Review Article

The role of hypervigilance in chronic esophageal diseases: a scoping review

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Background: Hypervigilance has emerged as an important construct in esophageal symptom reporting, but a review of the literature does not currently exist. This scoping review aimed to generate a comprehensive overview of the literature on hypervigilance in esophageal diseases and summarize the evidence for each esophageal disease.

Methods: Guided by the Joanna Briggs Institute scoping review methodology, articles that were peer-reviewed original studies, published in English, and included adult patients with at least one esophageal disease were included. Articles were retrieved from PubMed and Embase databases and screened first by title and abstract for an initial round of exclusions, and then again by full text for a second round of exclusions.

Results: Nineteen studies were included. Studies were categorized by primary diagnosis: achalasia (1, 5%), eosinophilic esophagitis (1, 5%), gastroesophageal reflux disease (GERD) (6, 32%), laryngopharyngeal reflux (3, 16%), non-cardiac chest pain (3, 16%), and multi-disorder samples (5, 26%). Studies primarily evaluated associations between hypervigilance and symptom severity, psychosocial functioning, health-related quality of life, and physiological disease variables. A number of studies also evaluated hypervigilance across esophageal diseases or presentations (e.g., across motility disorders, across GERD phenotypes).

Conclusions: The role of hypervigilance in symptom reporting has been investigated in multiple esophageal conditions. Findings suggest potential clinical utility in assessing hypervigilance, such as for disease conceptualization and treatment planning. Future research is needed in larger samples, with consistent measures of hypervigilance, and using data synthesis methodology (i.e., systematic reviews) to better compare and contrast findings across studies.

Keywords: Psychogastroenterology; behavioral medicine; esophageal disorders; health-related quality of life (HRQOL)

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Introduction

Esophageal diseases encompass a range of conditions with shared and distinct pathophysiology and symptoms. Diseases, such as gastroesophageal reflux disease (GERD) and eosinophilic esophagitis (EoE), are defined by presence of abnormal pathophysiology (i.e., abnormal acid exposure in GERD) (1). Meanwhile in esophageal disorders of gut-brain interaction (DGBI), including functional heartburn and functional dysphagia, symptoms are the result of dysregulation along the brain-gut axis instead of a structural abnormality (2).

However, there is a notable disconnect between a patient's symptom reporting and the physiological "reason" for said symptoms across esophageal diseases and disorders. For example, it has been demonstrated that the majority of symptoms reported are not related to abnormal acid reflux events in patients with GERD (3). Similarly, symptom severity only modestly correlates with histology in EoE (4,5), and there is a poor correlation between abnormal motor functioning (via high resolution manometry) and symptoms in patients with motility disorders (6). The lack of correlation across esophageal diseases suggests that factors outside of peripheral esophageal factors contribute to esophageal symptom perception.

Psychological processes are increasingly recognized as important factors contributing to esophageal symptom perception (7). One such process is esophageal hypervigilance, or the increased attention to the esophagus. Researchers in the chronic pain field postulate that hypervigilance develops when a person perceives symptoms as highly threatening, experiences fear, and is motivated to escape or avoid the symptoms (8). The increased attention is conceptualized as a way of trying to "be on the lookout" for a potential threat (i.e., symptoms) and therefore be able to more effectively avoid or protect oneself from said threat. Hypervigilance is believed to contribute to symptom perception, such that sensations are perceived as more intense and/or unpleasant when attended to (9). While pathophysiological differences exist across disorders, the psychological processes contributing to esophageal symptom perception are often believed to be universal, as they are centrally-acting processes (10) that can influence perception regardless of the underlying peripheral pathophysiology (7).

Hypervigilance as a construct has been described in other chronic illness populations, such as chronic pain (8), as well as mental health populations, such as post-traumatic stress disorder (11). However, a major limitation to measuring hypervigilance in gastrointestinal illness, especially in the esophagus, is the lack of validated measurement tools. Indeed, research has previously relied on adapted versions of other disease questionnaires [e.g., Pain Vigilance and Awareness Questionnaire for chronic pain (12)]. To address this need, researchers developed the Esophageal Hypervigilance and Anxiety Scale (EHAS) which was published in 2018 (13). The EHAS was the first questionnaire developed and validated specifically to assess esophageal-specific hypervigilance and anxiety, across a range of esophageal disorders. The questionnaire is comprised of a total score, as well as subscales for hypervigilance and symptom-anxiety, so researchers can tease apart the relative contribution of hypervigilance and anxiety.

The EHAS has prompted a surge in research in hypervigilance, across a range of esophageal diseases (14-18). However, there lacks an overview of the literature to date and summary of findings within and across esophageal diseases. Such an overview is needed to improve our general understanding of esophageal hypervigilance. For example, it is unclear if hypervigilance is important across esophageal conditions, or only in certain esophageal diseases or symptoms (e.g., pain-predominant disorders/symptoms). A

Highlight box

Key findings

- Esophageal hypervigilance has been studied across several esophageal diseases, including achalasia, eosinophilic esophagitis, gastroesophageal reflux disease, laryngopharyngeal reflux, and non-cardiac chest pain.
- Studies reported associations between hypervigilance and several important clinical outcomes, including symptom severity, psychosocial functioning, and health-related quality of life.

What is known and what is new?

- Esophageal hypervigilance has emerged as an important construct associated with esophageal symptom severity and overall quality of life in various esophageal conditions.
- Findings provide, for the first time, a comprehensive overview of the literature on hypervigilance in esophageal diseases, including summarizing the evidence for each esophageal disease by type and descriptively comparing similarities and differences in findings within and across esophageal diseases

What is the implication, and what should change now?

- Hypervigilance is a relevant construct that may be important in esophageal symptom perception.
- Future research is needed in larger samples, with consistent measures of hypervigilance, and using data synthesis methodology such that findings can be synthesized across studies.

scoping review of the literature is a first-step in addressing this question and can provide rationale to further evaluate the literature systematically using data synthesis methods (i.e., systematic review, meta-analysis). Further, it may underscore the potential clinical utility of assessing hypervigilance, such as to inform disease conceptualization and treatment planning. Thus, the aim of this scoping review was to generate a comprehensive overview of the literature on hypervigilance in esophageal diseases, including summarizing the evidence for each esophageal disease by type (e.g., GERD, EoE), and descriptively comparing similarities and differences in findings within and across esophageal diseases. We present this article in accordance with the PRISMA-ScR reporting checklist (available at https://tgh.amegroups.com/article/view/10.21037/tgh-23-120/rc).

Methods

The current study is a scoping review of the role of hypervigilance in chronic esophageal diseases. The study was guided by the Joanna Briggs Institute (JBI) methodology for scoping reviews (19,20). The protocol for this scoping review is available from the corresponding author upon request.

Search strategy

We searched PubMed and Embase databases in November 2023 for relevant articles (see https://cdn.amegroups.cn/static/public/TGH-23-120-Supplementary.docx for full details of keyword searches). We included studies based on the following criteria: (I) peer-reviewed original studies; (II) published in English; and (III) a clinical sample of adult patients with at least one esophageal disease. In addition, we included non-cardiac chest pain (NCCP) and laryngopharyngeal reflux (LPR) patient populations, as symptoms are similar to primary esophageal conditions (e.g., patients with LPR commonly have concomitant GERD symptoms) and therefore esophageal hypervigilance is also relevant in these patient populations. Any study that did not include peer-reviewed original research (e.g., case reports, reviews, letters, comments, and editorials) were excluded. We did not limit our search criteria by date of publication to ensure all available data was included.

Source of evidence screening and selection

Articles were retrieved from both databases and entered into separate EndNote (version 20.6) libraries, one for the PubMed search and one for the Embase search. The two EndNote libraries were merged and duplicates were automatically removed. A study member (L.G.) manually reviewed the remaining articles and removed any additional duplicates. The initial list was manually screened based on title and abstract and the articles that did not meet inclusion criteria were excluded. Next, the full text versions of the remaining articles were reviewed and irrelevant articles were again excluded. The first two rounds of screening were performed by one study member (L.G.). A second study member (R.Y.) independently reviewed the articles included/excluded from both screening rounds to confirm. Any disagreements were discussed between reviewers. In addition, we manually screened the reference lists of the full text articles for relevant articles to include.

Data extraction and analysis

Data charting (data extraction, analysis, and presentation) was conducted using guidance published by the JBI Scoping Review Methodology Group (21). We extracted data relevant to the study aim of generating a comprehensive overview of esophageal hypervigilance evidence within and across diseases. The extraction variables included authors, year of publication, country of origin (i.e., country the study was conducted in), study objective, sample size, primary diagnosis, study design, key findings, and funding. We also included a variable to indicate the measure used to assess hypervigilance. Of note, to avoid drawing conclusions about the construct of hypervigilance based on the EHAS total score, we limited our reporting of EHAS total score to those findings where the hypervigilance subscale was not available. For example, if a study conducted an analysis with both the EHAS total score and the hypervigilance subscale, we only reported the outcome from the hypervigilance scale. However, if an analysis only included the EHAS total score, that analysis was included but it was clearly stated that the outcome represents both hypervigilance and symptom-specific anxiety. One study member (L.G.) extracted the data into Microsoft Excel (Redmond, Washington, USA), which was reviewed by the other study member (R.Y.).

Studies were categorized and summarized by primary esophageal diagnosis, including achalasia, EoE, GERD, LPR, NCCP, and multi-disorder samples. Descriptive statistics (frequency/percentage) were used to evaluate the number of studies by primary esophageal diagnosis, country of origin, and measure of hypervigilance used.

Key findings were summarized based on primary outcome, which included either (I) evaluating associations between hypervigilance and other relevant variables [e.g., symptom severity, demographic and clinical information, health-related quality of life (HRQOL), psychological symptoms] or (II) evaluating the prevalence of hypervigilance across different esophageal disorders or phenotypes. When relevant, descriptive statistics (frequency/percentages) were used to indicate the number of studies within a diagnosis that evaluated the primary outcome. For example, the number of studies that evaluated the prevalence of hypervigilance scores across GERD phenotypes, or the number of studies evaluating an association between hypervigilance and chest pain in NCCP.

Results

Search outcomes

Our database search yielded 208 studies. Forty-four duplicates were removed (39 automatic and an additional 4 manually), resulting in 164 studies. An additional five studies were included following manual citation searching. As such, 169 studies were included in the initial search. 147 studies were excluded following title and abstract screening, and an additional three studies were removed following full text screening. The final study list included 19 studies (*Table 1*). *Figure 1* provides a PRISMA flow diagram of the article review and screening process. GERD was the primary diagnosis with the largest number of studies included (6, 32%), followed by multi-disorder samples (5, 26%), NCCP (3, 16%) and LPR (3, 16%), and finally achalasia (1, 5%) and EoE (1, 5%). The majority of studies (12, 63%) were conducted in the United States (13,17,18,22-24,26-28,30,31,34), followed by 3 studies (16%) in Taiwan (14,15,25), 1 study (5%) in Canada (29) and 1 study (5%) in France (33). Two studies were multicenter studies (11%), one study (16) included academic centers in the USA and France and the other (32) included centers in Spain and across Latin America (Chile, Colombia, Argentina, Mexico). The majority of studies (15, 79%) (13-18,22-25,27,28,32-34) used the EHAS (13) or an adaptation of the EHAS [e.g., the Laryngeal Cognitive-Affective Tool (LCAT)] (28) to measure self-reported hypervigilance. Two studies (11%) (30,31) used the Body Vigilance Scale (35), 1 study (5%) (26) used an adapted version of the Pain Vigilance and Awareness Questionnaire (12), and 1 study (5%) (29) used the heart-focused attention subscale of the Cardiac Anxiety Questionnaire (36). Of the 15 studies using the EHAS or an adaptation of the EHAS, 3 studies (20%) (16,24,25) only reported the total score, which includes items assessing both hypervigilance and symptom-specific anxiety, while 12 studies (80%) included analysis specifically with the hypervigilance subscale (13-15,17,18,22,23,27,28,32-34).

Achalasia

One study by Pandolfino *et al.* [2022] investigated hypervigilance in a sample of patients with achalasia. The main aim of the study was to validate a measure of achalasia symptom severity, the Achalasia Patient Reported Outcomes Questionnaire (22). However, the study also evaluated the relationship between this new measure of achalasia symptom severity with hypervigilance (via the EHAS hypervigilance subscale). Hypervigilance was correlated with increased achalasia symptom severity. Further, hypervigilance scores were higher in treatment naïve achalasia patients, compared to those treated for their achalasia and those with normal motility, as well as in patients using diet to manage symptoms.

In addition, the study evaluated factors associated with esophageal-specific HRQOL (22). Increased hypervigilance and achalasia symptom severity scores were significantly and independently associated with poorer esophageal-specific HRQOL. Further, a cluster analysis of symptom severity scores and EHAS total scores demonstrated that patients with high symptom severity and high EHAS total scores reported the poorest HRQOL, while those with low symptom severity and low EHAS total scores reported highest HRQOL.

EoE

One study by Taft *et al.* [2021] investigated esophageal hypervigilance (via EHAS total score and hypervigilance subscale) in a sample of patients with EoE (18). The study evaluated relationships between the EHAS hypervigilance subscale with dysphagia severity, difficulty swallowing foods, and HRQOL, while controlling for relevant disease severity variables such as the EoE endoscopic reference score, stricture presence, eosinophils per high-power field, and distal distensibility plateau. The study found that hypervigilance was the only variable significantly associated with both dysphagia severity and difficulty swallowing. For HRQOL, both hypervigilance as well as dysphagia severity

Table 1 Overview of studies evaluating hypervigilance in chronic esophageal disease

Diseases	Author, country/region	Year	Sample size	Study design	Hypervigilance measure	Major findings	Funding
Achalasia	Pandolfino, USA (22)	2022	296	Scale development	EHAS (total and hypervigilance subscale)	• Hypervigilance was positively correlated with increased achalasia symptom severity • Hypervigilance scores were higher in treatment naïve achalasia patients compared to those treated for their achalasia and those with normal motility • Patients using diet to manage symptoms reported higher hypervigilance • Hypervigilance and achalasia symptom severity was significantly and independently associated with HRQOL • Patients with high symptom severity and high EHAS total scores reported the poorest HRQOL, while those with low symptom severity and low EHAS total scores report highest HRQOL	NIH NIDDK, grant/award number: 1P01DK117824-01
Eosinophilic esophagitis	Taft, USA (18)	2021	103	Cross-sectional, retrospective	EHAS (total and hypervigilance subscale)	• Higher EHAS total scores were correlated with higher dysphagia severity and poorer HRQOL, but not disease variables • Hypervigilance was the only variable significantly and independently associated with dysphagia severity and difficulty swallowing foods when controlling for other relevant variables • PPI use was significantly and independently associated with decreased hypervigilance. For HRQOL, both hypervigilance and dysphagia severity were the only significant variables	NIH NIDDK, grant/award number: 1P01DK117824-01
Gastroesophageal reflux disease	Guadagnoli, USA (17)	2021	123	Cross-sectional, retrospective	EHAS (hypervigilance subscale)	• Hypervigilance was similar across groups based on number of days of positive AET/SI • Hypervigilance was significantly and independently associated with symptom frequency while controlling for symptom-specific anxiety	NIH NIDDK, grant/award number: 1T32DK101363
	Hill, USA (23)	2021	197	Cross-sectional, retrospective	EHAS (total and hypervigilance subscale)	• Hypervigilance was significantly correlated with increased symptom severity and decreased HRQOL, but not significant when controlling for age and gender	Unknown/not reported
	Hill, USA (24)	2022	102 (70 at 6-month post-surgical follow up)	Cohort study, retrospective	EHAS (total)	• Baseline EHAS total was significantly correlated with baseline symptom severity and HRQOL, but not disease pathology or type of surgery • EHAS total scores significantly decreased from baseline to 6-month post-LPR surgery follow up, but baseline disease pathology and type of surgery was not related to improvements in EHAS total scores	Unknown/not reported
	Wong, Taiwan (15)	2021	105	Cross-sectional, prospective	EHAS (hypervigilance subscale)	• Hypervigilance did not significantly differ across reflux phenotypes • Hypervigilance was significantly correlated with symptom severity, depression, and anxiety • Hypervigilance was not significantly correlated with AET, MNBI, or reflux event type (acid, weakly acid, non-acid)	MOST, grant/award number: 109-2314-B-303-027-MY2
	Wong, Taiwan (25)	2023	528 [110 with GERD symptoms (GerdQ >8); 418 without (GerdQ ≤8)]	Cross-sectional, prospective	EHAS (total)	• Patients with GERD symptoms had significantly higher EHAS total scores compared to those without GERD symptoms • Female gender and GerdQ scores were significantly and independently associated with EHAS total scores	MOST, grant/award number: 109-2314-B-303-027-MY2
	Yadlapati, USA (26)	2018	193 (125 on PPI; 67 off PPI)	Cross-sectional, prospective	PVAQ (adapted for heartburn)	• Hypervigilance was similar across GERD phenotypes in the sample tested on PPI • Hypervigilance was not significantly associated with abnormal GerdQ scores in normal or abnormal AET samples • Hypervigilance was not significantly associated with abnormal GerdQ scores in a group of FH patients tested off PPI	NIH NIDDK, grant/award number: 1T32DK101363
Laryngopharyngeal reflux	Krause, USA (27)	2023	77 [22 true LPR (AET ≥6%); 55 no LPR (AET <6%)]	Cross-sectional, prospective	EHAS (total and hypervigilance subscale)	• Hypervigilance was not significantly different between true LPR and no LPR groups • No difference in the proportion of patients reporting high EHAS total scores between groups	NIH NIDDK, grant/award number: 5T32DK007202 and K23 DK125266
	Krause, USA (28)	2024	260 (204 chronic laryngeal symptoms; 56 no chronic laryngeal symptoms)	Scale development	LCAT (hypervigilance subscale)	• Hypervigilance was significantly higher among the group with chronic laryngeal symptoms compared with the asymptomatic group • Hypervigilance was significantly correlated with increased symptom severity, anxiety and depressive symptoms, and thoughts of helplessness about their disease, as well as decreased esophageal-specific quality of life	NIH NIDDK, grant/award number: 5T32DK007202-46, DK125266, DK135513 and University of California San Diego Academic Senate Grant P025945
	Wong, Taiwan (14)	2023	269 (102 GERD; 32 LPR; 90 GERD + LPR; 45 controls)	Cross-sectional, prospective	EHAS (total and hypervigilance subscale)	• Patients with both GERD + LPR symptoms had significantly higher hypervigilance scores compared to controls, but similar to those with only LPR or GERD symptoms • No difference in hypervigilance scores across GERD phenotypes • Hypervigilance was positively correlated with reflux severity, and severity of postnasal drip, difficulty swallowing, choking episodes, annoying cough, globus, and heartburn • Patients reporting high total EHAS scores were older, reported greater reflux severity, had a higher proportion of concomitant GERD and LPR symptoms, and less reflux events compared to those with a normal EHAS total score	MOST, grant/award number: 109-2314-B-303-027-MY2 and 111-2314-B-303-004-MY3
Non-cardiac chest pain	Foldes-Busque, Canada (29)	2016	66 at baseline; 53 at 3-month follow up (patients with comorbid panic disorder)	Randomized cohort design	CAQ (heart-focused attention subscale)	• Baseline heart-focused attention and heart-focused fear was significantly correlated with baseline chest pain severity and heart-focused attention was significantly and independently associated with chest pain severity • Change in heart-focused attention was correlated with a reduction in chest pain severity at 3-months post-intervention, but not significantly and independently associated with chest pain reduction	Canadian Institutes of Health Research, grant/award number: 15324; The Fonds de recherche du Québec –Santé, grant/award number: 28882 and 29533

Table 1 (*continued*)

Table 1 (*continued*)

Diseases	Author, country/region	Year	Sample size	Study design	Hypervigilance measure	Major findings	Funding
	Pardue, USA (30)	2019	190	Cross-sectional, prospective	BVS	• Body vigilance was significantly correlated with chest pain severity and interference • Body vigilance was significantly and independently associated with chest pain severity, but not chest pain interference	NIH NIMH, grant/award number: MH63185; University of Missouri-Saint Louis (University Research Award)
	White, USA (31)	2010	229	Cross-sectional, prospective	BVS	• Patients with a DSM-IV Axis I comorbidity reported higher body vigilance compared to patients without a comorbid mental health condition • Body vigilance had a direct and indirect (partial mediation with interoceptive fear) association with chest pain in a latent variable path model	NIH NIMH, grant/award number: MH63185; University of Missouri-Saint Louis (University Research Award)
Multi-disorder (3+) sample	Carlson, USA and France (16)	2020	236 (23 chest pain; 87 dysphagia; 98 reflux; 26 other)	Cross-sectional, prospective	EHAS (total)	• EHAS total did not differ by Chicago Classification 3 diagnoses or presence/absence of major motor disorder (59 with major motor disorder; 177 without) • EHAS was positively correlated with dysphagia and reflux symptom severity • EHAS was greater for those reporting ≥1 food impaction or ED visit compared to those reporting 0 • EHAS was significantly and independently associated with dysphagia severity, two-fold higher than having a major motor disorder diagnosis, and HRM metrics were not significant	NIH NIDDK, grant/award number: R01 DK079902 and P01 DK117824
	Cisternas, Spain and Latin America (Chile, Colombia, Argentina, Mexico) (32)	2021	443 (16 chest pain; 133 dysphagia; 177 GERD; 42 GERD + dysphagia; 55 other)	Scale development	EHAS (total and hypervigilance)	• No differences in hypervigilance scores across Chicago Classification 3 diagnoses, category (obstructive, major, minor), or based on high-resolution manometry findings (normal *vs.* abnormal) • Patients reporting high EHAS total scores reported significantly higher dysphagia symptom severity, reflux symptom severity, and increased anxiety and depression	No funding declared
	Roman, France (33)	2021	469 (15 achalasia; 30 chest pain; 161 dysphagia; 164 GERD; 99 other)	Scale development	EHAS (hypervigilance subscale)	• Hypervigilance did not differ by diagnostic group, gender, or surgical history • Hypervigilance was significantly correlated with younger age, but not BMI	No funding declared
	Taft, USA (13)	2018	982 (79 chest pain; 524 dysphagia; 319 reflux; 60 other)	Scale development	EHAS (total and hypervigilance subscale)	• Hypervigilance was significantly correlated with increased dysphagia and reflux symptom severity and decreased overall and disease-specific HRQOL • Patients high on EHAS total were younger and reported significantly higher dysphagia and reflux symptom severity and worse overall and disease-specific HRQOL • No differences existed by sex for hypervigilance scores	NIH NIDDK, grant/award number: 1T32DK101363
	Taft, USA (34)	2023	149 (achalasia, EoE, GERD, or esophageal DGBI	Cross-sectional, prospective	EHAS (hypervigilance subscale)	• Hypervigilance scores were significantly correlated with increased global post-traumatic stress, as well as the negative mood/cognition and hyperarousal subscales	NIH NIDDK, grant/award number: 1P01DK117824–01

AET, acid exposure time; EHAS, Esophageal Hypervigilance and Anxiety Scale; FH, functional heartburn; GERD, gastroesophageal reflux disease; HRQOL, health related quality of life; HRM, high resolution manometry; LPR, laryngopharyngeal reflux; MNBI, mean nocturnal baseline impedance; MOST, Ministry of Science and Technology, Taiwan; NIDDK, National Institute of Diabetes and Digestive Disease and Kidney Diseases; NIH, National Institutes of Health; NIMH, National Institute of Mental Health; PVAQ, Pain Vigilance and Awareness Questionnaire; PPI, proton-pump inhibitor; SI, symptom index; LCAT, Laryngeal Cognitive-Affective Tool; CAQ, Cardiac Anxiety Questionnaire; BVS, Body Vigilance Scale; EoE, eosinophilic esophagitis; DGBI, disorders of gutbrain interaction; ED, emergency department.

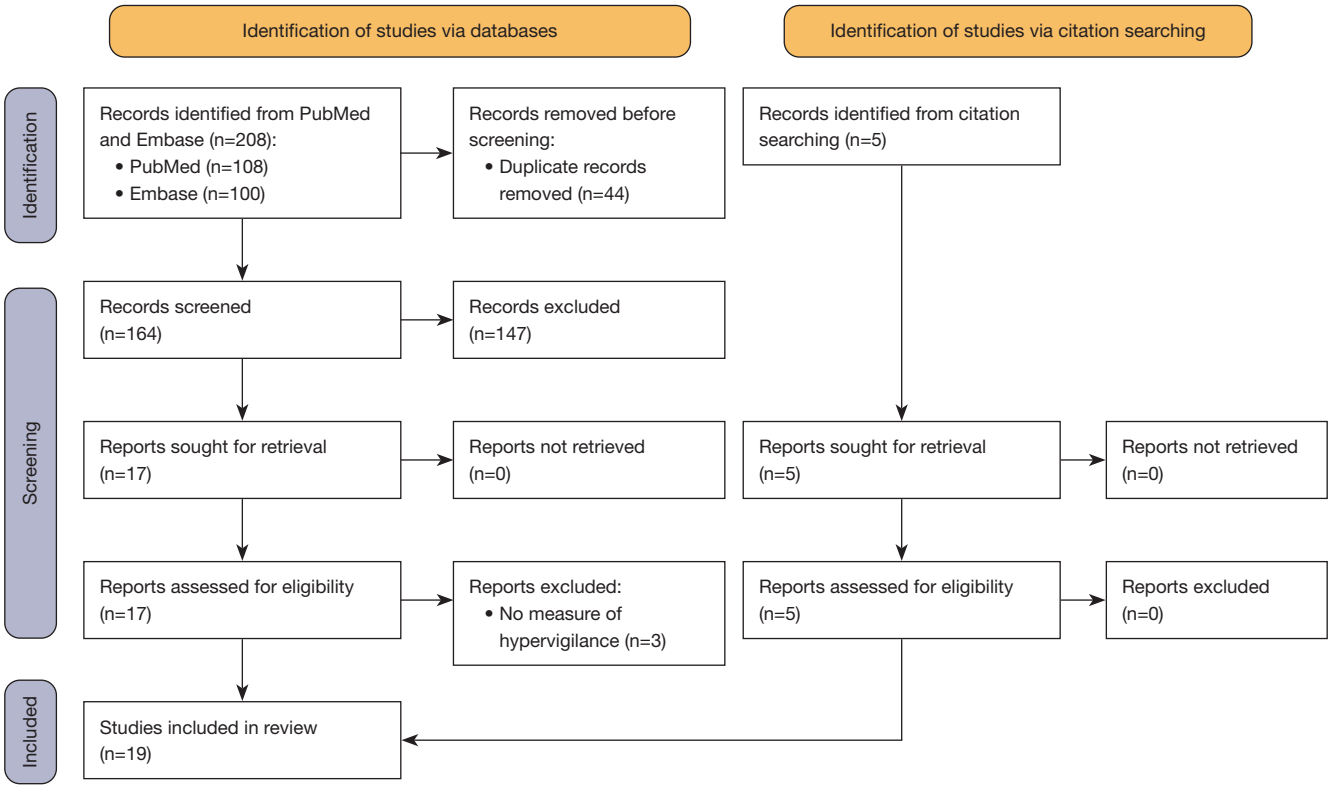

Figure 1 PRISMA 2020 flow diagram outlining the review process.

were significantly and independently associated with poorer HRQOL. Interestingly, EHAS total score was not correlated with disease severity variables (EoE endoscopic reference score, etc.) despite being significantly correlated with increased dysphagia severity and poorer HRQOL.

Taft *et al.* [2021] also evaluated clinical variables associated with hypervigilance, where hypervigilance was the main outcome. Patients on a proton-pump inhibitor (PPI) reported lower hypervigilance scores than those who were off PPI (18). Further, taking a PPI was significantly and independently associated with decreased hypervigilance.

GERD

Six studies evaluated hypervigilance in a sample of patients reporting reflux-related symptoms (e.g., heartburn and/or regurgitation) (15,17,23-26). Five of the studies (83%) used the EHAS, in which three of the five studies (15,17,23) (60%) included the hypervigilance subscale in analyses. The other two studies (24,25) reported only total EHAS scores, which includes both hypervigilance and symptom-specific anxiety. One study used a modified version of the Pain Vigilance and Awareness Questionnaire that was adapted for heartburn symptoms (26).

Comparison across GERD presentations and phenotypes

Three studies evaluated hypervigilance across various GERD presentations or phenotypes (15,17,26). Guadagnoli *et al.* [2021] stratified patients into groups based on the number of days of positive acid exposure time (AET; 0, 1–2, 3+ days) and then again by the number of days of positive symptom-index score (0, 1, 2+ days), following 96-hour wireless pH monitoring off PPI. Hypervigilance scores did not differ across any of the groups, while self-reported symptom severity and the number of symptoms reported during reflux texting differed significantly (17).

The other two studies stratified patients into defined GERD phenotypes based on 24-hour pH impedance monitoring and evaluated hypervigilance scores across the groups. Wong *et al.* [2021] grouped patients into non-erosive reflux disease, reflux hypersensitivity, and functional heartburn groups and found no difference in hypervigilance scores (via the EHAS hypervigilance subscale) across

phenotypes (15). Similarly, Yadlapati *et al.* [2018] found no difference in hypervigilance (via an adapted version of the Pain Vigilance and Awareness Questionnaire) amongst PPI non-responders stratified into normal, abnormal acid exposure, and reflux hypersensitivity groups (26).

Relationship with reflux symptom severity

All six studies assessed the relationship between hypervigilance and reflux symptom severity (15,17,23-26), with the majority being cross-sectional. In correlational analyses, two studies found hypervigilance was significantly correlated with increased symptom severity (15,23). Three studies evaluated if hypervigilance was independently associated with symptom severity, while controlling for other relevant variables (i.e., regression analyses). One study found that increased hypervigilance and younger age were significantly and independently associated with worsening symptom severity, while controlling for the symptom-specific anxiety subscale of the EHAS (17). Conversely, two studies did not find significant independent associations between hypervigilance and symptom severity (23,26). Hill *et al.* [2021] found that EHAS total scores were significantly and independently associated with symptom severity. However, the findings did not remain significant when evaluating this relationship using the hypervigilance subscale (23). Yadlapati *et al.* [2018] found that scores on the adapted PVAQ were not significantly associated with abnormal GerdQ (37) scores (GerdQ ≥8) in "Normal" reflux testing and "Abnormal AET" groups, when controlling for several demographic and clinical variables. Further, hypervigilance was not significantly associated with abnormal GerdQ scores in a group of functional heartburn patients tested off PPI (26).

Two studies evaluated EHAS total scores and symptom severity without including sub-analyses with hypervigilance-specific subscales. One study found that EHAS total was significantly correlated with reflux symptom severity (24), while another found that patients with reflux symptoms (GerdQ >8) report significantly higher EHAS total scores compared to those without reflux symptoms (GerdQ ≤8) (25). However, given that these relationships were not evaluated using the hypervigilance subscale, it is difficult to disentangle the relative contribution of hypervigilance *vs.* symptom-specific anxiety.

Relationship with psychological factors and quality of life

Three studies evaluated associations between hypervigilance, psychological factors (e.g., anxiety, depression) and/or disease-specific HRQOL (15,23,24). In cross-sectional analyses, hypervigilance was significantly correlated with increased depression and anxiety (15) as well as decreased HRQOL (23). However, when the relationship between hypervigilance and HRQOL was assessed while controlling for age and gender, hypervigilance was not significant (23). Finally, one study evaluating patients pre/post anti-reflux surgery found that baseline EHAS total scores were significantly correlated with baseline HRQOL, however, the study did not assess individual EHAS subscales and therefore the relative contribution of hypervigilance and/or anxiety cannot be disentangled (24).

Relationship with demographic and clinical disease outcomes

Two studies investigated correlations between hypervigilance (EHAS total and/or hypervigilance subscale) and physiological disease-related outcomes (15,24). In a sample of patients referred for anti-reflux surgery, baseline disease pathology (esophagitis, motility disorder, DeMeester score, hiatal hernia size) did not significantly correlate with baseline EHAS total scores or improvements in EHAS total scores 6-months post-surgery (24). Similarly, another study found that hypervigilance was not significantly correlated with acid exposure time, mean nocturnal baseline impedance, or acid event type (acid, weakly acid, non-acid) (15).

Factors contributing to EHAS

One study investigated the factors contributing to total EHAS scores and demonstrated that both female gender and reflux symptom severity were significantly and independently associated with EHAS total scores (25). Further, younger age was associated with increased EHAS total scores in a cross-sectional sample of patients referred for anti-reflux surgery (24).

Anti-reflux surgery

Hill *et al.* [2022] assessed hypervigilance (via EHAS total score), symptom severity, and disease-specific HRQOL at baseline and 6-month post-surgery in a sample of 102 patients with objective reflux, who underwent laparoscopic anti-reflux surgery. Of those who completed post-surgical questionnaires (70 patients), total EHAS scores significantly decreased from pre-surgery to 6-months post-surgery (24). Further, higher baseline EHAS total scores were significantly and independently associated with greater post-surgical improvements in symptom severity and HRQOL. Interestingly, baseline disease severity or type of

surgery did not correlate with the degree of improvements in symptom severity or HRQOL.

LPR

Three studies assessed hypervigilance in LPR using the EHAS (total score and hypervigilance subscale) (14,27) or the LCAT (28), a recently validated psychological questionnaire that was adapted from the EHAS specifically for laryngeal symptoms.

Comparison across disease presentations and phenotypes

Two of the studies evaluated hypervigilance scores across disease groups (14,27). Wong *et al.* [2023] found that patients with both GERD + LPR symptoms report significantly higher hypervigilance scores compared to controls, but similar to those with only LPR or GERD symptoms (14). Further, when evaluating patients with LPR symptoms by GERD phenotype (NERD, RHS, FH, inconclusive), hypervigilance scores did not differ across phenotype. Similarly, Krause *et al.* [2023] found that hypervigilance scores were not significantly different between patients with true LPR symptoms (e.g., acid exposure time ≥6%) and patients with LPR symptoms and normal acid exposure. There was also no difference in the proportion of patients reporting high EHAS total scores (EHAS >21) between groups, indicating that regardless of underlying pathology (e.g., abnormal *vs.* normal acid exposure), patients report similar rates of hypervigilance and elevated EHAS total scores (27).

Relationship with symptom severity

Two studies evaluated the relationship between EHAS (total and hypervigilance subscale) and symptom severity (14,28). Wong *et al.* [2023] found that patients who reported high EHAS total scores (score of >21) were older, reported greater reflux severity, and had a higher proportion of concomitant GERD and LPR symptoms, and less reflux events compared to those with a normal total EHAS scores (<21) (14). Using the hypervigilance subscale, authors found that hypervigilance was positively correlated with reflux severity as well as severity of postnasal drip, difficulty swallowing, choking episodes, cough, globus, and heartburn. Similarly, Krause *et al.* [2024] developed and tested the LCAT in patients with and without chronic laryngeal symptoms. The authors found that hypervigilance scores were significantly higher among the group with chronic laryngeal symptoms compared with the asymptomatic group. Further, hypervigilance was significantly correlated with increased symptom severity, including GERD, laryngeal and voice symptoms (28).

Relationship with psychological outcomes and quality of life

Krause *et al.* [2024] assessed associations between hypervigilance and psychosocial factors and found that hypervigilance was significantly associated with increased anxiety and depressive symptoms, and thoughts of disease-related helplessness, as well as decreased esophageal-specific quality of life (28).

NCCP

Three studies evaluated hypervigilance in patients with NCCP using two different measures and in populations both with and without comorbid mental health conditions (29-31). Two studies (30,31) used the Body Vigilance Scale (35), which measures general attention and interoceptive sensitivity to bodily sensations, including overall vigilance, attentional focus, sensitivity to changing bodily sensations, body scanning, and symptom-related vigilance. In addition, the Body Vigilance Scale includes domain-specific subscales for cardiopulmonary, gastrointestinal, dissociative (i.e., numbness), and temperature sensations. Foldes-Busque *et al.* [2016] used the Cardiac Anxiety Questionnaire (36), which includes fear, avoidance, and attention subscales, specific to cardiac-related anxiety in a sample of NCCP patients with comorbid panic disorder.

Relationship with chest pain symptom severity

All three studies evaluated the relationship between hypervigilance/attention and chest pain severity. White *et al.* [2010] used latent variable path models and found body vigilance was directly and indirectly associated with chest pain severity in a sample of NCCP patients with and without comorbid mental health disorders. In the indirect path, the effect of body vigilance on chest pain was partially mediated by interoceptive fear, indicating fear is likely an important factor contributing to the relationship between vigilance and symptom perception (31). Also using the Body Vigilance Scale, Pardue *et al.* [2019] found that body vigilance was significantly and independently associated with chest pain severity, when controlling for gender, anxiety sensitivity, and disease conviction (30). Finally, Foldes-Busque *et al.* [2016] assessed NCCP patients with

comorbid panic disorder at baseline and 3-months after completing evidence-based treatment for panic disorder (e.g., pharmacotherapy, cognitive behavioral therapy). The study found that at baseline, heart-focused attention and heart-focused fear were significantly correlated with chest pain severity (29). Further, heart-focused attention was significantly and independently associated with chest pain severity when controlling for heart-focused fear. At 3-month follow up, change in heart-focused attention (along with heart-focused fear, avoidance, and anxiety sensitivity) was correlated with a reduction in chest pain severity. However, when all the variables were entered into regression models, only change in heart-focused fear was significantly and independently associated with chest pain reduction (29).

Relationship with psychological outcomes

White *et al.* [2010] assessed for differences in vigilance between those with and without a comorbid mental health disorder. Results suggest patients with a comorbid DSM-IV Axis I mood/anxiety disorder reported higher body vigilance scores for all somatic domains (except heat), as well as higher overall vigilance, attention, sensitivity, scanning, and symptom vigilance compared to patients without a comorbid mental health condition (31). This effect was especially prominent for patients with a comorbid anxiety disorder, as they reported increased overall body and symptom vigilance compared to those without a comorbid anxiety disorder.

Multi-disorder patient samples

Five studies investigated hypervigilance (using the EHAS total and/or hypervigilance subscale) in a sample of patients with multiple disorders and/or indications (13,16,32-34). The studies included patients with varying esophageal symptoms, including chest pain, dysphagia, and heartburn, as well as diseases such as achalasia, EoE, GERD, and esophageal DGBI (e.g., functional heartburn/dysphagia). The exact symptoms/diagnoses included varied by study (see *Table 1* for overview).

Comparison across disease presentations and diagnostic groups

Two studies assessed hypervigilance across motility disorder diagnoses (16,32). Cisternas *et al.* [2021] found no differences in hypervigilance scores across Chicago Classification 3 diagnoses (achalasia, esophagogastric junction outflow obstruction, Jackhammer, diffuse esophageal spasm, absent contractility, ineffective esophageal motility), category (obstructive, major, minor), or based on high-resolution manometry findings (normal *vs.* abnormal) in a multi-center sample of patients in Spain and Latin America. Further, there were similar proportions of patients with "high" and "low" EHAS total scores between those with normal and abnormal manometry (32). Similarly, Carlson *et al.* [2020] found no difference in EHAS total scores across Chicago Classification diagnoses (achalasia, esophagogastric junction outflow obstruction, absent contractility, jackhammer, ineffective esophageal motility) or between those with normal and abnormal motility in a sample of patients in the USA and France (16). A third study evaluated differences in hypervigilance scores across esophageal diagnostic groups (dysphagia, GERD, other) and found no differences by diagnostic group (33).

Relationship with reflux and/or dysphagia symptom severity

Three studies investigated relationships between hypervigilance and symptom severity. Two studies report the EHAS total score (16) and the hypervigilance subscale (13) were significantly and positively correlated with dysphagia and reflux symptom severity. Further, when controlling for relevant physiological variables (e.g., motility disorder, basal esophagogastric junction pressure), both the presence of a major motility disorder and EHAS total scores were significantly and independently associated with dysphagia symptom severity (16). In fact, EHAS total scores had a two-fold higher contribution to dysphagia severity compared to having a major motor disorder diagnosis. Finally, two of the three studies grouped patients into high and low EHAS scores based on a median split. Both studies found that patients with the "high" total EHAS scores reported significantly greater dysphagia and reflux symptom severity compared to those reporting "low" total EHAS scores (13,32).

Relationship with psychological factors and quality of life

Three studies evaluated associations between hypervigilance (via EHAS total score and hypervigilance subscale) with psychological factors and quality of life (13,32,34). One study found that hypervigilance was significantly correlated with increased self-reported global post-traumatic stress, as well as negative mood/cognition and hyperarousal (34). Similarly, another study demonstrated that patients experiencing "high" EHAS total scores (score >37) report

significantly higher anxiety and depression (32). For HRQOL, Taft *et al.* [2018] found that hypervigilance scores were significantly correlated with decreased overall and disease-specific HRQOL, and those scoring "high" on EHAS total scores (based on median split) reported poorer overall and disease-specific HRQOL (13).

Relationship with demographic and clinical disease outcomes

In terms of disease-related outcomes, one study found that EHAS total scores were significantly higher in patients with ≥1 food impaction(s) or esophageal-related emergency department visits compared to those without (16). However, another study found that hypervigilance scores did not differ based on surgical history (33).

Two studies found that hypervigilance was associated with age, such that younger patients reported higher hypervigilance scores (33) and EHAS total scores (13). However, hypervigilance was not associated with gender and BMI (33), or sex (13).

Summary and future directions

Esophageal hypervigilance has been investigated across several different disorders, including GERD, achalasia, EoE, NCCP, and LPR, as well as in samples reporting several symptoms, such as heartburn, regurgitation, dysphagia, and chest pain. The current study reviewed 19 studies assessing hypervigilance in various esophageal diseases and reported similarities and differences within and across diseases. Here, we summarize the findings and discuss limitations and areas for future research.

Association between hypervigilance and increased symptom severity

The relationship between hypervigilance and increased symptom severity emerged as a theme across all six categories (achalasia, EoE, GERD, NCCP, LPR, and multi-symptom sample). Several studies found significant positive correlations between hypervigilance and symptom severity in achalasia (22), EoE (18), GERD (15,23,24), LPR (14,28), NCCP (29,30), and multi-disorder samples with GERD and dysphagia symptoms (13,16,32). Further, a number of studies evaluated the independent association between hypervigilance and symptom severity, while controlling for relevant demographic, clinical, and/or psychological variables, including in patients with GERD (17), EoE (18), NCCP (29-31), and in a multi-disorder sample (16). Finally, one study in a sample of LPR patients (14) and two studies of multi-disorder samples (13,32) grouped patients based on "high" and "normal/low" EHAS total score, and found those in the "high" group reported greater reflux and/or dysphagia symptom severity compared to the "normal/low" group.

Interestingly, when assessing independent associations between hypervigilance and symptom severity in GERD specifically, findings were inconsistent. One study found hypervigilance was independently associated with reflux symptom severity (17), which aligns with a recent study in nearly 400 patients with reflux symptoms that demonstrated psychological symptoms (e.g., depressive and anxiety symptoms) were the most important contributors to reflux symptom severity, while physiological parameters (e.g., number of reflux events) were not significant (7). However, two studies in the current review found no independent association (23,26). Differences between studies could be due to the sample type and size. Hill *et al.* [2021] included individuals with abnormal reflux who were referred for anti-reflux surgery, which is a very specific population and may not be reflective the general population of patients reporting heartburn/regurgitation symptoms (e.g., those with functional heartburn and reflux hypersensitivity). Another explanation for these findings may be due to differences in outcome variables. The study by Yadlapati *et al.* [2018] used binary logistic regressions with the main outcomes being abnormal/normal GerdQ scores compared to continuous outcomes used in other studies. Regardless, future research in large well-characterized samples should continue to investigate the relationship between hypervigilance and symptom severity, particularly in patients experiencing reflux.

Lack of association between hypervigilance and disease metrics

Studies across patients with EoE (18) and GERD (15,24) reported no association between hypervigilance and disease metrics. Indeed, EHAS total scores were not significantly correlated with disease severity variables (e.g., EoE endoscopic reference score) in a sample of EoE patients (18). Similarly, in patients with GERD, both hypervigilance scores (15) and EHAS total scores (24) were not significantly associated with disease-related variables such as acid exposure time (15), acid event type (15), esophagitis (24), and DeMeester score (24). This is logical given that hypervigilance and other psychological processes are

likely more related to symptom perception (e.g., symptom severity) than peripheral indicators of disease.

Interestingly, several studies found that hypervigilance was affected by treatment. Hypervigilance scores were higher in treatment naïve achalasia patients compared to those treated for their achalasia and those with normal motility (22), and EHAS total scores decreased from baseline to 6-months following anti-reflux surgery (24). However, in a sample of NCCP who underwent evidence-based treatment (e.g., cognitive behavioral therapy, pharmacotherapy), change in heart-focused attention was not significantly and independently associated with chest pain reduction (29). One reason for these differences may be due to the fact that the two studies that found significant results used the EHAS (total and/or hypervigilance subscale) while the study in NCCP used the attention subscale of the Cardiac Anxiety Questionnaire.

Lack of differences in hypervigilance scores within and across diseases

Several studies found that hypervigilance does not differ within and across esophageal diseases. Three studies in a sample of GERD patients (15,17,26) and two in a sample of LPR patients (14,27) found no differences in hypervigilance scores when evaluating hypervigilance by gastroesophageal reflux presentation/phenotype (e.g., non-erosive reflux disease *vs.* functional heartburn *vs.* reflux hypersensitivity, normal *vs.* abnormal acid reflux). Similarly in motility disorders, two studies that included multi-disorder patient samples found no differences in hypervigilance (32) or EHAS total scores (16) across Chicago Classification 3 diagnoses or between normal and abnormal motility based on manometry. Finally, two studies found no differences in hypervigilance scores between different diagnostic groups, such as between GERD and LPR (14) as well as between dysphagia, GERD, and a composite group of "other" diagnoses (e.g., chest pain, achalasia) (33).

These findings are consistent with a recent study that used traditional statistical methods (e.g., one-way ANOVA, logistic regression) and machine learning analyses to evaluate if a range of psychological symptoms were associated with GERD phenotype (38). The authors concluded that psychological symptoms were either not significantly different across phenotypes or extremely poor predictors of the phenotype a patient belonged to (38). These findings, taken together with the current review, lends evidence to the hypothesis that psychological processes such as hypervigilance are centrally-acting and therefore can be important to consider across esophageal conditions, regardless of underlying pathophysiology. However, future research specifically testing this hypothesis is needed.

Association between hypervigilance and demographic and psychosocial variables

In terms of psychological outcomes, hypervigilance was associated with depression and/or anxiety in GERD (15), NCCP (31), LPR (28), and in a multi-disorder sample of patients experiencing mostly dysphagia and reflux symptoms (heartburn/regurgitation) (32). Further, hypervigilance was significantly correlated with increased self-reported global post-traumatic stress symptoms in a multi-disorder sample of esophageal patients (34). It is logical that these processes would be mild-moderately correlated, as hypervigilance is conceptually similar to other psychological processes, specifically anxiety. If a patient is generally more anxious, they may experience more fear, threat, and tendency to want to avoid symptoms, which likely predisposes them to develop hypervigilance (8).

Hypervigilance was also consistently correlated with poorer HRQOL in patients with achalasia (22), EoE (18), GERD (23,24), LPR (28), and in a multi-disorder sample (13). Interestingly, when controlling for other relevant variables, this association remained significant in the study on achalasia patients (22) but not in one of the GERD samples, which controlled for age and gender (23). Thus, more research is needed to evaluate if hypervigilance is significantly and independently associated with HRQOL.

Finally, three studies across multiple symptom indications, including heartburn/regurgitation and dysphagia, found that younger age was correlated with increased hypervigilance scores (33) and EHAS total scores (13,24). However, one study in patients with LPR found that patients reporting high EHAS total scores (score of >21) were older compared to those reporting low EHAS total scores (14). Future research is needed to understand demographic and clinical variables that could potentially predispose patients to developing hypervigilance.

Limitations and future implications

There are several limitations to the current review. Scoping reviews are designed to provide a descriptive overview of the literature, not synthesize research (21). Thus, research methodology that involves data synthesis (i.e., systematic

reviews, meta-analyses) are needed to statistically examine key findings across studies. Most of the included studies were cross sectional, resulting in a lack of ability to make causational claims about the role of hypervigilance in chronic esophageal diseases. A key area for future research would be to include measures of hypervigilance in longitudinal samples, both observational and interventional, to assess if and how hypervigilance changes over time and in response to intervention. Further, the majority of studies evaluated hypervigilance as an independent variable (i.e., how does hypervigilance contribute to symptom severity), instead of an outcome (i.e., what factors contribute to hypervigilance). However, two studies evaluated variables with hypervigilance as an outcome. In a sample of EoE patients, PPI use was significantly and independently associated with decreased hypervigilance (18), while both female gender and reflux symptom severity were significantly and independently associated with total EHAS scores in a sample of GERD patients (25). Future research should include not only the role of hypervigilance in outcomes of interest (e.g., symptom severity), but also the variables associated with hypervigilance.

An additional limitation is that three of the 15 studies that used the EHAS or an adapted version of the EHAS (e.g., the LCAT) as their measure of hypervigilance only reported the EHAS total score. Further, even in the studies that reported the hypervigilance subscale, many included certain analyses with just total score. This makes it difficult to discern the contribution of hypervigilance *vs.* symptom-specific anxiety to the outcomes assessed. Future research should report both the total score as well as subscale scores to truly be able to discern the relative contributions of hypervigilance and symptom-specific anxiety. Finally, an additional limitation is that evaluating hypervigilance was not the main aim of the study for a number of studies. Instead, studies investigated other questions, such as the role of medical post-traumatic stress, or aimed to validate a measure, and hypervigilance was included as a variable amongst many other variables or explored as a secondary outcome. This could result in studies being underpowered to find effects in the analyses where hypervigilance was included and could therefore bias our results.

Conclusions

In conclusion, self-reported hypervigilance to esophageal symptoms and sensations has been measured in several esophageal disorders, including GERD, achalasia, EoE, NCCP, and LPR, and symptoms, such as heartburn, regurgitation, dysphagia, and chest pain. Several studies found that esophageal hypervigilance was associated with relevant outcomes, including esophageal symptom severity reporting and psychosocial functioning, and is similar across esophageal diseases. Further, a number of studies report a lack of association between self-reported hypervigilance and disease-related variables (e.g., acid exposure time in GERD). While we are careful not to overinterpret such descriptive results, findings suggest that hypervigilance may potentially be an important construct in esophageal symptom perception. Assessment of hypervigilance in a clinical context may provide information to clinicians that can aid in disease conceptualization and treatment planning. However, studies are limited by their cross-sectional nature and inconsistent measurement tools (e.g., EHAS total, EHAS hypervigilance subscale, Cardiac Anxiety Questionnaire). Future research is needed to replicate current results in larger samples, with consistent measures of hypervigilance, and with synthesis methods (i.e., systematic reviews) to better compare and contrast findings across studies.

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