• Clinical Research •

Renal dysfunction associated with clinical response to intravitreal conbercept therapy for diabetic macular edema

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Abstract

● **AIM:** To investigate the impact of renal dysfunction on clinical response to intravitreal conbercept injection (IVC) for diabetic macular edema (DME).

● **METHODS:** This retrospective study included a total of 100 eyes from 100 patients with DME treated with IVC with 3+PRN regimen. Based on the estimated glomerular filtration rate (eGFR), the patients were divided into normal renal function group (*n*=37), impaired renal function group (*n*=27), and renal insufficiency group (*n*=36). The main outcome measures were best-corrected visual acuity (BCVA) and central subfield macular thickness (CST). Clinical parameters included blood urea nitrogen, serum creatinine, serum uric acid, glycosylated hemoglobin (HbA1c), and hemoglobin.

● **RESULTS:** The mean follow-up time was 3.9mo. The mean number of IVCs was 2.07±1.22 in the three groups. Mean BCVA improved significantly from 0.81±0.49 logMAR at baseline to 0.72±0.52 logMAR in the three groups at the final visit (*P*<0.001). Mean CST decreased significantly from 427.85±148.99 μm at baseline to 275.31±108.31 μm at final visit (*P*<0.001). Patients in the normal renal function group had higher baseline hemoglobin levels and thinner baseline CST than those in the impaired renal function and insufficiency renal function group (all *P*<0.001). Patients in the normal renal function group had higher baseline hemoglobin levels and thinner baseline CST than those in the impaired renal function and insufficiency renal function group (all *P*<0.001). The three groups had no differences in baseline HbA1c levels (*P*>0.05). Good baseline BCVA (logMAR, *P*=0.001) and thicker baseline CST (*P*=0.041) were associated with visual acuity improvement. Higher eGFR (*P*<0.001), hemoglobin (*P*=0.032) and thicker baseline CST (*P*=0.017) were associated with macular edema retrogression in the conbercept-treated diabetic patients, which showed better anatomical response to IVC.

● **CONCLUSION:** Our results indicate that the renal dysfunction is the risk factor associated with the efficacy of IVC for DME.

● **KEYWORDS:** conbercept; diabetic macular edema; renal dysfunction

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INTRODUCTION

Diabetic macular edema (DME) is one of the leading causes of visual impairment worldwide. Totally 35 population-based studies reported that the global prevalence of DME was about 7.5%, influencing approximately 21 million individuals worldwide[1]. Vascular endothelial growth factor (VEGF) is crucial in the pathogenesis of DME, which promotes retinal neovascularization and increases the permeability of retinal vessels[2]. Anti-VEGF agents interfere with a critical stimulus for developing blood-retinal barrier breakdown in DME and ameliorate ischaemia-induced retinal neovascularization. Intravitreous injection (IVI) of anti-VEGF agents has been considered the first-line treatment of DME[3]. Conbercept (KH902; Chengdu Kanghong Biotech Co., Ltd.,

Sichuan Province, China) consists of the VEGF binding domains of the human VEGFR-1 and VEGFR-2 combined with the Fc portion of the human immunoglobulin G-1. It has a high affinity for all isoforms of VEGF-A, VEGF-B, and placental growth factor[4]. Several studies have shown that conbercept was safe and effective treating of DME, which could improve visual acuity and relieve macular edema[5-7].

However, only some DME patients responded well to the conbercept treatment in real-life clinical practice, reinforcing the multifactorial nature of DME. Previous studies have found that the occurrence and development of DME were related to systemic factors, including age, duration of diabetes, hypertension, and glycosylated hemoglobin (HbA1c) level[8-10]. Thus, it was necessary to investigate the impact of systemic factors on clinical outcomes of intravitreal conbercept injection (IVC). Diabetic nephropathy often coexists with diabetic retinopathy, indicating that they may have similar microvascular pathophysiology. A prospective study found that DME patients had higher serum creatinine (CREA) levels and lower estimated glomerular filtration rate (eGFR) levels than patients without DME[11]. A retrospective study reported that patients with severe proteinuria tended to gain better anatomical improvement after ranibizumab treatment. In comparison, those with lower eGFR were more likely to have poorer visual improvement[12]. Nevertheless, conflicting findings also exist, and few studies reveal the impact of baseline renal function on the visual and anatomical response of conbercept in patients with DME in the real-life clinical trial.

It was a real-world efficacy analysis, which had more clinical reference significance. Preoperative evaluation of renal function was not only beneficial for preliminary prediction of the approximate number of conbercept injections and effectiveness, but also reduced DME patients' economic burden, established reasonable expectations, and promoted better doctor-patient communication. Therefore, this study aims to investigate the risk of renal dysfunction in real-life clinical responses to conbercept of DME. Prediction of the real-life clinical effect of conbercept based on renal function in the treating of DME before onset holds great promise for reducing the risk of blindness and economic burden.

PARTICIPANTS AND METHODS

Ethical Approval This study adhered to the tenets of the Declaration of Helsinki and obtained approval from the Institutional Review Board of Zhujiang Hospital of Southern Medical University. The study was conducted in accordance with the Basic & Clinical Pharmacology & Toxicology policy for experimental and clinical studies[13]. This project has been approved by the Medical Ethics Committee of Guangzhou Red Cross Hospital (NO.20210513-07). Informed patient consent was not required by the ethics committee in view of the retrospective nature of the research and the anonymity of the study data.

Study Participants One hundred eyes from 100 DME patients who received IVC treatment in the Guangzhou Red Cross Hospital of Jinan University and Zhujiang Hospital of Southern Medical University between January 2018 and September 2023 were retrospectively enrolled in this analysis. The inclusion criteria included 1) type 2 diabetes mellitus; 2) DME diagnosed by spectral-domain optical coherence tomography (SD-OCT; Heidelberg Engineering, Heidelberg Spectralis OCT, Germany); 3) central subfield macular thickness (CST) ≥250 μm. Exclusion criteria were 1) the presence of significant media opacity that would affect the DME diagnosis in fundus examination and limit vision recovery (*e.g.*, significant cataract, vitreous hemorrhage, corneal scar); 2) the presence of any other ocular or systemic diseases that could induce retinopathy or macular edema; 3) previous intraocular surgery or intravitreal steroid injection within 6mo of initiation of anti-VEGF therapy; 4) presence of severe cardiovascular and cerebrovascular diseases and other systemic diseases, and long-term use of oral steroids. When both eyes met the inclusion and exclusion criteria, one of the eyes was randomly included (Figure 1).

Data Collection Baseline clinical characteristics were collected from the electronic medical records, including gender, age, duration of diabetes mellitus (years), the status of hypertension, levels of blood urea nitrogen (BUN), CREA, serum uric acid (UA), HbA1c, and hemoglobin. The eGFR was calculated using simplified modification of diet in renal disease (MDRD) equations. Ocular examinations, including measurement of best-corrected visual acuity (BCVA) and intraocular pressure, anterior segment slit-lamp examination, fundus examination, and measurement of CST by SD-OCT, were performed at each visit. The stage of diabetic retinopathy at baseline and the status of panretinal photocoagulation (PRP) were collected. IVC at 0.5 mg in 0.05 mL was performed in each treatment.

Outcome Measurement Based on eGFR, patients were divided into three groups: normal renal function group (eGFR≥90 mL/min·1.73 m^2), impaired renal function group (60≤eGFR<90 mL/min·1.73 m^2), and renal insufficiency group (eGFR<60 mL/min·1.73 m^2)[13]. The main outcome measures were change in BCVA and change in CST measured by SD-OCT. BCVA was converted to the logarithm of the minimum angle of resolution (logMAR). Effective treatment of IVC was defined as the change in BCVA (logMAR) <0 or CST reduction ≥20%[14-15]. Patients were divided into positive and negative functional response groups based on the functional outcome. Based on the anatomical outcome, patients were divided into positive and negative anatomical response groups.

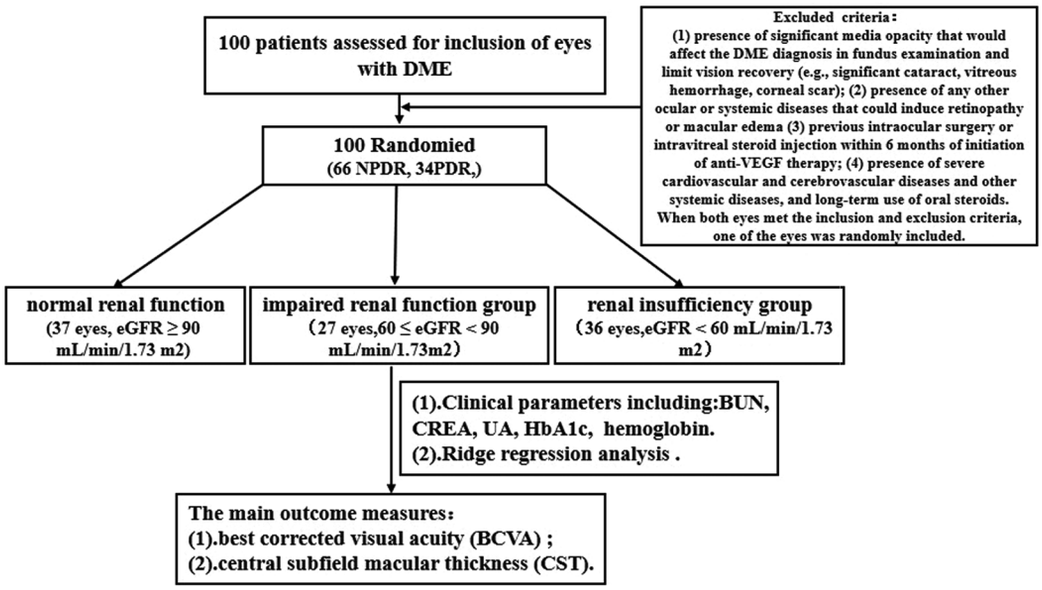

Figure 1 Design proposal of the research NPDR: Nonproliferative diabetic retinopathy; PDR: Proliferative diabetic retinopathy; eGFR: Estimated glomerular filtration rate; BUN: Blood urea nitrogen; CREA: Serum creatintine; UA: Uric acid.

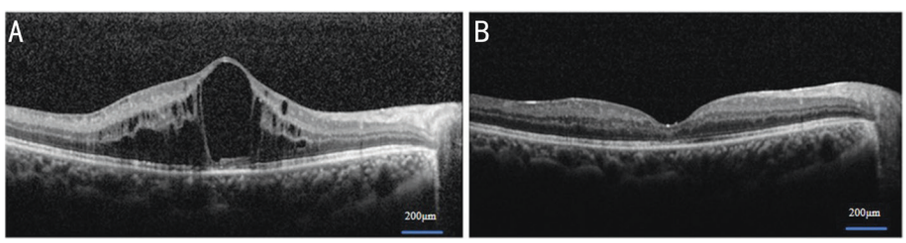

Figure 2 Alteration of CST during the follow-up visits by spectral domain optical coherence tomography A: DME patient with eGFR<30 mL/min•1.73 m^2, CST was 762 μm at baseline; B: CST decreased to 186 μm 1wk after 6 intravitreous conbercept injections. DME: Diabetic macular edema; CST: Central subfield macular thickness; eGFR: Estimated glomerular filtration rate.

Statistical Analysis All statistical analyses were performed using SPSS version 20.0 (SPSS, Inc., Chicago, IL. USA) and R version 4.0.1. When patients were divided into three groups according to eGFR value, categorical variables were compared using the Chi-square test or Fisher's exact test as appropriate, and continuous variables were compared using one-way ANOVA among three groups. When patients were divided into two groups according to functional and anatomical outcomes, an independent sample *t*-test was used to compare continuous variables. Ridge regression analysis was used to assess the associations of clinical parameters with the clinical response of IVC for DME when there was collinearity. A ridge regression model included predictors with a *P* value less than 0.2 in the univariate analysis in a *P* value <0.05 was considered statistically significant.

RESULTS

Baseline Demographics and Clinical Data A total of 100 patients were included in the study, including 60 males and 40 females, with an average age of 56.72±9.16y (range from 36 to 80). The mean duration of diabetes was 9.91±6.28y (range from 1 to 25). Fifty-five percent of them had hypertension. In terms of clinical parameters, the mean BUN was 6.68±3.23 mmol/L, the mean CREA was 93.33±61.41 μmol/L, the mean UA was 390.60±88.36 μmol/L, the mean eGFR was 86.91±25.55 mL/min·1.73m^2, the mean HbA1c was 8.49%±1.70%, and the mean hemoglobin was 123.64±17.63 g/L. Among the enrolled patients, 81 (81%) had HbA1c≥7%. Of the 100 eyes studied, 66 had nonproliferative diabetic retinopathy (NPDR), 34 had proliferative diabetic retinopathy (PDR), and 45 had previous history of PRP. After IVC treatment, mean BCVA improved significantly from 0.81±0.49 logMAR at baseline to 0.72±0.52 logMAR at the final visit (*P*<0.001). In addition, mean CST decreased significantly from 427.85±148.99 μm at baseline to 275.31±108.31 μm at final visit (*P*<0.001). The mean number of IVIs was 2.07±1.22. A comparison of these parameters among the three groups divided by eGFR was shown in Table 1. Patients in the normal renal function group had higher baseline hemoglobin levels and thinner baseline CST than those in the impaired renal function and insufficiency renal function group (all *P*<0.001). The three groups had no differences in baseline HbA1c levels (*P*>0.05). The mean follow-up time was 3.9mo (Figure 2, Table 1).

Functional and Anatomical Response in Three eGFR Groups Regarding visual outcomes, the positive functional

Table 1 Participant characteristics

Parameters	A (*n*=37)	B (*n*=27)	C (*n*=36)	*P*		
				A *vs* B	A *vs* C	B *vs* C
Sex, male/female	18/19	19/8	23/13		-	
Age, y	55.54±8.99	56.04±8.53	62.24±8.92		-	
Duration of DM, y	9.74±5.91	9.71±6.80	10.90±6.45		-	
Hypertension	51.4%	59.3%	55.6%		-	
HbA1c, %	8.50±1.68	8.43±1.80	8.53±1.59	0.134	0.663	0.137
Hemoglobin, g/L	129.42±14.91	119.14±17.09	111.55±18.95	<0.001	<0.001	<0.001
Stage of DR						
NPDR	95.0%	70.0%	33.3%		-	
PDR	5.0%	30.0%	66.7%		-	
Status of PRP	48.6%	51.9%	36.1%		-	
Baseline BCVA (logMAR)	0.80±0.51	0.71±0.41	1.01±0.53	<0.001	<0.001	<0.001
Final BCVA (logMAR)	0.73±0.52	0.65±0.53	0.81±0.50	<0.001	<0.001	<0.001
Change in BCVA (logMAR)	-0.07±0.46	-0.06±0.48	-0.20±0.54	0.89	<0.001	<0.001
Baseline CST, μm	421.11±154.92	432.02±117.92	444.00 ±176.20	0.007	<0.001	0.032
Final CST, μm	233.08±66.17	312.37±105.98	355.92±153.25	<0.001	<0.001	<0.001
Change in CST, μm	-188.03±172.52	-119.65±155.57	-88.08±151.23	<0.001	<0.001	<0.001
Number of IVI	1.99 ±1.19	2.06 ±1.29	2.40±1.12	0.12	<0.001	<0.001

A: Normal renal function; B: Impaired renal function; C: Renal insufficiency; DM: Diabetes mellitus; HbA1c: Glycosylated hemoglobin; DR: Diabetic retinopathy; NPDR: Nonproliferative diabetic retinopathy; PDR: Proliferative diabetic retinopathy; PRP: Panretinal photocoagulation; BCVA: Best corrected visual acuity; CST: Central subfield macular thickness; IVI: Intravitreous injection.

Table 2 Functional and anatomical responses according to eGFR levels *n* (%)

Parameters	Normal renal function (*n*=37)	Impaired renal function (*n*=27)	Renal insufficiency (*n*=36)	*P*
Change in BCVA (logMAR)				0.562
Positive functional response	18 (36.7)	15 (30.6)	16 (32.7)	
Negative response	19 (35.8)	12 (22.6)	22 (41.5)	
CST reduction				<0.001
Positive response	33 (49.3)	19 (28.4)	15 (22.4)	
Negative response	4 (12.1)	8 (24.2)	21 (63.6)	

eGFR: Estimated glomerular filtration rate; BCVA: Best corrected visual acuity; CST: Central subfield macular thickness.

response was obtained in 49 (49%) eyes. As for anatomical outcomes, the positive anatomical response was obtained in 67 (67%) eyes. There were statistically significant differences in anatomical response among the three eGFR groups (P<0.05; Table 2). Higher eGFR was associated with better anatomical outcomes. The normal renal function group gained superior anatomical response than the other two groups. There were no statistically significant differences in functional response among the three eGFR groups (P>0.05).

Clinical Parameters in Different Response Groups Compared to those in the negative functional response group, patients in the positive functional response group had higher BUN, UA and hemoglobin but lower CREA and HbA1c (all P<0.05). However, there was no difference in the level of eGFR (P>0.05). Patients with positive anatomical response had higher eGFR and hemoglobin, lower BUN, CREA, UA and HbA1c than the negative anatomical response group (all P<0.001). The eyes of the positive response groups had significantly worse BCVA and thicker CST than those of the negative response groups at baseline, respectively (P<0.001 for all). In contrast, the eyes of the positive response groups had significantly better BCVA and thinner CST at the last visit (all P<0.001). Compared to the positive response groups, the negative response groups received fewer conbercept injections in follow-up time, respectively (both P<0.001; Table 3, Figure 1).

Predictors of Functional Response BUN, CREA, UA, eGFR, and other covariates, including sex, age, duration of DM, hypertension, HbA1c level, PRP, baseline BCVA, baseline CST, and total injection numbers were also adjusted in the regression models. Patients who demonstrated a positive functional response were positively correlated with baseline BCVA (logMAR, P=0.001) and baseline CST (P=0.041; Table 4). Concerning the stage of DR, the number of patients with different levels was too small in the positive and negative

Table 3 Comparisons of clinical parameters between positive response group and negative response groups

Parameters	Change in BCVA		*P*	CST reduction		*P*
	Positive functional response (*n*=49)	Negative functional response (*n*=51)		Positive anatomical response (*n*=67)	Negative anatomical response (*n*=33)	
Sex (male/female)	29/20	31/20	0.516	39/28	21/12	0.602
Age, y	55.99±9.42	57.47±8.83	<0.001	56.11±9.24	58.79±8.54	<0.001
Duration of DM, y	9.26±5.77	10.58±6.70	<0.001	10.11±6.03	9.23±7.02	<0.001
Hypertension	59.2%	50.9%	0.267	56.7%	51.2%	0.673
BUN, mmol/L	7.19±3.02	6.12±3.35	<0.001	6.50±2.69	7.30±4.56	<0.001
CREA, μmol/L	91.39±55.86	95.30±66.56	0.008	84.38±43.24	123.69±95.05	<0.001
UA, μmol/L	398.33±78.78	382.71±96.56	<0.001	386.00±77.80	406.22±115.98	<0.001
eGFR, mL/min•1.73 m^2	86.64±23.56	87.18±27.45	0.376	92.14±21.82	69.16±29.09	<0.001
HbA1c, %	8.19±1.67	8.78±1.69	<0.001	8.43±1.70	8.66±1.69	<0.001
Hemoglobin, g/L	124.95±18.74	122.31±16.32	<0.001	126.41±17.48	114.25±15.06	<0.001
Stage of DR						
NPDR	89.8%	43.1%	<0.001	91.0%	15.1%	<0.001
PDR	10.2%	56.9%		9.0%	84.8%	
Status of PRP	53.0%	37.3%	0.112	49.3%	36.4%	0.286
Baseline BCVA (logMAR)	0.98±0.50	0.64±0.43	<0.001	0.82±0.53	0.75±0.34	<0.001
Final BCVA (logMAR)	0.56±0.41	0.88±0.57	<0.001	0.62±0.46	1.05±0.57	<0.001
Baseline CST, μm	455.88±153.08	399.21±138.99	<0.001	441.28±155.43	382.27±113.44	<0.001
Final CST, μm	238.39±71.19	313.03±125.40	<0.001	235.20±61.08	411.39±122.09	<0.001
Number of IVI	2.00±0.93	2.15±1.45	<0.001	2.10±1.22	1.99±1.23	0.002

DM: Diabetes mellitus; BUN: Blood urea nitrogen; CREA: Serum creatintine; UA: Uric acid; eGFR: Estimated glomerular filtration rate; HbA1c: Glycosylated hemoglobin; DR: Diabetic retinopathy; NPDR: Nonproliferative diabetic retinopathy; PDR: Proliferative diabetic retinopathy; PRP: Panretinal photocoagulation; BCVA: Best corrected visual acuity; CST: Central subfield macular thickness; IVI: Intravitreous injection.

Table 4 Ridge regression analysis between functional response and clinical parameters

Parameters	Estimate	Scaled estimate	Standard error	*t*	*P*
Baseline BCVA (logMAR)	0.622	3.057	0.950	3.218	0.001
Baseline CST	0.001	1.950	0.956	2.041	0.041

BCVA: Best corrected visual acuity; CST: Central subfield macular thickness.

Table 5 Ridge regression analysis between anatomical response and clinical parameters

Parameters	Estimate	Scaled estimate	Standard error	*t*	*P*
eGFR	0.011	3.810	0.994	4.035	<0.001
Hemoglobin	0.012	2.357	1.099	2.145	0.032
Baseline CST	0.001	2.657	1.109	2.396	0.017

eGFR: Estimated glomerular filtration rate; CST: Central subfield macular thickness.

functional response groups. Thus, ridge regression analysis was not feasible.

Predictors of Anatomical Response BUN, CREA, UA, eGFR, and other covariates, including sex, age, duration of DM, hypertension, HbA1c level, PRP, baseline BCVA, baseline CST, and total injection numbers were also adjusted in the regression models. Patients who demonstrated a positive anatomical response was positively correlated with eGFR level (P<0.001), hemoglobin level (P=0.032) and baseline CST (P=0.017; Table 5). Regarding the stage of DR, the number of patients with different levels was too small in the positive and negative functional response groups. Thus, ridge regression analysis was not feasible.

DISCUSSION

Intravitreous injection of anti-VEGF agents has been considered the first-line treatment for DME. IVC could improve the functional and anatomical outcomes of the patients with DME[5-7]. Previous studies have shown individual differences in clinical response to anti-VEGF therapy[16-18], suggesting that other factors influencing the treatment response. In this study, baseline BCVA and CST were associated with functional response to IVC. In contrast, eGFR, hemoglobin, and baseline CST were associated with anatomical response to IVC.

Several renal factors have been studied in previous analyses, but there were no consensus results from these studies. It was found that vision improvement was not influenced by renal function, including baseline CREA, eGFR, and BUN in the patients with DME treated with ranibizumab[18]. It was discovered that CREA and eGFR were unrelated to changes in BCVA and CST after anti-VEGF therapy[18]. It was found that renal function had a significant negative correlation with CST improvement after intravitreal bevacizumab injection and intravitreal dexamethasone implant in DME patients[19-21].

Glomerular filtration rate can be used to evaluate the degree of renal function damage and estimate the development and degree development of chronic kidney disease, which can guide diagnosis and clinical decision-making for renal diseases[22]. Our study found that higher baseline eGFR predicted a better anatomical outcome in DME patients treated with IVC, which was consistent with previous studies. It was found that lower eGFR levels were significantly associated with the presence of subretinal fluid before treatment and subretinal fluid residue after 3mo of treatment[23]. It was discovered that patients with poor response to intravitreal bevacizumab injection and steroid hormone implant had worse renal function[21]. The mechanism of eGFR affecting the therapeutic effect of IVC for DME remains unclear, and the explanations have been inconsistent. The perfusion density of the retinal surficial and deep vessels decreased in patients with low eGFR, and reduced retinal blood flow was independently associated with a lower level of eGFR[24-25]. It was speculated that the decrease of eGFR level reduced retinal blood perfusion, leading to macular ischemia and visual impairment[12]. In addition, patients with chronic kidney disease had elevated serum VEGF levels, and the level of VEGF was negatively correlated to the level of eGFR[26]. Increased levels of VEGF can result in changes in retinal vascular permeability and further cause macular edema. In summary, eGFR may influence the clinical response by affecting retinal blood flow perfusion and VEGF level. Other renal factors, BUN and CREA, were not associated with clinical response to IVC, the same as previous studies[19-20].

Higher hemoglobin at baseline was found to be associated with better anatomical outcomes. Anemia accompanies worsening chronic kidney disease as kidney production of erythropoietin declines[27]. It was found that low hemoglobin concentration was a risk factor for developing and increasing macular edema severity[28]. It was found that lower hemoglobin concentration associated with retinal ischemia because of low blood oxygen-transport capacity. They suggested that hypoxia stimulated the release of inflammatory mediators and vasoproliferative factors, such as VEGF[29]. We inferred that the hemoglobin decrease in the blood might lead to retinal ischemia and influence the clinical response of IVC.

Our study found that good baseline BCVA (logMAR) was associated with better functional response, and thicker baseline CST was associated with better functional and anatomical response. In previous studies, poor baseline BCVA seemed to have more visual gains after treatment[30-31]. It was found that treatment response was significantly influenced by baseline BCVA. They explained that this result was caused by “the ceiling effect”, meaning patients could return to normal vision and anatomy despite the differences in baseline BCVA and CST[32]. It was found that baseline CST was the strongest predictor of anatomical outcome, consistent with our research[31].

The impact of HbA1c on clinical response to conbercept of DME was also investigated in our study. In the previous studies, the relationship between HbA1c and the efficacy of anti-VEGF agents in the treatment of DME has been studied, whereas inconsistent results existed. It was discovered that HbA1c affected the visual and anatomic effects of anti-VEGF agents in DME. They highlight the importance of blood glucose control before and during treatment of DME[20]. It was evaluated the effect of blood glucose regulation on intravitreal injection of ranibizumab in treating DME. They found that serum HbA1c value was negatively correlated with change in CST[33]. However, it was found that improving visual acuity and reducing macular edema seemed independent of baseline HbA1c when treated with ranibizumab[34]. We also found that HbA1c was not associated with clinical response to IVC.

The present study was conducted in a real-life clinical setting, which did not meet the loading doses of 3 injections. In a real-world study investigating the efficacy and safety of ranibizumab in patients with DME, it was found that visual acuity was greater in patients who received five or more injections[35]. Many real-world studies[36-37] observed lower average intravitreal injection times than cohort studies[38-39]. The main factors for noncompliance included the cost of the anti-VEGF agent, the psychological burden, whether the patient was covered by medical insurance and the degree of patient’s satisfaction of visual outcome[40-41]. Due to repeated injections, it was difficult for most DME patients to bear this economic burden. We have confirmed that eGFR and hemoglobin could affect the clinical response of conbercept in the treatment of DME. In clinical practice, paying attention to these factors and taking timely intervention means is also expected to reduce the number of intravitreous injections and the economic burden on patients.

This study has several limitations. First, this study was conducted retrospectively. Despite the retrospective nature, however, the clinical data included in our analysis has been routinely recorded in the electronic medical record and could be collected reliably. Second, our study population was

relatively small sample size, so it could not fully represent the situation of the total population. Future studies need to be validated prospectively with large samples.

It was a real-world efficacy analysis, which had more clinical reference significance. Preoperative evaluation of renal function was not only beneficial for preliminary prediction of the approximate number of conbercept injections and effectiveness, but also for reducing the economic burden of DME patients and establishing reasonable expectations, which could promote better doctor-patient communication.

In conclusion, DME patients with good baseline BCVA (LogMAR) and thicker baseline CST showed better functional response to IVC. In contrast, those with high eGFR, high hemoglobin, and thicker baseline CST showed better anatomical response to IVC. The clinical response to IVC for DME may rely to some extent on the regulation of renal function. The prognosis of macular edema may also be an indicator for evaluating renal function.

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