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Latin American Journal of Ophthalmology

Retina *Original Article*

Serum creatinine as a predictor of functional and anatomical success in diabetic tractional retinal detachment

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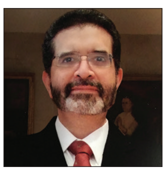

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Received : 20 October 2022
Accepted : 02 November 2022
Published : 24 November 2022

DOI
10.25259/LAJO_8_2022

Quick Response Code:

ABSTRACT

Objectives: The aim of the study was to evaluate pre-operative, intraoperative, and post-operative factors associated with functional and anatomical success in patients with diabetic tractional retinal detachment (TRD) treated with pars plana vitrectomy (PPV).

Material and Methods: We retrospectively reviewed the medical records of patients with diabetic TRD surgically repaired with PPV between March 2014 and February 2015 at the Instituto de Oftalmología Fundación de Asistencia Privada Conde de Valenciana, IAP in Mexico City. A total of 250 records were reviewed and 85 met the inclusion criteria. Pre-operative, intraoperative, and post-operative variables were obtained from all records. Statistical analysis included Fisher's exact test, Kruskal–Wallis test, and Mann–Whitney U test.

Results: A total of 88 eyes of 85 patients were included in the study. The average patient age at the time of the surgery was 51.53 years (SD ± 11.99). At post-operative month (POM) 1, a greater pre-operative serum creatinine value and a greater surgical duration were associated with a worse anatomical success (P = 0.032; P = 0.014). At POM 1, 31% of the eyes with macula-involved TRD and 57.5% of the eyes without macula-involved TRD achieved visual success (P = 0.013, Fisher's exact test).

Conclusion: A greater pre-operative serum creatinine value was associated with a worse visual and anatomical outcome at POM 1. A macula-involved TRD was associated with a worse visual outcome at POM 3. Post-operative complications were associated with a worse functional and/or anatomical success at the final follow-up visit ($P < 0.05$).

Keywords: Diabetes, Tractional retinal detachment, Vitrectomy, Clinical features, Visual improvement, Anatomical success, Serum creatinine

INTRODUCTION

Diabetic retinopathy (DR) is a leading cause of visual impairment in adults aged 20–74 years and is responsible for causing blindness in approximately 4% of individuals with Type 1 diabetes mellitus (DM) and in 1.6% of those with Type 2 DM.[1-3] DR is divided into non-proliferative and proliferative depending on the absence or presence of neovascularization and can be further classified by severity.[4] These stratifications have been useful in the analysis of indicators of disease progression and treatment strategies.

In the Wisconsin Epidemiologic Study of DR, higher glycosylated hemoglobin, higher blood pressure level, greater body mass index (BMI), severe DR, longer duration of diabetes, and gross proteinuria were associated with a higher incidence and/or progression of DR in patients with Type 1 DM.[5,6] Comparably, microalbuminuria has been associated with proliferative diabetic retinopathy (PDR) in patients with Type 2 DM.[7]

Diabetic macular edema (DME) and PDR are among the most common causes of persistent visual loss in DR.[8-10] Tractional retinal detachment (TRD) represents an advanced form of PDR that results from the development of neovascularization and contractile fibrous tissue into the vitreomacular interface. Excessive anteroposterior and tangential traction on the fibrovascular complex and ischemic retina causes the retina to detach. Diabetic TRD is then repaired with pars plana vitrectomy (PPV).[11,12]

Despite recent innovations in vitreoretinal surgery including high-speed and small-gauge vitrectomy systems, improved vitrectomy fluidics, bimanual surgery, and the development of anti-vascular endothelial growth factor (VEGF) intravitreal injections, surgical management of diabetic TRD continues to represent one of the most challenging surgeries for the vitreoretinal surgeon.[12,13] The presence of extensive fibrovascular membranes and an ischemic retina contribute to the complexity of the surgical repair.[12,14] Earlier studies have demonstrated that preoperative factors associated with poorer visual outcome include iris neovascularization, cataract, visual acuity <5/200, macular ischemia, and tractional or rhegmatogenous retinal detachment (RRD).[15-18]

Visual recovery after surgical management depends on the functional and structural recovery of the macula which may be severely injured by chronic macular detachment and edema.[19] Moreover, these eyes often have severe complications such as neovascular glaucoma and ischemic optic neuropathy which have been defined as predictors for low visual outcomes following surgery.[19,20] The unique set of characteristics of each patient with DR demonstrates the importance of undergoing an individualized and timely approach to treatment to preserve vision.

Hence, the aim of this study was to analyze the effect of pre-operative, intraoperative, and post-operative variables on visual and anatomical success in diabetic TRD treated with PPV at a single ophthalmological reference center. The evaluation of predictors associated with successful visual and anatomical outcomes may serve as guidance for improved surgical decisions and patient counseling.

MATERIAL AND METHODS

This study was approved by the Institutional Review Board and followed the tenets of the Declaration of Helsinki.

We retrospectively reviewed the medical records of patients with diabetic TRD surgically repaired with PPV between March 2014 and February 2015 at the Instituto de Oftalmología Fundación de Asistencia Privada Conde de Valenciana, IAP in Mexico City. The surgical approach, including the instrument gauge and the tamponade agent, was based on the surgeons' preference at the time of surgery.

Out of the 250 records reviewed, 85 met the inclusion criteria. All patients required a pre-operative internal medicine and anesthesiology assessment, a complete eye examination by a retina specialist, a pre-operative A-scan and B-scan ultrasonography, and a follow-up consultation 1 and 3 months after the surgery. Patients were excluded if they had a non-diabetic TRD or a previous surgically repaired retinal detachment. Pre-operative, intraoperative, and post-operative variables were obtained from all records and are summarized in [Table 1].

The pre-operative variables included: Age, type of DM (1 or 2), the period between the diagnosis of DM and the TRD in years, type of systemic treatment, microvascular or macrovascular systemic manifestations due to DM, BMI, creatinine level (mg/dl), best-corrected visual acuity (BCVA) measured on a Snellen chart, axial length (measured by an A-scan ultrasonography), the period between the onset of visual symptoms and the surgical intervention, lens status (phakic, aphakic, and pseudophakic), neovascular glaucoma, vitreous hemorrhage (VH), macula status assessed on the B-scan ultrasonography, and history of pre-operative panretinal laser photocoagulation (PRP) and/or anti-VEGF intravitreal injection.

The intraoperative variables included: Concurrent cataract extraction at the time of PPV, use of tamponade agent (silicone oil, air, octafluoro propane gas, or sulfur hexafluoride gas), duration of the surgery, presence of retinotomies and/or other surgical complications, intraoperative observations such as submacular hemorrhage, macular hole or optic disc pallor, and the use of special surgical techniques such as bimanual vitrectomy, viscodissection, or dissection with perfluoro-N-octane.

The post-operative variables included: The presence of VH, recurrent retinal detachment (tractional, rhegmatogenous, or combined), neovascular glaucoma, and glaucoma due to vitreoretinal surgery.

The main outcome measures were anatomical success and BCVA at post-operative month (POM) 3. A successful visual outcome was defined as gaining at least one line of vision at POM 3. Anatomical success was considered if a completely attached retina was observed at the final follow-up examination.

Statistical procedures used for this analysis included Fisher's exact test, Kruskal–Wallis test, and Mann–Whitney U test. $P < 0.05$ was considered statistically significant.

RESULTS

Pre-operative factors

A total of 88 eyes of 85 patients met the inclusion criteria for the study. The mean age at the time of the surgery was 51.53 ± 11.99 years. Eighty-two eyes were from patients with Type 2 DM and six eyes were from patients with Type 1 DM. Forty-eight patients (54.5%) had systemic microvascular complications, including chronic kidney disease in 47 patients and diabetic neuropathy in one patient.

Table 1: Pre-operative, intraoperative, and post-operative variables.

Variables

Pre-operative
- Age
- Type of DM (1 or 2)
- Systemic DM treatment
- The period between the diagnosis of DM and the TRD in years
- The period between the onset of visual symptoms and the surgical intervention in months
- Presence or absence of microvascular and/or macrovascular systemic manifestations due to DM
- Creatinine value
- BMI
- History of PRP
- History of preoperative anti-VEGF intravitreal injection
- BCVA on Snellen chart
- Axial length assessed by an A-scan ultrasonography
- Lens status
- Macula status assessed on the B-scan ultrasonography
- Iris neovascularization
- Vitreous hemorrhage.

Intraoperative
- Concurrent cataract extraction at the time of PPV
- Tamponade agent (silicone oil, air, octa-fluoro propane gas, or sulfur hexafluoride gas)
- Duration of the surgery
- Presence of retinotomies or other surgical complications
- Number of retinotomies
- Intraoperative observations
- The use of special surgical techniques.

Postoperative
- Vitreous hemorrhage
- Recurrent tractional, rhegmatogenous, or combined retinal detachment
- Neovascular glaucoma
- Glaucoma due to vitreoretinal surgery.

Main outcomes
- Visual success
- Anatomical success.

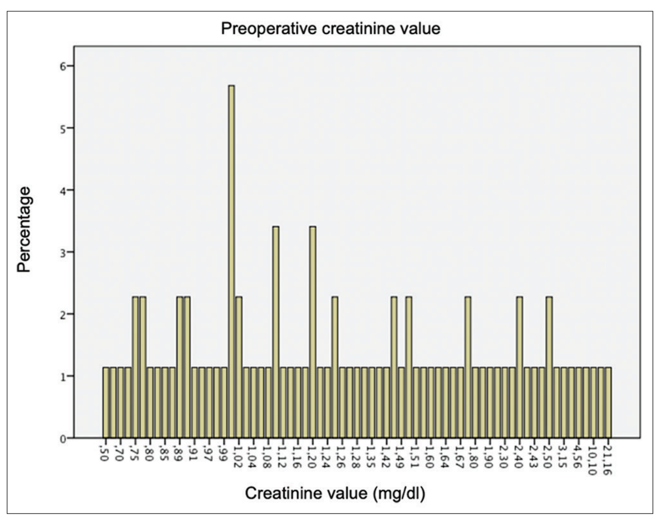
DM: Diabetes mellitus, TRD: Tractional retinal detachment, BMI: Body mass index, VEGF: Vascular endothelial growth factor, BCVA: Best corrected visual acuity, PRP: Panretinal laser photocoagulation, PPV: Pars plana vitrectomy

Six patients (6.8%) had macrovascular complications, including diabetic foot in five patients and upper limb arterial thromboembolism in one patient. The mean BMI was 26.29 ± 4.97, and 35.7% of the patients were categorized as obese (BMI >26.9). The median pre-operative creatinine value was 1.25 mg/dl (P25 = 1, P75 = 1.68) [Graph 1]. Most of the patients (44.3%) were being treated with only oral hypoglycemic medications, while 21.6% were being treated with both insulin and oral hypoglycemic medications. Six patients (6.8%) were not receiving systemic treatment.

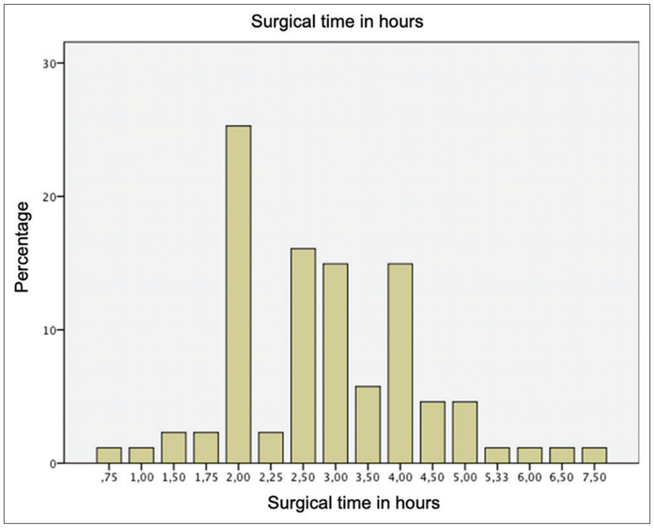
On average, the period between the diagnosis of DM and the TRD was of 15.72 ± 7.49 years with a median of 16.5 years (P25 = 10.25, P75 = 21). The median period between the onset of visual symptoms and the surgical intervention was of 8 months (P25 = 5, P75 = 12). The mean axial length was 22.84 ± 0.75 mm. Regarding the presence of VH, 22.7% of the patients had Grade 3, 20.5% had Grade 2, 12.5% had Grade 4, and 3.4% had Grade 1 VH. The Previous PRP had been performed in 47.7% of the eyes and only five eyes received pre-operative intravitreal anti-VEGF. Two eyes had pre-operative iris neovascularization. A total of 55 eyes (62.5%) had a macula involving TRD.

Intraoperative factors

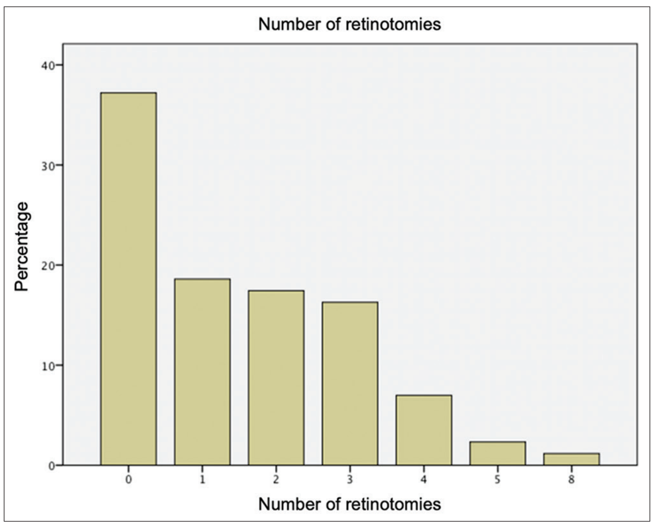
The median surgical time was of 2.5 h (P25 = 2, P75 = 4) [Graph 2]. A total of 78 eyes (88.6%) underwent concurrent cataract extraction at the time of the PPV. Of the 10 eyes that were treated with only PPV, six eyes had a clear lens, and four eyes were pseudophakic. Posterior capsule rupture occurred in five eyes, and in all cases, a three-piece lens was implanted in the sulcus. Incidental retinotomies occurred in 62.7% of the cases [Graph 3]. Regarding the tamponade agent, silicone oil was used in most cases (39 eyes) followed by C_3F_8 in 19 eyes (22%), SF_6 in 16 eyes, and air in 12 eyes (13.9%).



Graph 1: Distribution of pre-operative creatinine value (mg/dl).



Graph 2: Surgical time in hours.



Graph 3: Number of retinotomies.

Post-operative factors

Overall, functional success was achieved in 40.9% of the eyes at POM 1 and in 48.9% at POM 3. Although 78.4% of the eyes presented an attached macula at POM 1, only 71.6% of the eyes achieved a successful retinal reattachment at the final follow-up examination. Of the seventeen eyes (19.3%) that presented post-operative complications, the most common complication encountered was secondary RRD which occurred in 6 eyes (6.8%). Other complications included persistent VH at POM 3 (3.4%), secondary combined rhegmatogenous and TRD (1.1%), neovascular glaucoma (1.1%), and endophthalmitis (1.1%) [Table 2].

Table 2: Clinical factors.

Factors	Overall (*n*=88)
Eye with TRD	
Right	43 (48%)
Left	45 (52%)
Age, mean	51.53 years (SD±11.99)
Type of DM	
Type 1	6 (7%)
Type 2	82 (93%)
Period between the diagnosis of DM and TRD, mean	15.72 years (SD±7.49)
Systemic microvascular manifestations	48 (54.5%)
Chronic kidney disease	47 (53%)
Diabetic neuropathy	1 (0.01%)
Systemic macrovascular manifestations	6 (6.8%)
Diabetic foot	5
Upper limb arterial thromboembolism	1
BMI, mean	26.29 (SD±4.97)
BMI >26.9	31 (35.7%)
Pre-operative creatinine value, median (95% CI)	1.25 mg/dl (P25=1, P75=1.68)
Systemic DM treatment	
Oral hypoglycemic medication	39 (44.3%)
Insulin + oral hypoglycemic medication	24 (27.3%)
Insulin	19 (21.6%)
Without treatment	6 (6.8%)
Months of symptoms, median (95% CI)	8 months (P25=5, P75=12)
VH grade	
Grade I	3 (3.4%)
Grade II	18 (20.5%)
Grade III	20 (22.7%)
Grade IV	11 (12,5%)
PRP	42 (47.7%)
Iris neovascularization	2 (2%)
Macula-involved TRD	55 (62.5%)
Surgical duration, mean	2.5 h
Type of surgery	
PPV	10 (12%)
PPV + phacoemulsification	78 (88%)
Retinotomies	55 (62.7%)
Tamponade	
Silicone oil	40 (45.3%)
C_3F_8	20 (22%)
SF_6	16 (18.6%)
Air	12 (13.9%)
Overall visual success	
POM 1	36 (40.9%)
POM 3	43 (48.9%)

SD: Standard deviation, DM: Diabetes mellitus, POM: Postoperative month, BMI: Body mass index, PPV: Pars plana vitrectomy, VH: Vitreous hemorrhage, PRP: Panretinal laser photocoagulation, TRD: Tractional retinal detachment

Visual predictive factors

A univariate analysis using the Mann–Whitney U test demonstrated that a greater pre-operative creatinine value was correlated with a worse visual outcome (P = 0.01). Moreover, a longer surgical time and a greater number of intraoperative retinotomies were associated with a worse visual outcome at the final follow-up examination ($P < 0.001$ and $P < 0.001$, respectively). Altogether, visual success at the final follow-up examination was achieved in 76.6% of the eyes with TRD not involving the macula and in 44.4% of the eyes with TRD involving the macula ($P = 0.005$).

At the final follow-up examination, visual success was achieved in 68.3% of the eyes without post-operative complications and in 13.3% of the eyes with post-operative complications ($P < 0.001$). At the initial post-operative visit, 53.1% of the eyes without intraoperative retinotomies improved vision, while 33.3% of the eyes with intraoperative retinotomies gained at least one line of vision ($P = 0.045$). Comparably, at the final visit, 80.7% of the eyes without intraoperative retinotomies achieved a successful visual outcome, while only 44.6% of the eyes with retinotomies gained vision ($P = 0.03$).

Fifty-nine eyes (67.7%) with pre-operative Grades 3 and 4 VH presented visual improvement at the initial post-operative examination. Conversely, only 26.3% of the eyes without pre-operative VH presented visual improvement during the same evaluation period ($P < 0.001$). Similarly, at POM 3, 81.4% of the eyes with pre-operative Grade 3 or 4 VH improved vision, while only 43.9% of the eyes without pre-operative VH attained functional success ($P = 0.03$) [Tables 3 and 4].

Anatomical predictive factors

A greater pre-operative creatinine value was related to a worse anatomical outcome at the first POM ($P = 0.032$; Kruskal–Wallis test). A prolonged operative time was also associated with a worse anatomical outcome at the first follow-up examination ($P = 0.014$; Kruskal–Wallis test). At the first POM, anatomical success was achieved in 98.4% of the eyes without post-operative complications and in 70% of the eyes with post-operative complications ($P < 0.001$). Comparably, at the final follow-up examination, anatomical success was achieved in 95% of the eyes without post-operative complications and in 46.1% of the eyes with post-operative complications ($P < 0.001$) [Tables 5 and 6].

DISCUSSION

In this study, we report pre-operative, intraoperative, and post-operative factors associated with functional and anatomical success in patients with diabetic TRD treated with PPV at a single reference ophthalmological center.

Table 3: Factors associated with a worse visual outcome (continuous variables with statistically significant results).

Worse visual outcome	Pre-operative creatinine value	Number of retinotomies	Surgical duration
Post-operative month 1	Greater creatinine value (P=0.01)	Greater number of retinotomies (P=0.012)	Greater surgical duration (P<0.001)
Post-operative month 3		Greater number of retinotomies (P<0.001)	Greater surgical duration (P<0.001)

Table 4: Percentage of eyes with functional success (categorical variables with statistically significant results).

	Macula-involved TRD (B-scan ultrasonography)	Retinotomies	Pre-operative Grade 3 or 4 VH	Post-operative complications
Post-operative month 1	No=57.5% Yes=31% (P=0.013)	No=53.1% Yes=33.3% (P=0.045)	No=67.7% Yes=26.3% (P<0.001)	No=46.4% Yes=17.6% (P=0.026)
Post-operative month 3	No=76.6% Yes=44.4% (P=0.005)	No=80.7% Yes=44.6% (P=0.003)	No=43.9% Yes=81.4% (P=0.03)	No=68.3% Yes=13.3% (P<0.001)

TRD: Tractional retinal detachment, VH: Vitreous hemorrhage

Table 5: Factors associated with a worse anatomical outcome (continuous variables with statistically significant results).

	Pre-operative creatinine value	Number of retinotomies	Surgical duration
Post-operative month 1	Greater creatinine value (P=0.032)	Greater number of retinotomies (P=0.012)	Greater surgical duration (P=0.014)

Table 6: Percentage of eyes with anatomical success (categorical variables with statistically significant results).

	With postoperative complications	Without post-operative complications	*P*-value
Post-operative month 1	70%	98.4%	<0.001
Post-operative month 3	46.1%	95%	<0.001

A limited number of studies have analyzed the effect of renal function on the outcomes of vitrectomy for TRD and DME. An earlier study led by Kojima *et al*. did not find a correlation between the pre-operative serum creatinine level and a change in post-operative retinal morphology in patients who underwent PPV for DME.[21] Similarly, a study led by Larrañaga-Fragoso *et al*. reported that a reduced renal function does not adversely affect visual outcomes of patients with TRD repaired with PPV.[22] Comparably, Tokuyama *et al*. demonstrated that hemodialysis has little effect on macular leakage in patients with DME and DR. The authors described that a possible explanation for the lack of change in macular leakage after hemodialysis despite clinical expectations could be the presence of a sufficiently preserved inner blood-retinal barrier and retinal blood flow autoregulation capable of protecting the capillaries from the dynamic changes in fluid and plasma volumes.[23] Contrary to these findings, in our study, patients with a greater pre-operative serum creatinine level achieved a worse functional and anatomical outcome 1 month after the PPV. A possible explanation for this observation could be that patients with greater serum creatinine levels have greater microvascular damage overall.[24] In patients with PDR and renal disease, high blood pressures and low protein serum levels may affect the hydrostatic and plasmatic osmotic pressures, respectively, which increase vascular leakage.[23]

The complexity of the surgical repair of diabetic TRD largely depends on the amount of vitreoretinal traction since the dissection of firmly adhered fibrovascular membranes may lead to incidental retinotomies and prolonged operative duration.[15] Consistent with these observations, we found that fewer retinotomies and a shorter surgical duration were associated with a better visual outcome at the initial and final follow-up examinations. Overall, patients with worse functional and anatomical outcomes were those who underwent complex surgeries due to a friable and ischemic retina.

Supporting the findings of earlier studies, our results demonstrate that a pre-operative macula involving TRD is an important predictor for a worse post-operative outcome.[15] Overall, eyes with pre-operative macula involving TRD achieved worse functional and anatomical outcomes at POMs 1 and 3.

Initially, patients with a pre-operative Grade 3 or 4 VH had a significantly lower visual acuity than those with Grade 1 or 2 VH. Unpredictably, patients with pre-operative Grade 3 or 4 VH presented better final visual and anatomical outcomes than those with a lower grade of VH. Finally, a greater number of post-operative complications was found to be associated with a worse overall final outcome.

CONCLUSION

Consistent with earlier studies, we demonstrate that timely PPV is an effective procedure for diabetic TRD repair and that due to the often-unpredictable results; it is of utmost importance to fully grasp all the variables that could affect the patient's outcome. We conclude that greater preoperative serum creatinine levels correlate with a worse final functional and anatomical outcome.

The limitations of our study include the retrospective design, the lack of a long-term follow-up, and the variability of surgeons. Thus, further research is warranted to better elucidate the relationship between pre-operative serum creatinine levels and/or renal function and overall surgical success.

Declaration of patient consent

Patient's consent not required as patient's identity is not disclosed or compromised.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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How to cite this article: Cano-Hidalgo RA, Urrea-Victoria T, Kim-Lee JH. Serum creatinine as a predictors of functional and anatomical success in diabetic tractional retinal detachment. Lat Am J Ophthalmol 2022:5:4.