (60.5%) [10]. In addition, we reported a similar high retinal attachment rate in both groups in the short-term follow-up (97.2%, 99.3%), similar to previously reported rates of 90.6–92.0% [28]; a 100% macular attachment rate in patients who underwent silicone oil removal, similar to previously reported rates of 66–88% [28]; a low occurrence of POVH in both groups (4,8), compared to previously reported rates of 15–32% [16, 29, 30]; and a zero occurrence of NVG in both groups, which has been reported to be 5.3–11.8% [31–33] previously.

The poor VA outcome was known to be related to macular-involved TRD, incomplete PRP, severe neovascular elsewhere (NVE), the presence of NVI, disc or macular-involved tRD, poor pre-PPV VA, and the combination of tRD and a retinal tear [34]. In this study, the condition of high-risk PDR and the combination of retinal tears (32.9%, 39.7%) were similar in the two groups. Patients in the impaired renal function group had a higher percentage of incomplete PRP, macular-involved tRD, and broader FVP that involved the disc (77.5%, 28.9%), which implied the risk of worse VA outcomes. However, both groups of patients achieved similar VA outcomes. Our results indicated that PDR patients with impaired renal function could achieve comparable VA outcomes if appropriately treated.

The goal of PPV in PDR patients is to clear the VH, release vitreoretinal traction, and complete PRP. There was no significant difference in the operation time, intraoperative laser points, or percentage of silicone oil tamponade between the two groups during PPV. However, we found that patients with impaired renal function had a higher percentage of subretinal fluid drainage, and severe intraoperative bleeding required endodiathermy.

Previous work showed that subretinal fluid could spontaneously resolve 2–12 months after PPV, and long-standing subretinal fluid is unrelated to visual prognosis [15–17]. Contrary to previous works focusing on the influence of subretinal fluid on visual recovery in PDR patients who underwent PPV, we focused on the presence of long-standing subretinal fluid, which may hold back the application of PRP and, in turn, increase the chance of postoperative NVI. Post-PPV NVG indicates poor visual prognosis in PDR patients [31–33], and complete intraoperative photocoagulation can effectively prevent post-PPV NVG [35]. Previous work performing PPV without subretinal fluid drainage on PDR patients showed that in a group of PDR patients with 41% of patients with macular-involved tRD and 48% of patients who had complete PRP before PPV, 7% of them developed NVG in the follow-up [36]. Compared to previous work, our study had fewer patients with complete PRP before PPV (3/71) and a similar percentage of patients with macular-involved tRD (46.5%), but we had no NVG in the follow-up. If the subretinal fluid is left untreated, patients without complete PRP may develop NVG because it is difficult to perform additional PRP on the retina with extensive, long-standing subretinal fluid to correct retinal ischemia. Therefore, we performed subretinal fluid drainage in cases with a large area of tRD. In patients with impaired renal function, the higher percentage of patients with macular-involving tRD may explain the higher percentage of subretinal fluid drainage (45.1%, 22.1%). Our data suggested that subretinal fluid drainage in PPV in PDR patients, especially in patients with impaired renal function, should be performed considering the risk of NVG in addition to visual outcomes.

POVH is a common complication of PPV in PDR patients. Previous work indicated that pre-PPV IV anti-VEGF agents may lessen the chance of intraoperative bleeding and prevent

POVH [37, 38]. Although we had widely applied anti-VEGF injection treatment in both groups (81.7%, 88.6%) and the FVP was more commonly observed as predominantly fibrotic (43.7%, 25.5%), the occurrence of severe intraoperative bleeding requiring endodiathermy was higher in the group of patients with impaired renal function (56.3%, 32.3%). It is known that extensive vitreoretinal adhesion is related to the aggression of NVE [39]. We could not tell the role of long-term use of anticoagulant or antiplatelet medication or sustained those therapy during PPV on the severe intraocular bleeding. The high prevalence of extensive vitreoretinal adhesion in patients with impaired renal function (77.5%, 28.9%) may help to explain the high occurrence of severe intraoperative bleeding. The occurrence of POVH in both groups (4/71,8/149) was lower than previously reported as 15–32% [16, 29, 30]. Our results suggested that preoperative IV-anti-VEGF agents and the use of endodiathermy in cases with extensive FVP may be practical to lessen the chance of POVH.

Limitations. Previous research showed that 44–72% of VH in PDR patients could resolve after IV-anti-VEGF agents in a follow-up of 16–52 weeks; only 7.04–33.0% of patients required PPV [29, 40–42]. Since our study was a retrospective study with a relatively low percentage of patients who received IV-anti-VEGF agents after VH occurrence (6.5%, 7.5%), we could not show the influence of anti-VEFG agents injection on the resolution of VH and the chances of gaining a second PRP. The high prevalence of severe FVP in patients with impaired renal function in our patients suggested that the observation for VH absorption after IV-anti-VEGF agents in PDR patients combined with impaired renal function should not be too long in case of progression of tRD. The safe length of the observation period in patients with CKD after IV anti-VEGF agents should be further investigated.

We only had serum creatinine, blood urine nitrogen, and urine protein tests; we did not have a urinary albumin-to-creatinine ratio test. We could not show the influence of CKD with relatively normal renal function on the PDR characteristics or PPV details.

It is well known that incomplete PRP is related to the progression of PDR [43, 44] and the occurrence of VH [45], POVH [27], and postoperative NVI [31–33]. We reported a low prevalence of completion of PRP (3/71, 3/149) before PPV and a high number of laser points during the surgery (980, 1092) in both groups. We had noticed that the reason for incomplete PRP and progression of PDR might be: 1) the improper PRP treatment by the ophthalmologists, 2) the development of VH or tRD at initial presentation, 3) the progression of PDR before PRP completion due to the reluctance of patients to continue PRP. However, we did not investigate the role of the patient's poor compliance on the incomplete PRP due to the retrospective characteristics. Further investigation of the reason for incomplete PRP may provide more information on the influence of CKD on DR patients' treatment before ophthalmic surgery.

Since the OCT assessment could not be applied in cases of severe macular involved TRD, dense VH, or severe FVP involved macular, the high proportion of patients with dense VH (74.6%, 33.6%), macular involved TRD (46.5%, 24.1%) and macular involved FVP (77.5%, 28.9%) in our patients made most of preoperative OCT macular measurement unavailable. Thereby, we failed to show the OCT evaluation of anatomic macular changes before and after PPV.

Conclusions

We showed that in PDR patients who underwent PPV, the prevalence of impaired renal function was relatively high, while the awareness of the renal condition among PDR patients was relatively low. Thus, screening for CKD was required before PPV.

We also found that PDR patients with impaired renal function had a high prevalence of extensive FVP, macular-involved tRD, and retinal vessel closure. In patients with extensive tRD, subretinal fluid drainage and photocoagulation are recommended to lessen the chance of NVG; moreover, pre-PPV injection of anti-VEGF agents and endodiathermy during PPV could lessen the chance of POVH. In addition, patients with and without impaired renal function can achieve comparable PPV outcomes after proper management during PPV.

Supporting information

S1 Checklist.
(DOCX)

Author Contributions

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