

Phantom Eye Syndrome

Patient Experiences after Enucleation for Uveal Melanoma

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Purpose: Patients undergoing enucleation for uveal melanoma need to be informed of the possibility of phantom eye syndrome (PES). The number with uveal melanoma in PES studies has been small. Aims were to: (1) determine the prevalence, symptoms, and characteristics of PES and to test associations of PES symptoms with sociodemographic and clinical characteristics; (2) examine the interrelatedness of PES symptoms; and (3) explore the emotional valence of PES and the relationship to anxiety and depression.

Design: Cross-sectional questionnaire.

Participants: Patients (n = 179) with uveal melanoma enucleated 4 to 52 months previously.

Methods: Questionnaire on PES. Responses to a routine audit of mood obtained from clinical records.

Main Outcome Measures: Patients were asked about 3 symptoms: pain, visual sensations, and a feeling of seeing through the removed eye. Mood was assessed by the Hospital Anxiety and Depression Scale.

Results: Of 179 respondents, 108 (60.3%) experienced symptoms: 86 reported (48%) visual sensations, 50 reported (28%) seeing, and 42 reported (23%) pain; 14 (7.8%) reported all 3 symptoms. At the time of the questionnaire, 31 (17%) experienced 1 or more symptoms daily. Women were more likely to report pain (odds ratio [OR], 2.18; 95% confidence interval [CI], 1.08–4.40). Younger patients at enucleation were more likely to report pain ($t = 4.13$; degrees of freedom [df], 177; $P < 0.001$) and visual sensations ($t = 2.11$; df, 177; $P < 0.05$). Patients studied sooner after enucleation were more likely to report seeing (Mann–Whitney U , 2343; $P < 0.05$). Pain and seeing were intercorrelated (chi-square, 5.47; $\Phi = 0.18$; df, 1; $P < 0.05$), pain with visual sensations (chi-square, 3.91; $\Phi = 0.15$; df, 1; $P < 0.05$) and seeing with visual sensations (chi-square, 34.22; $\Phi = 0.45$; df, 1; $P < 0.001$). Twenty of 108 patients (18.5%) found symptoms disturbing, and 21 of 108 (19.4%) pleasurable. Patients reporting pain were more anxious (OR, 3.53; 95% CI, 1.38–9.03) and depressed (OR, 13.26; 95% CI, 3.87–46.21).

Conclusions: Patients should be informed of PES symptoms. Pain may indicate anxiety or depression; this needs research to determine cause and effect. *Ophthalmology* 2015;■:1–6 © 2015 by the American Academy of Ophthalmology.

Uveal melanoma is the most common primary intraocular malignancy in adults. Approximately 30% of patients are treated by enucleation.¹ A poorly understood consequence of enucleation is phantom eye syndrome (PES), which refers to sensations that a patient experiences as a result of the amputated eye. In studies of patients who underwent enucleation for a variety of clinical reasons, symptoms of PES are common, occurring in 46% to 72% of patients.^{2–5} Pain in the eye or in the area around the missing eye is experienced daily by approximately one-third of patients and can be intense, although other tactile sensations are very rare.⁴ Visual phenomena in the removed eye range from simple sensations that lack meaning to complex sensations, including structured scenes and objects. Some patients also have the sensation of being able to see with the enucleated eye.^{4–8} However, in these studies only small numbers of patients have undergone enucleation for uveal melanoma. In 2 studies, 22 of 112 enucleated patients and 43 of 173 enucleated patients had unspecified ocular cancer.^{3–5} In a third study,² 53 patients underwent enucleation for ocular cancer, of whom 51 had choroidal

melanoma. Aspects of PES may differ between patients undergoing enucleation for cancer or other conditions. In particular, the experience of cancer may change people's psychological responses to symptoms associated with enucleation.

Identification of risk factors and correlates of PES in uveal melanoma requires large samples that are clinically homogeneous. We therefore conducted a survey of patients who had been treated for uveal melanoma by enucleation. Our first aim was to identify the proportion of patients who experienced the principal symptoms of PES; to characterize those symptoms according to their form, frequency, and triggers; and to examine whether PES symptoms were associated with sociodemographic and clinical characteristics. It is unclear whether PES should be considered a syndrome or a concurrence of distinct symptoms. This can be inferred from estimates of symptom covariance, but previous estimates of interrelationships between symptoms differ markedly,^{2–5} possibly because samples have been mixed clinically, with composition differing between studies. Our second aim therefore was to find out how

strongly the 3 symptoms were interrelated in patients undergoing enucleation for uveal melanoma. Phantom pain predisposes limb amputees to depression and anxiety,^{9–11} and PES symptoms also may be expected to be distressing. Our third aim was to explore the emotional valence of PES symptoms and their relationships to depression and anxiety.

Methods

Study Design

A cross-sectional, self-report questionnaire-based survey was approved by Royal Liverpool & Broadgreen University Hospital Trust regulatory authority as a service evaluation (reference no., 4017-10/11).

Participants and Procedure

Two hundred thirty-nine patients treated 4 to 52 months previously by enucleation for uveal melanoma at the Liverpool Ocular Oncology Centre were identified from the Centre's database. They were sent a questionnaire about PES (see below) by mail and were asked to return this in a reply-paid envelope. One hundred and seventy-nine of 239 patients (75%) responded. Patients completed the Hospital Anxiety and Depression Scales (HADS¹²) at 6- to 12-month intervals as part of routine clinical audit. Scores provided at the time closest to the PES questionnaire completion were obtained for these patients from clinical records. The mean time between HADS and PES questionnaire completion was 2.9 months (standard deviation, 5.63).

Questionnaire

Questions were adapted from the interview questions reported by Rasmussen et al.^{4,5} Patients were asked about 3 types of symptoms in the removed eye: (1) pain (the question asked by Rasmussen et al referred to pain "in the eye or in the area around the missing eye," but for greater specificity, we asked only about pain in the removed eye); (2) visual sensations, including colors, shapes, and images; and (3) the feeling of seeing with the removed eye. Patients also were asked to describe any visual sensations as free text. Patients who experienced 1 or more of those types of symptoms since enucleation were considered to have experienced PES. The questionnaire also asked about frequency of symptoms, about symptom triggers, and about what caused the symptoms to stop. Emotional valence was determined by asking patients to report whether they found the symptoms of PES disturbing, pleasant, or other. If other, they were asked to describe in free text how they experienced them. Those responses were used to allocate symptoms to 3 categories: disturbing, pleasant, and neutral. The 2 subscales of the HADS measure anxiety and depression; higher scores indicate greater distress, and scores exceeding 7 can be regarded as indicating probable clinical levels of distress.^{12,13}

Data Analysis

Prevalence and Characteristics of Phantom Eye Syndrome and Association with Clinical and Sociodemographic Characteristics. After describing the prevalence of PES symptoms, the chi-square test was used to examine the relationship of the 3 PES symptoms with categorical variables (gender, marital status, and preoperative pain in the affected eye). The Mann-Whitney *U* test was used to test associations of PES symptoms with time since

enucleation and visual acuity in the remaining eye. Because age was distributed normally, its relation to PES symptoms was tested by independent *t* tests.

Coherence of Phantom Eye Syndrome as a Syndrome. The chi-square test was used to determine the interrelationship between the 3 constituent types of symptoms of PES with the Φ coefficient used to indicate effect size.

Emotional Valence and Mood. First, the emotional valence of PES was described and the association of emotional valence with anxiety and depression was tested by the chi-square test. Second, logistic regression analysis tested the cumulative effect of the 3 constituent symptoms on whether patients had clinical levels of anxiety or depression (defined by scores exceeding 7), controlling for age when completing the questionnaire, gender, marital status, time since enucleation, and pain before enucleation.

Results

Of the 179 patients who responded 103 (57.5%) were men and 76 (42.5%) were women. Eight of 179 patients were aware of having metastases when completing the questionnaire. One hundred forty-one of 179 (78%) also responded to the HADS questionnaire. The median time since enucleation was 12.8 months (range, 4–52 months).

Prevalence, Symptoms, and Characteristics of Phantom Eye Syndrome and Association with Clinical and Demographic Characteristics

Characteristics of PES in this sample are summarized in [Table 1](#). Symptoms of PES were reported by 108 of 179 patients (60.3%). For half these patients, symptoms started within 6 weeks of enucleation. The most common were visual sensations. Free text responses indicated that these generally were elementary shapes and colors, but 11 of 179 patients (6.1%) described more complex images, for example, resembling wallpaper, a kaleidoscope, or fireworks, or even specific scenes and people ([Table 2](#)). Fewer patients reported seeing with the removed eye or experiencing pain in that eye. Forty of 179 patients (23%) reported more than 1 of these 3 types of symptoms, and 14 of 179 patients (7.8%) experienced all 3 symptoms. At the time of the questionnaire, more than one third of patients with PES experienced symptoms daily. Patients mostly cited darkness or tiredness as triggers of PES, with a few citing light, sounds, stress, closing and opening eyes, sitting quietly, concentrating, or reading. Episodes of PES ceased spontaneously in 46 of 108 patients (42.6%), with others citing distraction, sleep and darkness, light, alcohol, and blinking causing PES to stop.

Sociodemographic and clinical characteristics are summarized in [Tables 3 and 4](#), respectively. No symptom was related to marital status. The feeling of seeing and visual sensations were unrelated to gender, but women were more likely to report pain (odds ratio [OR], 2.18; 95% confidence interval [CI], 1.08–4.40). Patient age was related to visual sensations and pain, but not to the feeling of seeing; specifically, patients with visual sensations were younger than others at both questionnaire completion ($t = 2.20$; degrees of freedom, 177; $P < 0.05$) and enucleation ($t = 2.11$; degrees of freedom, 177; $P < 0.05$). Patients with pain also were younger at questionnaire completion ($t = 4.22$; degrees of freedom, 177; $P < 0.001$) and enucleation ($t = 4.13$; degrees of freedom, 177; $P < 0.001$). Pain before enucleation predicted pain after enucleation (OR, 3.01; 95% CI, 1.35–6.70) but not visual sensations or the feeling of seeing. Patients studied sooner after enucleation were more likely to report the feeling of seeing (Mann-Whitney *U* test, 2343;

Table 1. Phantom Eye Syndrome: Symptoms and Characteristics

Symptoms and Characteristics (n = 108)	No.	%*
Time since enucleation (until first episode of PES)		
<2 wks	37	34.3
2–6 wks	18	16.7
>6 wks–3 mos	6	5.6
>3–6 mos	7	6.5
>6 mos	2	1.9
Not reported	38	35.2
Symptoms and sensations†		
Pain since enucleation	42	38.9
Feeling of seeing with enucleated eye	50	46.3
Visual sensations in enucleated eye	86	79.6
Colors	38	35.2
Shapes	56	51.9
Images	31	28.7
Triggers of PES symptoms†		
Darkness	40	37.0
Light	10	9.3
Sounds	6	5.6
Stress	10	9.3
Tiredness	33	30.6
Other	7	6.5
Reported reasons causing PES symptoms to stop†		
Spontaneous (just went away)	46	42.6
Darkness	2	1.9
Distraction	15	13.9
Sleep	24	22.2
Other	4	3.7
Frequency of experience of PES symptoms		
Discontinued	7	6.5
Rarely to 1/wk	26	24.1
>1/wk	22	20.4
Every day	31	28.7
Not reported	22	20.4
Emotional valence of PES symptoms		
Pleasant	20	18.5
Disturbing	21	19.4
Neutral	31	28.7
Not reported	36	33.3

PES = phantom eye syndrome.

*Denominator is the 108 patients reporting PES.

†Patients could endorse more than 1 item, so percentages do not sum to 100.

$P < 0.05$), but time since enucleation was unrelated to visual sensations or pain. Visual acuity in the remaining eye was unrelated to any symptom. The number of patients who believed they saw complex images ($n = 11/179$) was too small to examine statistically whether this sensation was related to sociodemographic or clinical characteristics.

Coherence of Phantom Eye Syndrome as a Syndrome

The 3 PES symptoms were interrelated: pain and seeing with the removed eye (chi-square, 5.47; $\Phi = 0.18$; degrees of freedom, 1; $P < 0.05$), pain and visual sensations (chi-square, 3.91; $\Phi = 0.15$; degrees of freedom, 1; $P < 0.05$), and the feeling of seeing with the removed eye and visual sensations (chi-square, 34.22; $\Phi = 0.45$; degrees of freedom, 1; $P < 0.001$). However, the Φ values for the associations of pain with both visual sensations and seeing with the removed eye denote only small effect sizes.

Table 2. Examples of Free Text Descriptions of Complex Visual Phenomena

“[A] figure walking at side of me”: 82-year-old man.
“Moving images of people. They disappear when I look to the right”: 78-year-old man.
“People passing and light and items that were not there”: 77-year-old man.
“In the dark I can see people”: 77-year-old woman.
“As though I am swimming underwater through reeds. There is never any colour”: 52-year-old man.
“Once I awoke to find a person unidentified standing next to the bed”: 70-year-old woman.

Emotional Valence of Phantom Eye Syndrome and the Relationship of Phantom Eye Syndrome and Its Constituent Symptoms with Mood

The emotional valence of PES is shown in Table 1. Only a minority of patients found symptoms distressing, whereas a similar proportion found them pleasurable. The emotional valence was unrelated to anxiety and depression. For the 141 patients with HADS data, Table 5 shows the numbers of cases of anxiety or depression. Logistic regression analyses examined how PES symptoms were related to clinical levels of anxiety or depression. The regression models predicting both anxiety (chi-square, 18.52; degrees of freedom, 8, Nagelkerke $R^2 = 0.18$; $P < 0.05$) and depression (chi-square, 29.13; degrees of freedom, 8; Nagelkerke $R^2 = 0.32$; $P < 0.001$) were significant, but only 1 symptom, pain since enucleation, was associated with anxiety (OR, 3.53; 95% CI, 1.38–9.03) or depression (OR, 13.26; 95% CI, 3.87–46.21). No control variables predicted either anxiety or depression.

Discussion

We surveyed uveal melanoma patients treated with enucleation to identify the prevalence and characteristics of PES symptoms, to assess whether the symptoms cohere sufficiently to regard PES as a syndrome, and to explore the emotional valence of PES symptoms and their relationship with mood. More than half of patients with uveal melanoma who had undergone enucleation experienced at least 1 symptom of PES, particularly younger female patients. Visual sensations and experiences of seeing through the affected eye tended to occur in the same patients, but these symptoms were only weakly related to pain. The feeling of seeing through the affected eye became slightly less prevalent as the interval after enucleation increased, but there was no evidence that prevalence of pain or visual sensations differed according to time since enucleation. Only a minority of patients were disturbed by their symptoms, and a similar proportion found them pleasurable. Nevertheless, those experiencing pain were more anxious and depressed.

Comparison with Published Research

Our finding that 60% of patients who had undergone enucleation for uveal melanoma experienced 1 or more symptoms of PES is similar to previous reports of enucleated patients.^{2–5} Similarly, patient description of visual experiences broadly resembled those reported previously.^{3–5,8}

Table 3. Sociodemographic Characteristics in Groups Defined by the Presence or Absence of Specific Phantom Eye Syndrome Symptoms

Characteristics	Full Sample (n = 179)	Pain		Seeing*		Visual Sensations	
		Absent (n = 137)	Present (n = 42)	Absent (n = 120)	Present (n = 50)	Absent (n = 93)	Present (n = 86)
Gender (n = 179), no. (%)							
Male	103 (57.5)	85 (82.5)	18 (17.5)	67 (69.1)	30 (30.9)	53 (51.5)	50 (48.5)
Female	76 (42.5)	52 (68.4)	24 (31.6) [†]	53 (72.6)	20 (27.4)	40 (52.6)	36 (47.4)
Age (yrs; n = 179), mean (SD)							
At enucleation	64.1 (12.5)	66.1 (11.7)	57.4 (12.7) [‡]	64.7 (12.1)	63.5 (14.1)	66.0 (11.2)	62.2 (13.5) [‡]
At questionnaire	66.7 (12.4)	68.7 (11.7)	59.9 (12.1) [‡]	66.9 (12.0)	65.8 (13.8)	68.6 (11.2)	64.6 (13.2) [‡]
Marital status (n = 172), no. (%)							
Living with partner	124 (72.1)	91 (73.4)	33 (26.6)	82 (68.9)	37 (31.1)	59 (47.6)	65 (52.4)
Not living with partner	48 (27.9)	41 (85.4)	7 (14.6)	35 (77.8)	10 (22.2)	30 (62.5)	18 (37.5)
Employment status (n = 156), no. (%)							
Employed or homemaker	56 (35.9)	43 (76.8)	13 (23.2)	38 (73.1)	14 (26.9)	24 (42.9)	32 (57.1)
Retired	80 (51.3)	65 (81.3)	15 (18.8)	56 (70.9)	23 (29.1)	49 (61.3)	31 (38.8)
Other	20 (12.8)	15 (75.0)	8 (40.0)	16 (80.0)	4 (20.0)	9 (45.0)	11 (55.0)

SD = standard deviation.

*One hundred seventy patients responded to the seeing question; thus, cells do not sum to 179.

[†]P < 0.05.

[‡]P < 0.001.

Complex visual images were reported by 6.1% of our participants, compared with 20% reported by Sörös et al³ and 1% reported by Rasmussen et al⁴ and Rasmussen.⁵ Triggers of PES also reflected previous findings, that is, darkness, closing the eyes, and psychological stress.^{4,5,8} Although our patients reported that many instances ended spontaneously, patients also could end them by distraction or sleep. Our finding that younger patients were more likely than older ones to report visual sensations and pain concurs with the findings of Sörös et al,³ but not with those of Rasmussen et al⁴ and Rasmussen,⁵ who reported that visual sensations were more common in older patients. Unlike previous studies, we

found an association with gender: women were more likely than men to experience pain in the removed eye. We also tested the theory that preoperative pain in the removed eye is a precursor to PES symptoms. Preoperative pain was associated with pain in the removed eye but, unlike in the studies by Rasmussen et al,⁴ Rasmussen,⁵ and Sörös et al,³ it was unrelated to the feeling of seeing or visual sensations. As with previous reports, no PES symptoms were associated with eye laterality or visual acuity in the fellow eye. Inconsistency in correlates of PES in previous studies may reflect the smaller samples and diverse clinical groups studied.

Table 4. Clinical Characteristics in Groups Defined by the Presence or Absence of Specific Phantom Eye Syndrome Symptoms

Characteristics	Full Sample (n = 179)	Pain		Seeing*		Visual Sensations	
		Absent (n = 137)	Present (n = 42)	Absent (n = 120)	Present (n = 50)	Absent (n = 93)	Present (n = 86)
Eye (n = 179)							
Right	85 (47.5)	66 (48.2)	19 (45.2)	53 (44.2)	25 (50.0)	42 (45.2)	43 (50.0)
Left	93 (52.0)	70 (51.1)	23 (54.8)	66 (55.0)	25 (50.0)	51 (54.8)	42 (48.8)
Both	1 (0.5)	1 (0.7)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	1 (1.2)
Pain before enucleation (n = 177)							
No	143 (80.8)	116 (84.7)	27 (64.3)	100 (83.3)	36 (74.0)	75 (80.6)	68 (79.1)
Yes	34 (19.2)	20 (15.3)	14 (35.7) [†]	20 (16.7)	13 (26.0)	17 (19.4)	17 (20.9)
Visual acuity in remaining eye (n = 179)							
6/6–6/12	167 (93.3)	129 (94.2)	39 (92.9)	112 (93.4)	47 (94.0)	86 (92.5)	82 (95.3)
6/15–6/60	9 (5.0)	7 (5.1)	2 (4.8)	7 (5.80)	2 (4.0)	7 (7.5)	2 (2.4)
3/60	1 (0.5)	0 (0.0)	1 (2.4)	0 (0.0)	1 (2.0)	0 (0.0)	1 (1.2)
Enucleated	1 (0.5)	1 (0.7)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	1 (1.2)
Time since enucleation (mos; n = 179), median (interquartile range)	7.0 (11.6)	7.2 (13.2)	6.8 (9.8)	7.4 (16.4)	6.4 (6.4) [‡]	7.3 (14.7)	6.8 (9.5)

Values are no. (%) unless otherwise indicated.

*One hundred seventy patients responded to the seeing question; thus, cells do not sum to 179.

[†]P < 0.01.

[‡]P < 0.05.

Table 5. Number of Probable Cases of Anxiety or Depression Indicated by a Score of More than 7 on the Respective Subscale of the Hospital Anxiety and Depression Scale¹²

	Full Sample (n = 141)	Pain (n = 141)		Seeing (n = 134)		Visual Sensations (n = 141)	
		Absent (n = 107)	Present (n = 34)	Absent (n = 95)	Present (n = 39)	Absent (n = 75)	Present (n = 66)
Anxiety							
Yes	42 (29.8)	24 (22.4)	18 (52.9)*	27 (28.4)	12 (30.8)	17 (22.7)	25 (37.9)
No	99 (70.2)	83 (77.6)	16 (47.1)	68 (77.5)	27 (69.2)	58 (77.3)	41 (62.1)
Depression							
Yes	24 (17.0)	8 (7.5)	16 (47.1)†	14 (14.7)	10 (25.6)	10 (13.3)	14 (21.2)
No	117 (83.0)	99 (92.5)	18 (52.9)	81 (85.3)	29 (74.4)	65 (86.7)	52 (78.8)

Values are no. (%).

* $P < 0.01$.

† $P < 0.001$.

Although visual sensations and the feeling of seeing in the removed eye were associated strongly, pain in the removed eye was associated only weakly with each of these. Moreover, the different symptoms of PES had different demographic and clinical correlates. Therefore, PES cannot be regarded as a coherent syndrome and, contrary to suggestions that preoperative pain may underlie PES,^{3–5} a single pathologic cause is unlikely.

Only a minority of patients found PES symptoms disturbing, a similar finding to that in the only previous study to report this.^{4,5} Moreover, equal numbers in our study found them pleasurable. In free text responses, 1 patient even reported being disappointed when a symptom ceased. One reason why patients were so sanguine about their symptoms may be because they viewed the enucleation that gives rise to the symptoms as a life-saving procedure. Patients undergoing enucleation for other reasons may prove to be more disturbed. Although neither the feeling of seeing nor visual sensations were associated with clinical levels of anxiety or depression, reporting pain in the removed eye increased the odds of anxiety by 3.53 and that of depression by 13.26, indicating that pain is a strong marker for emotional distress. Crawford et al¹⁴ report United Kingdom population norms of 33.2% probable cases for anxiety and 11.4% for depression. Comparing prevalences of anxiety and depression in our sample (Table 5) with population norms shows that sample prevalences of both were similar to norms among those who did not report pain but greater than norms among those who did.

Strengths and Weaknesses

To our knowledge, this is the largest sample of patients undergoing enucleation solely for uveal melanoma that has been investigated for PES. The high participation rate (75%) indicates that the findings are likely to be representative of the population of patients undergoing enucleation for uveal melanoma at this center. Rather than assume that PES is a unitary syndrome, we specifically tested the interrelationships between its constituent symptoms.

Although we did have some information as to when patients first experienced PES, many patients could not

recall this, and we lack information on the duration of the syndrome and on how the frequency and nature of the symptoms change over time. Patients in our sample were enucleated up to 4 years previously; a longer follow-up would be necessary to study the time course of PES. Our characterization of PES was restricted to visual and pain phenomena, and we may have missed other types of symptoms, particularly tactile sensations other than pain, although Rasmussen et al⁴ and Rasmussen⁵ previously reported that these are rare. Our questions were presented in a paper questionnaire, whereas questions by Rasmussen et al, on which they were based, were administered during an interview. Patients may respond differently to these different formats. Anxiety and depression data were not available for all patients and were not contemporaneous with the PES questionnaire. We did not investigate whether any patients with anxiety or depression received treatment for such morbidity. In future studies, it would be interesting to determine the impact on phantom pain of treatment that improves depression and anxiety. Although we have shown a relationship between mood and PES, the cross-sectional design cannot confirm causality.

Clinical Usefulness

Our findings have clear implications for patients dealing with uveal melanoma and for their clinicians. First, although symptoms were statistically associated with age, gender, and preoperative pain, this information does not allow accurate identification of patients who will experience PES. Therefore, because the symptoms can be disturbing to patients, it is important to inform all patients routinely of the possibility of PES symptoms but to assuage any distress. Second, in the absence of a cure for PES symptoms, patients should be advised that they will need to manage them if they wish by discovering their own symptom triggers and ways of reducing symptom impact. Information in this report could help clinicians advise patients about this. Third, pain in the enucleated eye is a marker for depression and anxiety; clinicians treating patients who report this symptom therefore should be alert to this possible comorbidity.

Future Directions

These findings indicate the need for prospective, longitudinal study of PES symptoms and their precursors and consequences. In particular, it will be important to describe how symptoms change over time since enucleation and to identify whether pain is a cause or consequence of anxiety and depression. This could be approached, for example, by examining whether pain is reduced by effective treatment for anxiety and depression.

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Abbreviations and Acronyms:

CI = confidence interval; **df** = degrees of freedom; **HADS** = Hospital Anxiety and Depression Scales; **OR** = odds ratio; **PES** = phantom eye syndrome.

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