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Psychological, Social, and Behavioral Conditions of Anti-VEGF Patients: Results from the ALBATROS Data Collection

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Keywords: Anti-VEGF; patient perspective; attitude; psychology; health care; fear; vision loss; blindness

Article

The Psychological, Social and Behavioral Impact of Intravitreal Anti-VEGF Therapy: Analysis from the ALBATROS Data

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Abstract: Background: Retinal diseases such as neovascular age related macular degeneration (nAMD), diabetic macular edema (DME) or branch-/central retinal vein occlusion (B/CRVO) have significant implications for patients' social and psychological well-being. To gain a comprehensive understanding of patients' backgrounds and attitudes, we developed an exploratory questionnaire, the Basic Care and Patient Satisfaction Questionnaire (BPZ-9). **Methods**: The ALBATROS study aimed to assess the care situation of treatment-naïve patients diagnosed with either nAMD, DME or B/CRVO. The data collection took place at the beginning of treatment and after twelve months of anti-VEGF (vascular endothelial growth factor) therapy. The BPZ-9 instrument comprises nine questions to evaluate patients' psychological and social situation and their satisfaction with treatment. **Results**: Data were collected from 1,478 nAMD (mean 78 years), 445 DME (67 years), 233 BRVO (70 years) and 144 CRVO (71 years) patients at 102 study centers throughout Germany. Approximately one third of the patients was living alone and six percent were in organized care. One in four patients had difficulties to walk and one in five needed accompany for treatment. Anxiety to lose vision was present in three out of four patients at the beginning and slightly decreased to two out of three over the 12-month treatment period. The distress of having a retinal disease was generally higher than the distress related to treatment. Most patients reported high treatment satisfaction (73%) and felt well informed (81%). **Conclusion**: Patients receiving anti-VEGF therapy commonly experience impaired mobility, dependency on others and the fear of vision loss.

Keywords: Anti-VEGF; patient perspective; attitude; psychology; health care; fear; vision loss; blindness

1. Introduction

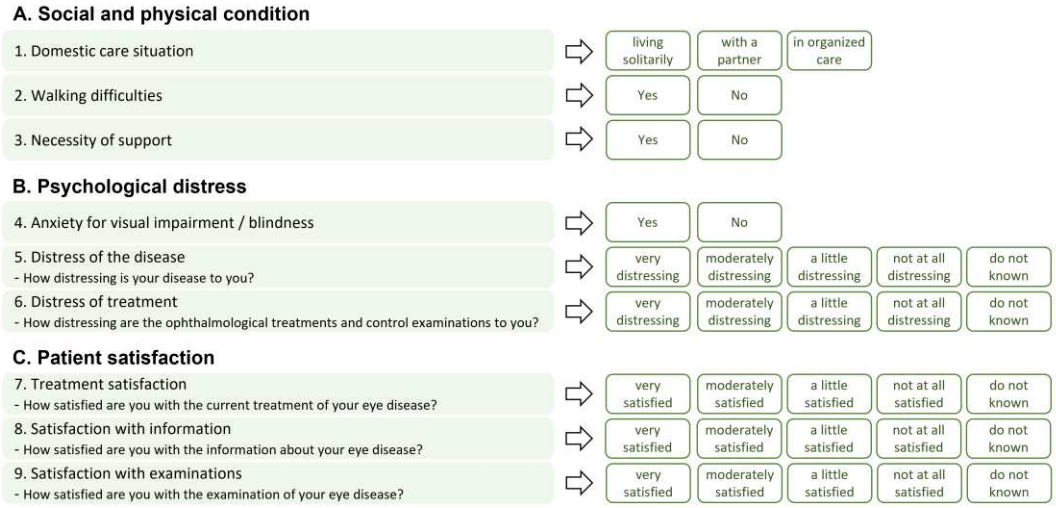
Intravitreal injections are among the most performed procedures in medicine. Their positive impact on preserving vision in retinal diseases such as neovascular age-related macular degeneration (nAMD), diabetic macular edema (DME) and retinal vein occlusions (RVO) has been extensively demonstrated [1–4]. The widespread use of these injections has contributed to a reduction in blindness and low vision [5,6]. However, individual perspectives on treatment may differ from a population health standpoint, as they require continuous motivation over many years [7,8]. Consequently, non-persistence and non-adherence remain significant challenges that threaten the long-term maintenance of visual function [9]. It is essential to understand the patients´ attitudes and commitment to treatment in order to explain and enhance treatment adherence [10]. Previous publications have revealed substantial disparities in treatment practices between clinical studies and real-life scenarios. Notably, the injection frequency and treatment adherence are often much lower in the real-world-settings compared to clinical trials [11,12]. As a result, the patients' perspective has garnered increased attention in recent years to gain a deeper understanding of their concerns, relevant barriers, and behavioral aspects.

Retinal diseases and comorbidities have a profound impact on the quality of life (QoL) [13]. Since a significant portion of treated patients are elderly, this target group often suffers from other health problems and experiences daily limitations even before regular treatment visits and ocular discomfort introduce additional burdens for both patients and potential caregivers [14]. Questionnaires that focus solely on QoL dimensions do not adequately capture the personal situations and treatment commitment of patients. Therefore, we have developed an exploratory tool aimed at comprehensively elucidating patients' social, physical, and psychological conditions. This tool should aid in understanding the utilization of care by patients and in potentially identifying internal or external barriers and limitations to therapy.

2. Materials and Methods:

The exploratory questionnaire was implemented within the multi-centered ALBATROS data collection to monitor the situation of anti-VEGF-patients when receiving treatment for neovascular age-related macular degeneration (nAMD), diabetic macula edema (DME) or retinal vein occlusion (RVO) in Germany. The study design and clinical outcomes have been recently reported [15]. One hundred and two study centers participated in the project throughout Germany. Patients were invited to join the data collection before commencing their therapy and were followed-up over the first twelve months of treatment. No specifications regarding anti-VEGF treatment or treatment frequency were given. Only patients without prior anti-VEGF treatment, aged ≥18 years and a written informed consent for participation were included in the study.

The questionnaire about the patients' situation of Basic care and Patient satisfaction (in German: "*Fragebogen zur Basisversorgung und Patientenzufriedenheit*", BPZ-9) comprised nine questions in three different domains about social, physical, and psychological conditions. Patients' distress and satisfaction with treatment were assessed using a five-point Likert-scale. The answers were collected at baseline and the final study visit (after twelve months). An overview of the questions and answer options is provided in Figure 1.



A. Social and physical condition

1. Domestic care situation	⇨	living solitarily	with a partner	in organized care		
2. Walking difficulties	⇨	Yes	No			
3. Necessity of support	⇨	Yes	No			

B. Psychological distress

4. Anxiety for visual impairment / blindness	⇨	Yes	No			
5. Distress of the disease - How distressing is your disease to you?	⇨	very distressing	moderately distressing	a little distressing	not at all distressing	do not known
6. Distress of treatment - How distressing are the ophthalmological treatments and control examinations to you?	⇨	very distressing	moderately distressing	a little distressing	not at all distressing	do not known

C. Patient satisfaction

7. Treatment satisfaction - How satisfied are you with the current treatment of your eye disease?	⇨	very satisfied	moderately satisfied	a little satisfied	not at all satisfied	do not known
8. Satisfaction with information - How satisfied are you with the information about your eye disease?	⇨	very satisfied	moderately satisfied	a little satisfied	not at all satisfied	do not known
9. Satisfaction with examinations - How satisfied are you with the examination of your eye disease?	⇨	very satisfied	moderately satisfied	a little satisfied	not at all satisfied	do not known

Figure 1. Questions and answer options of the exploratory BPZ-9 questionnaire.

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For this analysis data from patients who completed the full 12-month observation period were included. Statistical analyses were descriptive with absolute and relative frequencies, tabulated using SAS Version 9.4 (SAS Institute Inc., Cary, North Carolina, United States of America).

3. Results:

In total 1,478 patients with a baseline and a 12-month visit were included in the completed analysis set (CAS) of the ALBATROS data collection. During the 12-month observation period, patients received on average (mean±SD) 6.1±3.2 anti-VEGF injections.

The mean(±SD) age of the study population was 74.5±10.9 years, with 54.9% female patients. Irrespective of sex, older patients experienced worse visual acuity (Figure S1). Nearly two thirds of the study population (65.2%) were treated for nAMD, with 32.8 % receiving bilateral treatment (DME: 9.9%). Demographic parameters varied across different indications, e.g., patients diagnosed with nAMD were generally older and more likely to be female, while patients diagnosed with DME were younger and more likely to be male (Table 1).

Table 1. Demographics & baseline characteristics.

	Total	nAMD	DME	BRVO	CRVO
Demographics & baseline characteristics					
Patients, n	1.478	964	272	140	102
Age, years	74.5±10.9	78.3±8.0	65.9±12.3	68.7±11.4	70.4±11.8
Sex, female (%)	54.9	61.1	38.6	52.1	43.1
BCVA study [fellow] eye, letters	56.1±19.6 [65.8±25.0]	54.4±19.6 [62.2±27.2]	65±14.2 [69.2±20.4]	59.1±19.1 [77.2±13.9]	44.9±23.1 [75.3±16.4]
Better eye at baseline is fellow eye, n (%)	1028 (69.6)	643 (66.7)	172 (63.2)	123 (87.9)	90 (88.2)
Neovascular / exudative disease of the partner eye (%)	23.9	32.8	9.9	4.3	3.9
If not otherwise indicated, data are presented as mean±SD					

Social and physical condition: The living situation of patients varied significantly. At baseline, 4.9% of the patients lived in organized care, 62.5% lived with a partner and approximately one third (32.7%) lived alone. At baseline, 24.7% of the patients reported walking impairments and 18.9% reported dependency on an accompanying person. The percentages varied by indication as demonstrated in Figure 2 and showed that nAMD patients more often suffered from walking difficulties and required more assistance. In contrast BRVO-patients were less often living in an organized care and reported a better walking situation and less need for accompany.

After twelve months of treatment, the proportion of individuals in a single household increased from 32.7% to 34.0% and the percentage of those in organized care rose from 4.9% to 6.3%. Walking difficulties slightly increased from 24.7% to 26.5% and the need for assistance during anti-VEGF-treatment from 18.9% to 19.7%. Fewer patients with DME were dependent of support than in the beginning of treatment (20.2% vs. 17.2%).

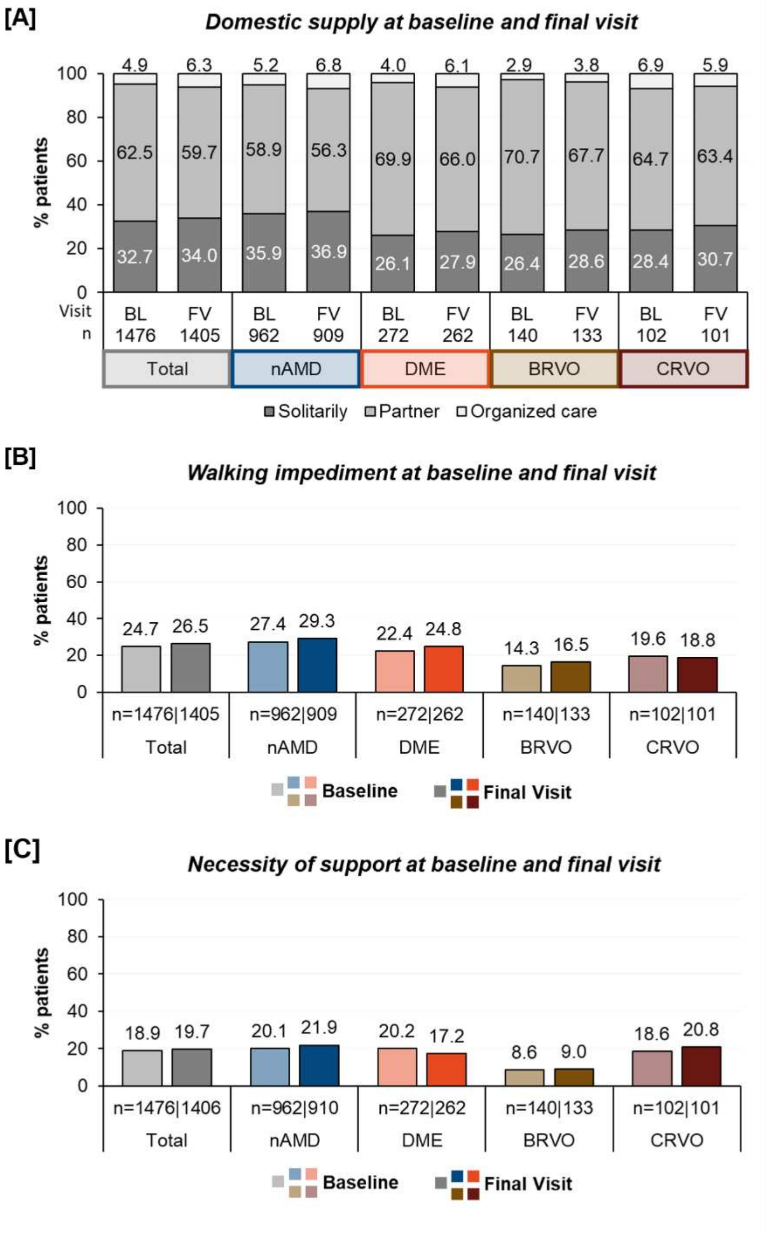

Figure 2. Domestic care situation [A], prevalence of walking difficulties [B] and need for an accompanying person [C] at baseline and after twelve months of treatment. BL, baseline; FV, final visit.

Psychological distress | Anxiety of vision loss: Prior to the first anti-VEGF therapy, most patients (74.1%) expressed anxiety about developing visual impairment and blindness. This concern remained present in 67.2% of the patients after twelve months. When examining different underlying indications, the fear for vision loss was less prominent in branch retinal vein occlusions (BRVO) and more prominent in nAMD. Over the course of one year of treatment, a reduced prevalence of anxiety was observed across all indications (Figure 3). However, while 15.5% had less anxiety about vision loss, a small group (8.6 % of patients) reported being more anxious than prior to the anti-VEGF therapy.

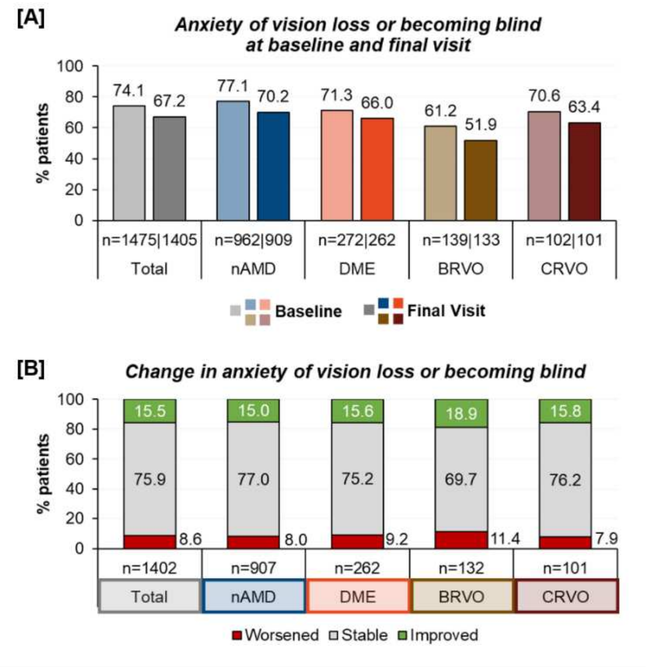

Figure 3. Anxiety of vision loss and blindness [A] and change in anxiety from baseline to final visit for all indications [B].

Psychological distress | *Disease and treatment-related distress*: At baseline, 71.9 % of patients perceived their disease as moderately to very distressing, while 25.8 % perceived it as little or not at all distressing. At the final visit, fewer patients reported disease-related distress, but it was still prevalent in nearly two thirds of the patients (65.6%). Regarding treatment distress, we found that a majority (52.5%) experienced it as little or not at all distressing as compared to 44.5% who valued treatment as moderately to very distressing. After twelve months the ratio had not changed substantially (55.1% - "little/not at all distressing" vs. 43.9% - "moderately/ very distressing").

Comparing disease- and treatment-related distress, patients more frequently struggled with the disease itself than with treatment (Figure 4).

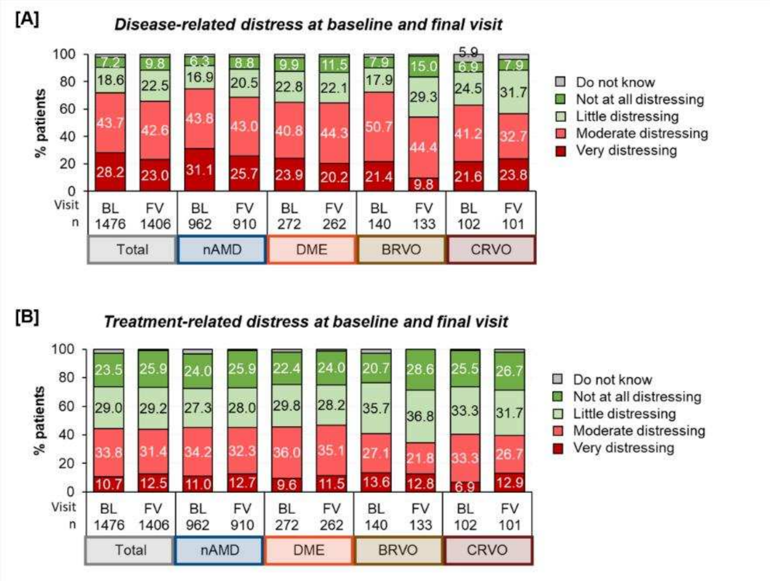

Figure 4. Disease-related distress [A] and treatment-related distress [B] for all indications. Note: For clarity reasons, labels for values <5% were omitted.

Regarding differences in disease- and treatment-related distress at the beginning and after twelve months of treatment, we observe that about half of the patients reported similar emotional views. At least, more patients experienced a reduction of disease related distress than an increase in distress. The results differed by indication, showing that more BRVO patients experienced improvement than patients of other indications. However, 18.2 % of all patients reported more distress in dealing with the retinal disease, which was also less pronounced among those with BRVO.

Concerning treatment-related distress, about three out of four patients (73.4%) did not change their perception of treatment distress or even found it improved, with little variation among the different indications (Figure 5, upper part of the figures).

Improvements in distress estimation were correlated with changes in the best corrected visual acuity (BCVA), as shown in Figure 5 (lower part of the figures). A heat map analyzing the correlation of patients` disease and treatment distress perception, showed no clear correlation of disease and treatment distress, highlighting the value of separately assessing both disease and treatment distress (Figure S2).

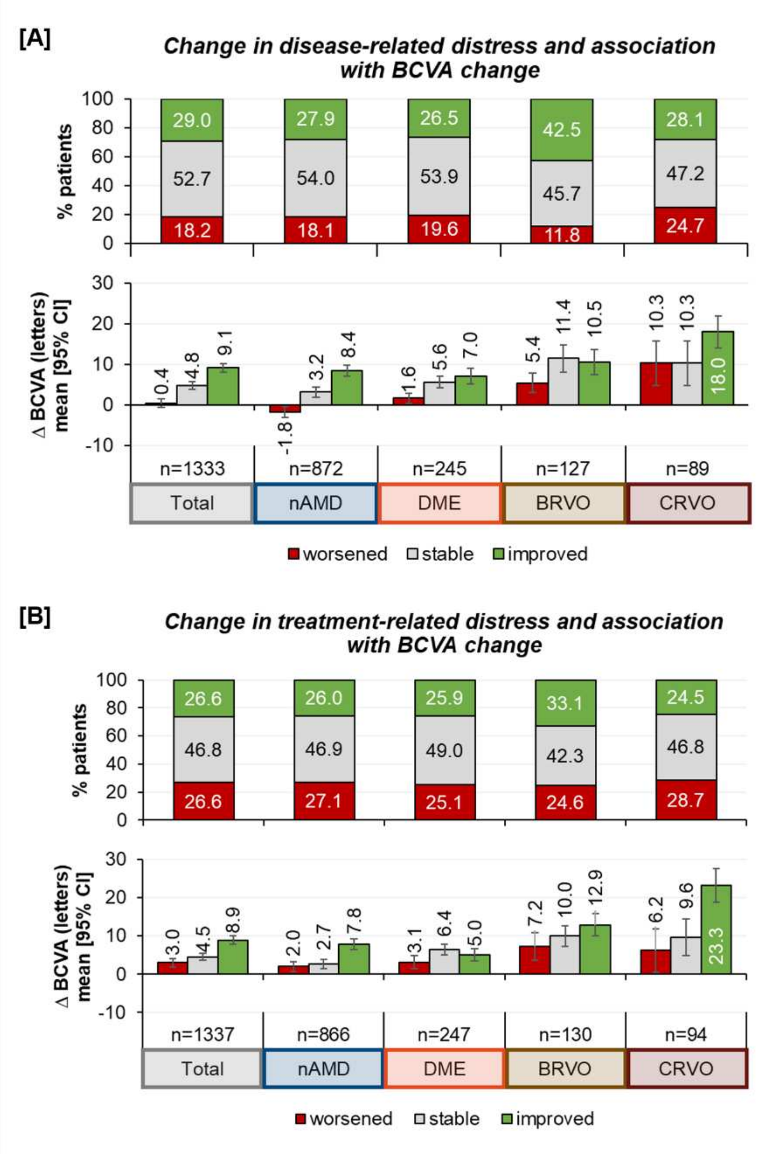

Figure 5. Change from baseline to final visit for disease-related distress [A] and for treatment-related distress [B] in association with the best corrected visual acuity (BCVA).

Patient Satisfaction: Most patients were generally highly satisfied regardless of the underlying indication. The satisfaction varied across different areas with the highest satisfaction seen for ‘control examinations' (seven out of eight patients being "very satisfied"), followed by 'information about the disease' (four out of five being "very satisfied") and 'satisfaction with treatment' (three of four being "very satisfied"), see Figure 6. Over the course of twelve months, satisfaction remained generally stable for the patients under study observation.

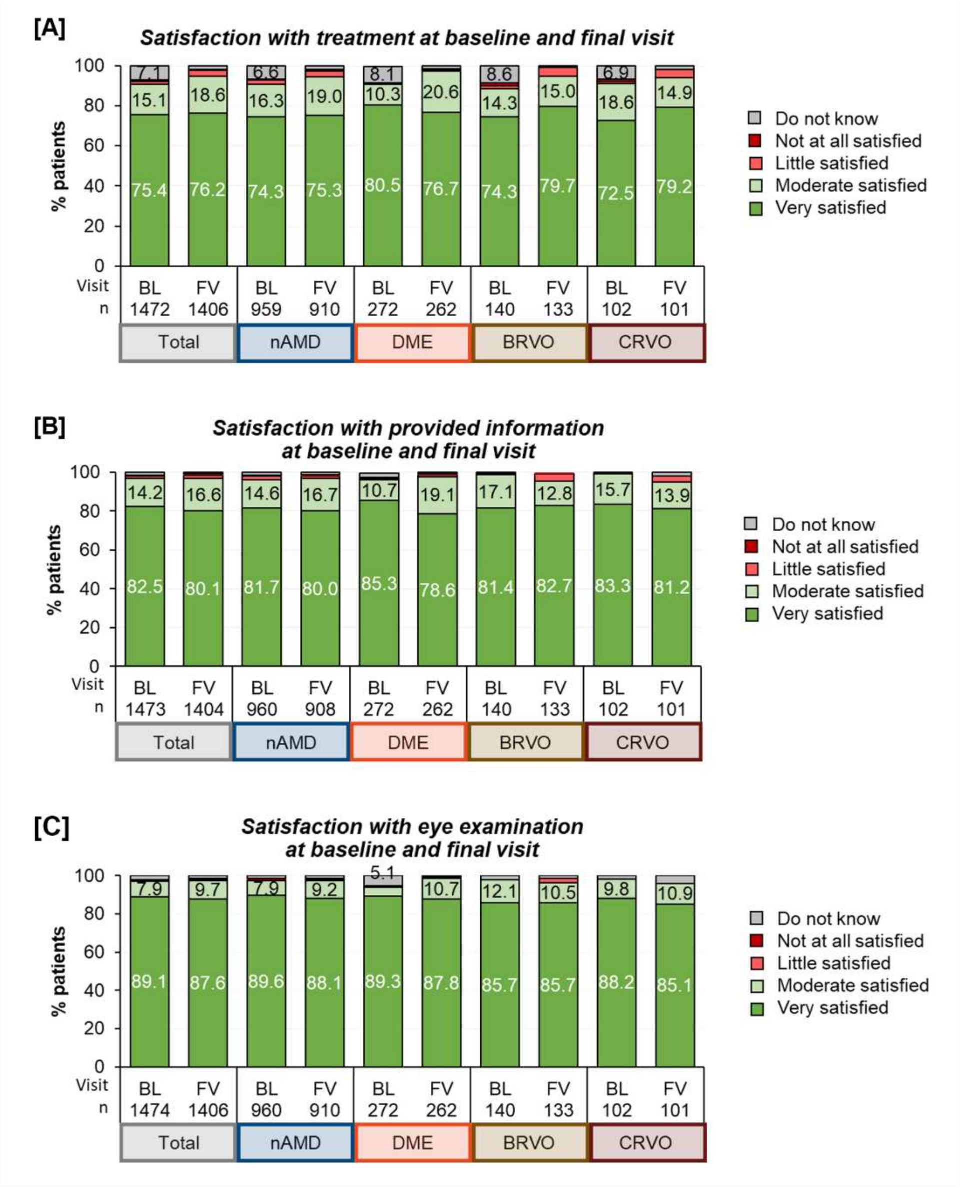

Figure 6. Treatment satisfaction [A], satisfaction with eye and control examinations [B] and satisfaction with information about disease [C] at baseline. Note: For clarity reasons, labels for values <5% were omitted.

4. Discussion

The findings from the ALBATROS study provide intriguing insights into the patients' social, physical, and psychological conditions, when confronted with a retinal disease and intravitreal anti-VEGF treatment. The extensive size of this study cohort with data collected from more than one hundred study centers throughout Germany helped to capture a realistic picture. The broad categories hinted at the variety of practical issues and concerns patients face when receiving injection therapy.

The social backgrounds of anti-VEGF patients are naturally diverse, as reflected in the ALBATROS data, which represented the affected population [16]. Although the vast majority was found to live in their own homes, attention should be given to difficulties or mobility restrictions. Roughly six percent of patients in our cohort resided in a domestic care situation. More than one-fifth of patients needed to be accompanied and even every forth patient experienced walking difficulties. These facts reveal that logistical issues and limitations may frequently hinder the daily practice of anti-VEGF treatment.

Previous studies have already demonstrated a high need of support. For instance, a survey among nAMD patients reported that even 82.1% of patients received assistance from a caregiver [17]. In contrast to support in daily activities (57.8%), other studies described a higher rate (77%) of patients, attending medical appointments without assistance [18]. This corroborates our findings that 18.9% of anti-VEGF-patients required an accompanying person. The accessibility of care should be closely monitored. Previous surveys suggest that means of transportation does not influence the dependency of affected individuals [19]. Even in cities with a good and efficient public transport, visually impaired might not manage the injection visit without caregivers.

However, even more important than the issues of transport and mobility, the doctor-patient relationship proved to have a significant impact on patients [20]. Accompanying persons were able to enhance adherence by overcoming barriers and increasing self-efficacy [21].

The fact that patients experienced more distress due to their disease than the actual treatment underscores the high psychological burden of having a retinal disease. A review on the psychological impacts of neovascular macular degeneration described that up to 42% of patients showed signs of depression [22]. Other studies reported a prevalence of depression among anti-VEGF-patients ranging between 20% and 26% [23] and also among caregivers to AMD-patients, with 24.4% affected [17]. Our findings emphasize the specific impact of anxiety for vision loss as a key psychological element, which was present in as much as 74.1% of patients at the beginning of their treatment. This high prevalence of anxiety for vision loss confirmed anxiety to be a psychological dimension with a lower threshold than depression, as described in the literature. Assessing anxiety can identify that there is also a fear of the injection itself during treatment and that efficacy of the treatment is the most important outcome for patients as previous studies pointed out [24,25]. Patients therefore declared their willingness to take certain risks or accept discomfort and inconveniences [26,27]. Although aversions and unconscious preferences cannot be ruled out, the acceptance of intravitreal therapy is generally very high [28], supported by the very positive findings for treatment satisfaction observed in our study.

Our analysis has highlighted psychological and logistical dimensions of treatment. Literature has described treatment barriers for patients that can be categorized into four groups [20]: tolerability, clinical factors, logistical parameters and human factors, which can all contribute to a low confidence in their therapy and its effects resulting in the decision to discontinue treatment. The experience of side effects was identified as the most important factor for non-adherence [20]. Previous investigations demonstrated that 28.8% of anti-VEGF-patients were lost to follow up during treatment, defined as a discontinuation of therapy for at least six months [29]. Other studies described that 32% of patients considered to interrupt their anti-VEGF therapy [30] and that up to 50% of patients stopped treatment within 24 months [31]. Possible reasons may be disbelief in the benefit of treatment or fear of the injection [32]. The follow-up of this study might have been too short to access the full impact of longer treatment durations [33].

Non-adherence is therefore a major issue in retinal care, found to be higher in DME than in nAMD and other indications [32]. A key role in maintaining adherence was seen in the quality of the relationship between physician and patient [32]. Practical recommendations include better monitoring of the patients’ treatment course to identify interruptions or non-adherence [32] and actively assessing the patients' expectations regularly along the course of treatment [32]. Even though our analysis focused primarily on those patients who adhered to their therapy, we do observe that psychological and logistical problems are very common already among these patients. We can assume that such issues are even more important for those, who have difficulties to commit to a continuous therapy [34]. Future “real-world”- research should therefore focus even more on those patient groups who do not continue treatment and further investigate behavioral factors.

Our findings were limited because patients may have responded in an overly positive way and avoided being critical (social desirability bias). In real-world care practice satisfaction values as demonstrated here may be too high and practical barriers or comorbidities may be more prevalent among those who interrupted or even stopped treatment within the first year. Furthermore, our research questions were exploratory, and we cannot supply final information about the validity and reliability of our questionnaire at this point. Further methodological validation is needed to measure accuracy and consistency of our research questions. The introduction of validated questionnaires can complement established instruments of life-quality and patient-related outcome measures. Future research may also introduce possible means to measure commitment and adherence to ease the delivery of retinal care. As anti-VEGF-treatment remains one of the most performed medical procedures, even minor improvements can have a greater impact for the needs in the population.

5. Conclusions

In summary, having a retinal disease and undergoing a continuous anti-VEGF treatment was shown to be challenging for patients both logistically as well as psychologically. On the other hand, patients demonstrated high levels of satisfaction with their treatment. Understanding patients` needs and fears are prerequisites to help patients overcoming logistical and psychological barriers and may result in enhanced and maintained commitment, adherence, and treatment satisfaction. Our exploratory study questions may help to widen the understanding of the patients' background, attitudes and behavior and may serve as a useful complement to other instruments of patient-related outcome measures.

Supplementary Materials: The following supporting information can be downloaded at the website of this paper posted on Preprints.org. **Figure S1**: Box-Whisker-Plot of worst eye visual acuity vs age group and sex at baseline. Note: Distribution of worst eye visual acuity (VA): Study eye=69.6%, Partner eye=30.4%. Horizontal lines show median, boxes indicate the interquartile range (IQR) with whiskers providing 1.5xIQR and black dots showing outlier values. **Figure S2**: Heat maps showing correlation of disease- and treatment distress at baseline [A], final visit [B] and change from baseline to final visit [C] for the overall population. Numbers indicate patients with a distinct combination of distress perception. Shadings show frequencies. The darker the color, the higher the frequency.

Author Contributions: Conceptualization, A.K.S., B.S., C.W., M.R., N.P.; Methodology, A.K.S, B.S., C.W., F.Z., M.R., N.P.; Software, n/a.; Validation, A.K.S, B.S., C.W., F.Z., M.R.; Formal Analysis, n/a; Investigation, A.K., A.K.S, C.W., T.H., F.Z. and N.P.; Resources, A.K., A.K.S, B.S., C.W., F.Z., M.R., T.H., N.P.; Data Curation, B.S., M.R.; Writing – Original Draft Preparation, C.W., A.K.S, F.Z.; Writing – Review & Editing, A.K.S, C.W., T.H., A.K., F.Z., N.P.; Visualization, A.K.S, B.S., F.Z.; Supervision, M.R., B.S., N.P.; Project Administration, B.S., M.R.; Funding Acquisition, M.R.

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Institutional Review Board Statement: ALBATROS: The study was conducted according to the guidelines of the Declaration of Helsinki. According to national law, the ALBATROS data collection did not require formal vote in favor by an independent ethics committee (IEC) but was reviewed by the IEC according to medical professional code of conduct of state Rhineland-Palatinate (EC State Medical Association of Rhineland-Palatinate) for the corresponding investigator.

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The data presented in this study are available on request from the corresponding author. The data are not publicly available due to intellectual property reasons.

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