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Research Article

Long Term Outcomes of Pars Plana Vitrectomy in Diabetic Eyes with Poor Baseline Visual Acuity

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Abstract

Purpose: To investigate the long-term visual outcomes of patients undergoing pars plana vitrectomy for diabetic retinopathy-related complications and determine factors that predict final visual acuity.

Design: Retrospective study of 37 eyes in 33 diabetic patients who underwent pars plana vitrectomy (PPV) for diabetic retinopathy at a single institution. The study included patients with type 1 or 2 diabetes mellitus who had PPV for persistent vitreous hemorrhage or macula-threatening tractional retinal detachment. Surgeries were performed by the same vitreoretinal surgeon using standard 23-gauge needle vitrectomy, and complete pan-retinal photocoagulation was performed in all cases.

Results: A study analyzed data from 37 eyes over an average 4.84 ± 2.74 years. Most had type 2 diabetes and were treated for macula-threatening tractional retinal detachment or non-clearing vitreous hemorrhage (NCVH). Visual acuity improved in year 1 and remained stable at 5 years. Only 6 eyes needed vitreous washout. Regression models revealed 6-month visual acuity as the sole predictor for final visual acuity in years 2 and 5.

Conclusions: This study adds to existing knowledge about long-term outcomes in diabetic eyes undergoing vitrectomy for NCVH and macula threatening TRD. Most eyes show positive 2- and 5-year visual outcomes, regardless of the initial reason for surgery. 6-month VA appears to be the strongest predictor of final VA. Further research is needed to identify baseline ocular characteristics using objective metrics to better predict surgical benefits.

Keywords: Pars Plana Vitrectomy; Diabetic Retinopathy; Long Term Outcome

Introduction

Diabetic retinopathy is one of the leading causes of blindness among working-age adults and elderly. There is a global increase in the prevalence of diabetes mellitus with an estimated prevalence in 2019 of about 9.3%, rising to 10.2% (More than half a billion individuals) by 2030 and 10.9% (700 million) by 2045 [1]. Fifty percent of the diabetic patients are accidentally discovered and are referred with advanced retinopathy and late complications with potentially irreversible vision loss.

About 5% of the patients with diabetic retinopathy despite appropriate ophthalmic care and strict metabolic control still develop ocular complications requiring surgical treatment [2]. Non-clearing vitreous hemorrhage (NCVH), tractional retinal detachment (TRD) involving the macula, combined tractional and rhegmatogenous retinal detachment and neovascular glaucoma are the most common complications requiring a vitreoretinal surgical intervention.

Since the advent of vitrectomy in the 1970s, surgical techniques and instrumentation have improved to a great extent. However, prior investigations have shown that nearly a third of patients who underwent vitrectomy for TRD require a second operation [3]. Accelerated cataract progression and recurrent vitreous hemorrhage are the most common complications in eyes receiving vitrectomy [4]. Some of the more established risk factors that increase the likelihood of recurrent VH include fibrovascular ingrowth at sclerotomy sites which could be present in about 85% of cases, incomplete PRP and younger patients [5].

Anatomical and visual outcomes are quite often unpredictable after vitrectomy for PDR. Anatomical results are often limited by the extent and degree fibrous tissue, vitreoretinal adhesion, and iatrogenic tears. Functional visual outcome is also limited due to macular dysfunction from a long duration of macular traction and ischemic maculopathy [6]. There are a limited number of published articles discussing the long-term visual outcomes of PPV for DR complications.

Therefore, the purpose of the current study was to assess long term visual outcomes for patients undergoing PPV for diabetic retinopathy associated complications and to determine baseline characteristics that predict final VA and determine which eyes are likely to achieve good visual outcomes.

Methods

This was a retrospective non-comparative chart review of 37 eyes of 33 diabetic patients with PDR who underwent PPV between Feb 2010 and Jan 2018 at a single institution (Alex iCare) and had at least 6 months of follow up. The study was approved by the IRB of the Alexandria Faculty of medicine (IRB number 00012098). The need for consent forms was waived by the IRB given that it was a retrospective chart review.

The study included patients with type 1 or 2 DM, who had PPV for diabetic retinopathy related complications either vitreous hemorrhage or macula threatening tractional retinal detachment. The study excluded any patients with concomitant retinal diseases that may or may not have contributed to the need for surgery (retinal vein occlusion, macular dystrophy, trauma, rhegmatogenous retinal detachment, etc.) or patients with less than 6 months of follow up.

Patient records were reviewed for demographic and clinical data such as sex, age, type, and duration of diabetes mellitus, coexisting ophthalmological disease (such as glaucoma), coexisting systemic diseases (e.g., hypertension), use of oral anticoagulant/antiplatelet medications, and history of previous interventions (phacoemulsification, vitrectomy, PRP laser or anti-VEGF injection). In addition, ocular data acquired from the pre-operative (pre-op) exam was obtained such as BCVA, IOP and indication for surgery (non-clearing vitreous hemorrhage (NCVH) or macular threatening TRD). Post operative data included BCVA at each visit, IOP, results of the dilated fundus exam or imaging, subsequent surgeries, and their indication. Snellen best corrected visual acuity (BCVA) for each patient was collected from their files and for the purposes of statistical data analysis it was converted to ETDRS letter equivalent.

All cases were operated under general anesthesia by the same vitreoretinal surgeon (AAS), by using standard 23-gauge needle vitrectomy and complete pan-retinal photocoagulation (PRP) was performed in all cases.

Statistics

The Shapiro-Wilk test was used to test for normality. Comparison between VA pre-operative and at years, 1,2,3,4 and 5 were performed using a repeated measures general linear model. Wilcoxon Rank was used to compare between VA in the vitreous hemorrhage and tractional RD groups at each time point. Multivariate regression models were run looking at the association between age, duration of DM, pre-operative VA and 6-month VA with VA at 2 and 5 years. In addition, a binary regression model was run looking at the association of age, duration of DM, hypertension, prior PRP, pre-operative VA, pre-op anti-VEGF use, pre-operative VA and 6-month VA with good VA outcomes (20/40 or better) at year. We used SPSS statistical software version 23 (SPSS, Inc., IBM Company, Chicago, IL, USA) for statistical analysis. A P value of <0.05 was considered significant for these exploratory analyses.

Results

The study included 37 eyes of 33 patients with a mean follow up duration of 4.84 ± 2.74 years. Approximately 88% and 70% of patients completed the 2 and 3 years of follow up respectively. 55% and 33% of patients completed the 4 and 5 years follow ups.

A summary of demographic, ocular and prior ocular treatment history is summarized in table 1. The mean age of patients was 60.64 ± 10.03 year with 60.6% of patients being female. (87.9%) of patients had type 2 DM with a mean duration of 24.4 ± 6.78 years. Prior to surgery 48.8% of eyes had prior PRP and 40.5% had prior anti-VEGF injections. 27% of eyes were pseudophakic. The indications for surgery were evenly split with 43.2% undergoing surgery for macula threatening TRD while 56.8% had surgery for NCVH. Most patients had air tamponade placed at the end of surgery (73%) while the remaining had either silicone oil (18.9%) or SF6 gas (8.1%).

Table 1: Demographic, eye and operative data for patients included in the study.

Demographic data	37 eyes/33 patients
Age (years, mean ± SD)	60.64 ± 10.03
Female	60.6%
Type 2 DM	87.9%
Duration DM (years, mean ± SD)	24.4 ± 6.78
Hypertension	51.5%
Eye Characteristics	
Prior PRP	18/37 (48.6%)
Prior PPV	2/37 (5.4%)
Prior anti-VEGF	15/37 (40.5%)
Pseudo phakic	10/37 (27.0%)
Mean Duration of follow up (years, mean ± SD)	4.84 ± 2.74
Indications for PPV	
Macula threatening TRD	16/37 (43.2%)
Non clearing VH (NCVH)	21/37 (56.8%)
Tamponade	
Air	27/37 (73.0%)
Silicone	7/37 (18.9%)
Gas	3/37 (8.1 %)
Anti-VEGF	
Intraoperative	15/37 (40.5%)
1-2 days Pre-operative	1/37 (2.7%)
Phacoemulsification	
Same time as PPV	4/27 (14.8%)
Post PPV	16/27 (59.3%)

PPV; pars plana vitrectomy, VEGF; vascular endothelial growth factor, PRP; panretinal photocoagulation, DM; diabetes mellitus, VH; vitreous hemorrhage, NCVH; non clearing VH, TRD; tractional retinal detachment.

Figure 1 shows the change in ETDRS equivalent VA from a baseline to year 5. BCVA improved significantly from baseline to year 1. The VA achieved in year 1 remained stable at 5 years, however the number of eyes completing follow up decreased from 31 at year 1 to 18 by year 5. There was a statistically significant improvement from the pre-operative baseline to year 1, but no significant differences were noted between any of the subsequent years. Of note the VA at each of the subsequent years of follow up remained significantly greater than the baseline.

When stratifying eyes based on the indication for surgery (persistent VH vs tractional RD), both groups showed a statistically significant improvement in VA at year 1 compared to baseline and

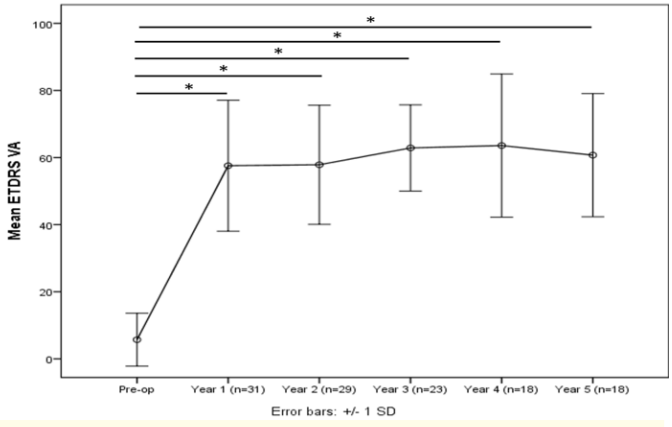
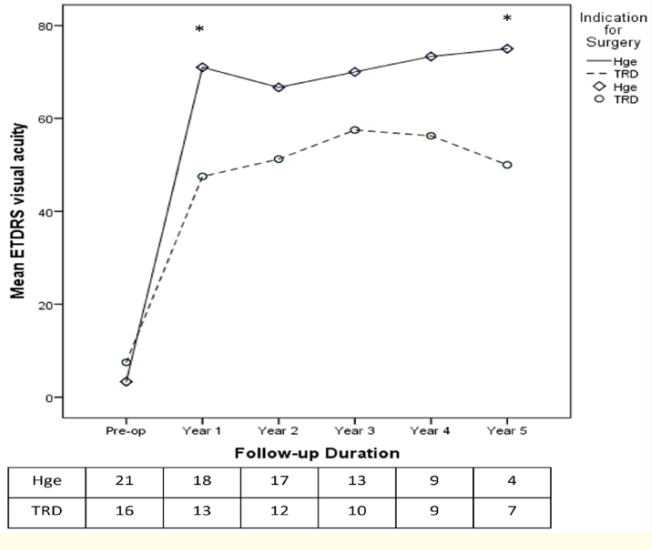


Figure 1: VA outcomes in eyes undergoing diabetic eyes undergoing PPV.

this VA gain was maintained at years 2, 3, 4 and 5. Although VA gain in eyes being treated for VH was significantly greater at the year 1 follow up compared to the TRD group (63.39 ± 20.33 vs 40.00 ± 26.54, p = 0.009), by year 2 this difference was no longer statistically significant (Figure 2 and supplementary table 1).



Hge	21	18	17	13	9	4
TRD	16	13	12	10	9	7

Figure 2: Comparison between VA outcomes in the group undergoing surgery for persistent VH and tractional retinal detachment.

Supplementary table 1: Comparison between VA in the group undergoing PPV for persistent VH and tractional retinal detachment.

Visit (numbers in each group – Hge/TRD)	Persistent vitreous Hemorrhage	Tractional Retinal Detachment	P-value (t-test)	P-value (Wilcoxon Rank)
Pre-operative (21/16)	16.19 ± 27.47	18.13 ± 25.55	0.828	0.820
Year 1(18/13)	63.39 ± 20.33	40.00 ± 26.54	0.009	0.12
Year 2(17/12)	57.82 ± 31.12	41.67 ± 34.13	0.197	0.195
Year 3(13/10)	56.54 ± 27.34	45.80 ± 30.16	0.389	0.410
Year 4(9/9)	65.00 ± 18.03	57.22 ± 20.64	0.407	0.297
Year 5(4/7)	77.50 ± 5.00	50.71 ± 28.78	0.05	0.073

TRD; tractional retinal detachment

Most eyes (n = 23) who were phakic pre-operatively, did not undergo simultaneous phacoemulsification and did not require silicone oil tamponade, needed cataract surgery (56.23%) with the mean duration to surgery being 1.2 years. Of the eyes that had silicone oil injected at the end of surgery, 71.4% had the oil removed within 1 year of having the initial surgery. Only 6 eyes (16.22%) required a vitreous wash out for persistent vitreous hemorrhage post-surgery within 2-3 months of the original intervention (Table 2).

Table 2: Interventions required after the primary surgery for diabetic eyes undergoing PPV for either VH or TRD.

	Number at risk	Number receiving intervention	Percentage	Duration to intervention (years)
Phaco	23	13	56.52	1.2
Phaco+SOR	4	3	75.00	0.9
Rhegmatogenous RD repair	37	1	2.70	0.31
AC wash	37	1	2.70	0.07
Vit wash	37	6	16.22	0.23
SOR	3	2	66.67	0.71
IOL dislocation	27	1	3.70	11.3
Post operative Anti-VEGF	37	2	5.41	1.6
Cyclodiode	37	1	2.70	1.7

SOR; silicone oil removal, RD; retinal detachment, AC; anterior chamber, IOL; intraocular lens, VEGF; vascular endothelial growth factor.

Figure 3 shows the visual acuity outcomes for 29 cases that completed the 2 years follow up post-surgery. Most eyes had a visual acuity improvement compared to baseline and many of those eyes had a persistent improvement in VA that was maintained at the 2 years follow up. Only 2 eyes had a VA at year 2 that was lower that the pre-operative VA (case 5 and 17), while 3 eyes showed an initial VA improvement at year 1 only to return to baseline VA at year 2.

Linear regression models showed that only VA at 6 months was associated with the VA at year 2 and year 5 (Supplementary table 2 and Figure 4). Baseline VA, age, sex, prior PRP and HTN were not associated with final VA at either year 2 or 5. Binary logistic models looking at possible associations between baseline characteristics and good visual outcome (20/40 or better) at year 2 did not find any significant associations (Supplementary table 3).

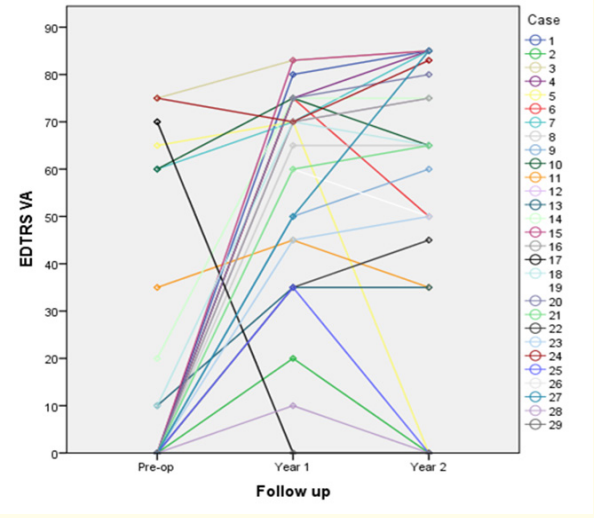


Figure 3: Line graphs showing the VA outcomes at year 2 for individual cases undergoing PPV.

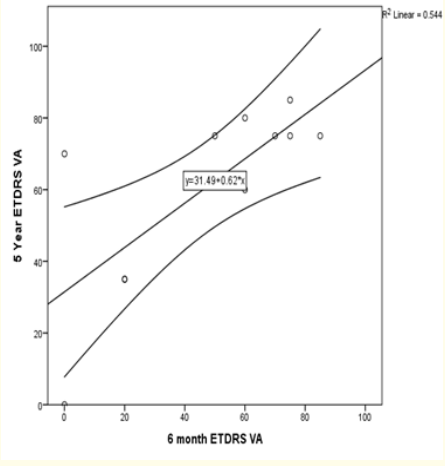
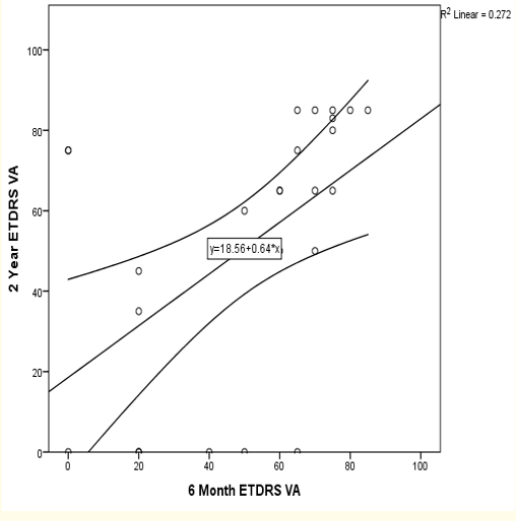


Figure 4: Scatter plots showing the association between VA at 6 months and the VA at year 2 and 5 of follow up.

Supplementary table 2: Multivariate linear Regression model to predict 2-year VA outcomes in diabetic eyes underdoing PPV for either VH or TRD.

	B	Lower Bound	Upper Bound	P-value
Age	-0.136	-1.869	1.597	0.871
Duration DM	-0.843	-2.723	1.038	0.360
Pre-op VA	0.008	-0.528	0.545	0.974
6 Month VA	0.637	0.147	1.126	0.014

DM; diabetes mellitus, VA; visual acuity.



Supplementary table 3: Binary logistic regression model looking at parameters that can predict good VA outcomes (20/40 or better) at year 2.

	95% CI for Exp(B)			
	Exp(B)	Lower	Upper	P-value
Age	0.996	0.923	1.075	0.919
Duration DM	0.935	0.819	1.066	0.314
Hypertension	2.187	0.469	10.210	0.319
Prior PRP	0.960	0.213	4.335	0.935
Pre-Op anti-VEGF	1.009	0.982	1.037	0.503
Pre-Op VA	2.667	0.529	13.43	0.234
6-month VA	1.024	0.990	1.060	0.173

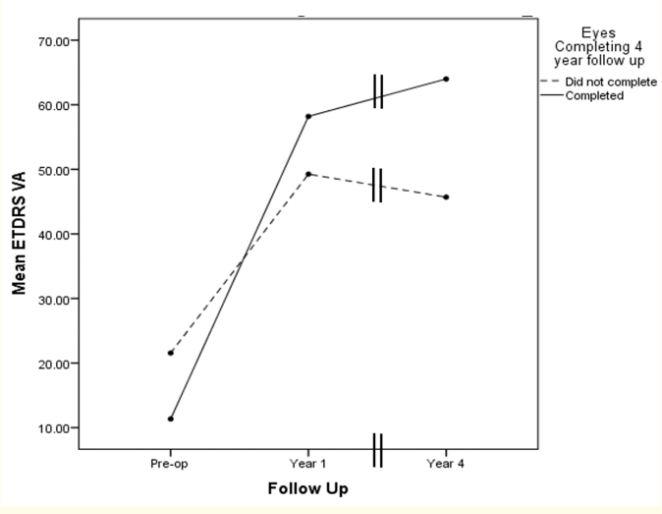
DM; diabetes mellitus, PRP; panretinal photocoagulation, VA; visual acuity, VEGF; vascular endothelial growth factor

Given that only 50% of eyes had 4 years follow up, a sensitivity analysis was conducted looking at eyes that completed the 4 years follow up versus those that did not and found no significant differences between both groups in terms of pre-operative VA as well as VA at years 1 and 2 (Supplementary table 4 and supplementary figure 1).

Supplementary table 4: Comparison between VA at 1 year in the groups that did and did not complete 4 years follow up post PPV.

	Completed 4 year follow up (n = 15)	Did not complete 4 years follow up (n = 16)	P-value (t-test)
Pre-op VA	11.33 ± 18.37	21.56 ± 21.56	0.302
Year 1 VA	58.20 ± 14.83	49.25 ± 32.56	0.338
Year 2 VA	60.76 ± 16.94	43.31 ± 40.43	0.132

VA; visual acuity.



Supplementary Figure 1: Comparison between VA outcomes in the group completing 4 years of follow up versus the group that did not complete 4 years of follow up with last VA measured carried forward.

Discussion

The current study looked at long-term outcomes for patients undergoing pars plana vitrectomy for diabetic retinopathy related complications. It adds to the current literature exploring long term visual outcomes for these patients and suggests good long term visual outcomes regardless the surgical indication and tamponading agent. More than half of our patients managed to complete the 5 years of follow-up visits and we found that there was no significant difference in visual acuity at year one and year two, regardless of the baseline visual acuity. Visual acuity at 6 months post-surgery was a predictor of final visual outcome at both the 2nd and 5th year. In most patients' visual acuity improved significantly from baseline to year 1 and remained stable to the fifth year suggesting that initial visual benefits post-surgery is maintained in the long term.

We observed that visual improvement at year 4 did not differ significantly between patients with VH and TRD. On the contrary, other studies showed that the final VA might be affected by both the pre-operative degree and density of VH as well as pre-operative VA and there exists a significant correlation between pre- and post-operative visual acuity for both TRD and NCVH [7]. They imputed the variation in functional visual acuity to the extended periods of macular traction as well as macular ischemia [8,9]. It is not clear why such a difference exists, but it could be driven by different patient populations and demographic factors.

The most common complication after vitrectomy is immediate or delayed post-operative vitreous hemorrhage, with approximately 16.22% of patients requiring intervention within 2-3 months. The percentage of patients requiring re-intervention is in line with other studies (9.7- 23.0%). The incidence of recurrent vitreous hemorrhage and the need for re-intervention after pars plana vitrectomy in diabetic patients varies in different studies. Recurrent vitreous hemorrhage was observed in a total of 31 patients out of 217 (14.3%) of which 20 eyes required re-intervention [10]. A retrospective study from the Joslin Diabetes Center reported that 12.4% of cases required re-intervention [11]. The Diabetic Retinopathy Vitrectomy Study (DRVS) reported 14-23% of cases needing another surgery [12], and Goupta., *et al*. reported 9.7% requiring a second surgery out of the 43.25% with post-vitrectomy VH [6]. The similarity in the post vitrectomy hemorrhage and re-intervention rates suggests that while vitrectomy is highly effective in managing diabetic retinopathy complications, in some patients' additional surgery is required and should be part of the patient discussion pre-operatively. It is unclear how the time to intervention, use of anti-VEGF and experience of the operating surgeon can affect these rates. Further research is necessary to understand the underlying causes and identify solutions.

Multiple systemic factors can limit visual gains after PPV. The use of insulin and having ischemic heart disease was associated with poor visual outcomes and less visual improvement post-surgery in the DRIVE UK study [6]. In the current study, there was no association with baseline systemic diseases and demographic

characteristics at baseline and VA improvement at 1 and 5 years. However, the current study did not explore DM treatment and the presence/absence of ischemic heart disease was missing for a vast majority of patients. In addition, there was no association with baseline characteristics and the rate of reintervention. As such this adds to the importance of adding more global experiences to the current literature and exploring outcomes in previously unexplored ethnic populations.

Limitations of the study include its retrospective study design, relatively small sample size, and the inability to obtain a 5-year follow-up for all patients. In addition, there fundus photographs and OCT scans were not available for most patients on most post operative visits which limited additional analysis and post operative assessments. The lack of pre-operative ultrawide field imaging also limited our ability to determine the extent of the macula threatening TRD and extent/density of VH, which could provide valuable insights into the severity of the retinopathy and its impact on surgical outcomes. This study's strengths include that all surgical interventions were performed by a single surgeon in the same center under similar circumstances. This ensures that the surgeon's experience and technique was not a factor in final outcomes. In addition, the long follow-up duration, meticulous evaluation of best corrected visual acuity and assessment of pre and post operative retinal characteristics by a trained retina specialist (AAS) ensured that data collected was accurate.

The current study adds to the current literature looking at long term outcomes in eyes with DM undergoing PPV for NCVH and macula threatening TRD demonstrating that most eyes have good visual outcomes at 2 and 5 years. A small percentage of eyes required re-intervention and regardless the initial reason for surgery (NCVH vs TRD) most eyes achieved good VA outcomes with the strongest predictive feature for final VA was the VA at 6 months. The results of the study are in line with other long-term studies and re-affirm some of the previous findings. However, more prospective studies are required to identify baseline ocular characteristics including the extent of TRD and density of NCVH using objective quantitative metrics are necessary to better predict which patients may benefit the most from surgery.

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