



# General Well-being and Coping Strategies in Adult Eosinophilic Esophagitis Patients

Willemijn E de Rooij,<sup>1\*</sup> Floor Bennebroek Evertsz,<sup>2</sup> Aaltje Lei,<sup>1</sup> and Albert J Bredenoord<sup>1</sup>

Departments of <sup>1</sup>Gastroenterology and Hepatology, and <sup>2</sup>Medical Psychology, Amsterdam University Medical Center, Amsterdam, the Netherlands

## Background/Aims

Growing evidence suggests a negative effect of eosinophilic esophagitis (EoE) on patients' general health-related quality of life (HRQOL). However, the relevance and use of coping strategies and its relation to (disease specific) HRQOL as well as its determinants have not been studied well.

## Methods

Adult EoE patients were invited to complete standardized measures on general HRQOL (Short Form-36 Health Survey [SF-36]) and coping strategies (Utrechtse Coping Lijst [UCL]). Scores were compared to general population norms. The disease specific Adult Eosinophilic Esophagitis Quality of Life (EoE-QOL-A) measure was used to assess EoE-HRQOL. Socio-demographic and clinical factors were also evaluated.

## Results

In total, 147 adult EoE patients (61% males), age 43 (interquartile range, 29-52) years were analyzed. Mental health-scores (SF-36) were significantly lower in EoE patients, whereas physical health-scores (SF-36) were similar in EoE patients (vs the general population;  $P = 0.010$  and  $P = 0.240$ ), respectively. The subdomain "disease anxiety" (EoE-QOL-A) was mostly affected, determinants were; female gender, younger age, severe clinical disease activity, higher number of food bolus extraction, and more recent EoE-diagnosis. Less effective coping styles (ie, passive/palliative reaction) were associated with a significant impact on each individual EoE-HRQOL-subdomain as well as lower scores of the Mental Health Component Scale in male EoE patients. Passive reaction in female EoE-patients correlated with impairment of the EoE-HRQOL-domains "emotional impact" and "disease anxiety." Active problem solving was significantly related to better perception of mental HRQOL (SF-36) in both males and females.

## Conclusions

EoE has a significant negative impact on mental HRQOL, with less effective coping strategies—specifically in males, being a relevant determinant. Thus, a pro-active approach towards coping mechanisms is needed in order to enhance HRQOL and manage patients' burden of EoE.

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## Key Words

Adaptation, psychological; Eosinophilic esophagitis; Mental health; Quality of Life

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\*Correspondence: Willemijn E de Rooij, MD

Department of Gastroenterology and Hepatology, Amsterdam University Medical Center, 22660, 1100 DD Amsterdam, the Netherlands

Tel: +31-(0)20-566-6961, Fax: +31-(0)20-691-7033, E-mail: [w.e.derooij@amsterdamumc.nl](mailto:w.e.derooij@amsterdamumc.nl)

## Introduction

Eosinophilic esophagitis (EoE) is a chronic allergic disease, characterized by eosinophilic mucosal infiltration of the esophagus and symptoms of esophageal dysfunction.<sup>1-3</sup> Now widely recognized by gastroenterologists and allergists, EoE has rapidly evolved into an important cause of upper gastrointestinal morbidity in children and adults.<sup>4-9</sup> The first line management of EoE consists of medical therapy (ie, proton pump inhibitors or topical corticosteroids) or dietary elimination of culprit foods and medications.<sup>3</sup> Maintenance treatment is indicated in EoE, since disease activity recurs quickly after cessation of therapy and ongoing eosinophilic inflammation is associated with narrowing of the esophagus and stricture formation.<sup>10-13</sup> In general, health-related quality of life (HRQOL) is a multi-dimensional concept that is determined by patients' physical, psychological and social status, as well as attitudes, concerns, and behaviors in response to having a (chronic) disease.<sup>14</sup> Previous literature confirms that EoE significantly impacts on patients' daily life.<sup>15,16</sup> Yet, data remains scarce on to which demographic, clinical, or cognitive/behavioral factors influences (illness specific) HRQOL in EoE. From the patients' perspective, being diagnosed with this "relatively new" disease with need for life-long treatment and subsequent invasive procedures for disease monitoring may be of specific concern.<sup>17</sup> Moreover, most patients have developed adapted eating behaviors (eg, taking smaller bites and avoid highly textured foods) or use dietary restrictions (avoidance of culprit foods) in order to manage symptoms and avoid food impactions in particular.<sup>17</sup> EoE patients generally display avoidance behaviors of eating (alone or with others) in daily social-life, due to swallowing anxiety or fear of giving others the impression of a state of illness.<sup>18,19</sup> Hence social situations may lead to stress, anxiety symptoms, and embarrassment. Coping refers to emotional, cognitive, and behavioral efforts that affects the way each individual handles the physical, social, and mental burden that is linked to stressful life events, such as having a chronic illness. Stress management seems to be crucial in general health. Despite a wide range of different coping mechanisms, 2 main categories are generally mentioned: problem- and emotion-focused coping.<sup>20,21</sup> Problem focused-coping refers to efforts to change a stressful situation (eg, taking action and seeking information), whereas emotion-focused coping involves strategies that regulate emotional distress that is being associated with the situation (eg, expression of emotion and anger, and distraction). Moreover, also gender differences in the selection of different coping styles have also been well-described.<sup>22-24</sup> How individuals cope

with a chronic illness determines patients' quality of life and has shown to be an important outcome in a number of chronic disease populations, eg, rheumatoid arthritis and inflammatory bowel disease (IBD).<sup>25-30</sup> At present, no studies are available that have evaluated coping strategies in adult EoE patients. More importantly, the degree to which different coping styles are related to (disease specific) HRQOL is unknown as well. Therefore, we aim to assess (1) general and disease specific HRQOL, (2) coping strategies and their relationship with general and disease specific HRQOL, and (3) determinants (ie, clinical and socio-demographic factors) of disease specific HRQOL.<sup>31</sup>

## Materials and Methods

An observational cross-sectional study design was used to assess mental distress among adult EoE patients. Consecutive patients who attended the outpatient clinic of the Amsterdam University Medical Center Motility Center, were invited to participate in the study. An informed consent letter including self-reported questionnaires was distributed at the outpatient clinic between July 2019 and February 2020. Patients with a documented diagnosis of EoE, aged 18 and over, with a sufficient command of written Dutch to complete a self-reported survey were considered eligible for inclusion.<sup>32</sup> Once consented, all patients completed a paper or digital version of the questionnaires. All data were safely collected and stored by using the Electronic Data Capture Castor.

## Patients and Procedures

A cross-sectional study design was used to assess for disease specific and general well-being (ie, EoE-HRQOL) and coping strategies in an adult EoE population. Inclusion criteria were a minimum age of 18, a sufficient command of written Dutch to complete self-reported questionnaires and documented diagnosis of EoE according to consensus guidelines.<sup>3</sup> All patients received an informed consent letter including questionnaires. Once written consent was obtained, all eligible patients completed a paper or digital version of the study questionnaires and data was subsequently stored by using the Electronic Data Capture Castor.

## Measures

### Demographics and clinical data

Socio-demographic characteristics (eg, gender and marital status) as well as EoE related clinical information concerning year of symptom onset and diagnosis, history of endoscopic interventions

and dilation, EoE management (medical or dietary treatment), atopic comorbidities, and adapted eating behavior (ie, taking smaller bites, more chewing, eating slowly, or drinking more water during meals) were evaluated by a standard fixed choice questionnaire. Clinical disease activity, defined as symptoms related to esophageal dysfunction (dysphagia and/or food impaction) were assessed by the Straumann Dysphagia Instrument-measure.<sup>33</sup>

### General health-related quality of life

General HRQOL was evaluated with the Short Form-36 Health Survey (SF-36) and has been widely validated for the use in different health care settings and patients. General HRQOL is measured in 36 items across 8 domains, including: physical functioning, role limitations due to physical problems, bodily pain, general health, vitality, role limitations due to emotional problems, social functioning, and mental health. The items of the SF-36 are combined to form the Physical Health Component Scale (PCS) and the Mental Health Component Scale (MCS).<sup>34</sup> All SF-36 scores of our EoE patients, stratified for gender and age were compared to a national reference cohort, containing a random sample of the Dutch population (n = 1742).<sup>35</sup>

### Disease specific health-related quality of life

The impact of EoE on psychosocial functioning was measured by means of the Adult Eosinophilic Esophagitis Quality of Life (EoE-QOL-A) measure.<sup>36</sup> This tool was developed to assess disease specific EoE-HRQOL in EoE populations and has not been validated in the Dutch population. The EoE-QOL-A consists of 24 items (Cronbach's  $\alpha = 0.94$ ) across 5 subscales, including; eating/diet impact, social impact, emotional impact, disease anxiety, and swallowing anxiety (Supplementary Table 1). Each item score ranges from 4 (very good QOL) to 0 (very poor QOL). Overall scores range from 0 to 96, with higher scores indicating better quality of life. The total EoE-QOL-A index score includes the weighted average of all subscales.

### Coping strategies

Patients coping styles were measured by using the validated Utrechtse Coping Lijst (UCL).<sup>21,37</sup> The UCL consists of 47 items, which represent 7 different coping styles. The coping subscales are: active problem solving (ie, not having to deal with a problem by looking for distraction and getting away from the situation) and palliative reaction, avoidance and passive expectancy, seeking social support, and passive reaction (ie, expression of emotions and anger as well as fostering reassuring thoughts) (Supplementary Table 2).

Different coping strategies of our EoE sample were compared to a reference group, including normative data of the Dutch population, stratified by gender and age. The reference groups are described in the UCL manual.<sup>38</sup>

## Statistical Methods

Statistical analysis was performed with IBM SPSS Statistics

**Table 1.** Socio-demographic and Clinical Characteristics

| Characteristics                                       | EoE (N = 147) |
|---|---------------|
| Socio-demographic characteristics                     |               |
| Age (yr)  | 43 (29-52)    |
| Gender (male)   | 90 (61)       |
| Alcohol use (yes)                                     | 115 (78)      |
| Smoking (yes)   | 9 (6)         |
| Level of education                                    |               |
| Primary or secondary school                           | 49 (33)       |
| College or university                                 | 98 (67)       |
| In domestic partnership (living together or married)  | 96 (65)       |
| Working status  |               |
| Student   | 9 (6)         |
| Employed  | 121 (82)      |
| Unemployed  | 9 (6)         |
| Stayed at home parent                                 | 1 (1)         |
| Retired   | 7 (5)         |
| Clinical characteristics                              |               |
| Atopic diatheses                                      | 119 (81)      |
| Allergic rhinitis                                     | 106 (72)      |
| Oral allergy syndrome                                 | 52 (35)       |
| Food allergy  | 50 (34)       |
| Asthma  | 49 (33)       |
| Atopic dermatitis                                     | 37 (25)       |
| Clinical disease activity <sup>a</sup>                | 97 (66)       |
| Adapted eating behavior                               | 93 (64)       |
| Number of endoscopic interventions                    | 3 (2-6)       |
| Diagnostic delay (yr) <sup>b</sup>                    | 5 (2-14)      |
| Disease duration (yr) <sup>c</sup>                    | 3 (1-6)       |
| Age at diagnosis (yr)                                 | 39 (26-48)    |
| Previous dilation                                     | 21 (14)       |
| Current treatment                                     |               |
| PPIs  | 34 (23)       |
| Topical steroids                                      | 35 (24)       |
| Topical steroids with additional dietary restrictions | 14 (10)       |
| Empiric food elimination                              | 36 (25)       |
| No treatment  | 28 (19)       |

<sup>a</sup>Clinical disease activity, defined as SDI-PRO score  $\geq 1$ .

<sup>b</sup>Diagnostic delay is the time interval between the first symptoms and the diagnosis.

<sup>c</sup>Disease duration, measured from year of diagnosis.

EoE, eosinophilic esophagitis; PPIs, proton pump inhibitors.

Data are presented as median (interquartile range) or n (%).

(version 25.0) (IBM Corp, Armonk, NY, USA). To characterize our sample, descriptive statistics were used to assess socio-demographic and clinical variables. Categorical data are described as percentages and continuous data are expressed as mean ( $\pm$  SD) or median (interquartile range [IQR]). SF-36 scores and UCL scores were compared to previously published reference norms from the Dutch general population, stratified by gender and age.<sup>35,38</sup> Independent sample *t* tests were used to compare SF-36 and UCL scores from our EoE cohort to the general population. Univariate linear regression analysis was used to assess clinical and socio-demographic factors (independent variables) that are possibly associated with EoE-QOL-A subscale scores (dependent variables). Subsequently, a multiple linear regression model was fitted for each subdomain of the EoE-HRQOL-A survey to identify determinants. Factors with a liberal *P*-value of  $< 0.2$  were entered for multiple linear regression analysis with backward selection. A *P*-value of  $< 0.05$  was considered to be statistically significant. Associations between coping styles and EoE-HRQOL were assessed by Pearson's or Spearman's rank correlations coefficients, as appropriate. Level of significance was set at  $< 0.05$  for the PCS and MCS as well as  $P < 0.01$  to correct for multiple testing for all 5 subdomains of the EoE-QOL-A.

## Ethical Considerations

This study was conducted according to the principles of the Declaration of Helsinki and in accordance with the Dutch Medical Research Involving Human Subjects Act (WMO). Our study was reviewed by the Medical Ethics Committee of the Amsterdam

University Medical Center and formal evaluation was waived according to Dutch law (W19\_103#19.136).

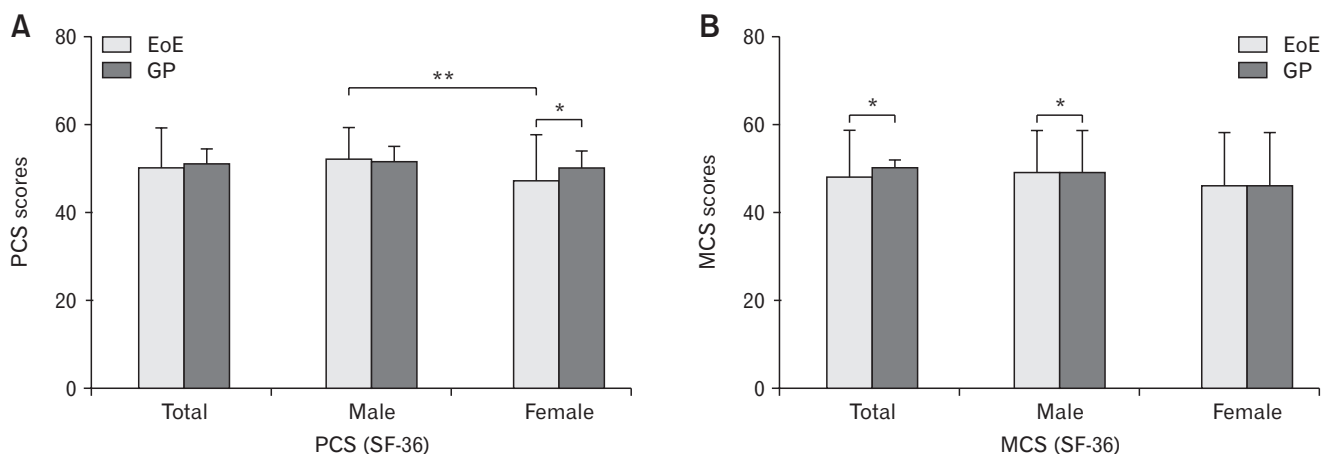
## Results

### Patient Characteristics

In total, 147 patients (out of 209 patients) completed the self-reported questionnaires (response rate 71%). A male predominance (61%) was confirmed, with a median age of 43 (IQR, 29-52) years. The median time interval between the first reported EoE symptoms and diagnosis (diagnostic delay) was 5 (IQR, 2-14) years, with a median age at diagnosis of 39 (IQR, 26-48) years. The majority of our cohort (66%) reported experiencing ongoing symptoms of dysphagia and/or food impaction. Ninety-three (64%) patients noted to have currently adapted their eating behavior (eg, more chewing) as a result of EoE symptoms. Empiric elimination of causative foods was reported in 36 (25%) patients, of which 18 (12%) patients stated to be on an elimination diet under guidance of a specialized dietician at present. More details on patients' characteristics of our EoE sample are listed in Table 1.

### General Health-related Quality of Life

General HRQOL (SF-36) levels of the PCS of EoE patients showed no difference compared to the general population ( $50.5 \pm 8.6$  vs  $51.4 \pm 3.2$ ;  $P = 0.244$ ). Although PCS levels of male EoE patients vs males of the general population were not significantly different ( $P = 0.453$ ), female EoE patients scored significantly



**Figure 1.** General health-related quality of life in patients with eosinophilic esophagitis (EoE) compared to the Dutch general population (GP), stratified for gender. (A) Physical Health Component Scale (PCS; Short Form-36 Health Survey [SF-36]) of EoE patients compared to the Dutch GP. (B) Mental Health Component Scale (MCS; SF-36) of EoE patients compared to the Dutch GP. \**P*-value of  $< 0.05$ , indicating a significant outcome, \*\**P*-value of  $< 0.01$ .

lower compared to females of the general population ( $P = 0.030$ ). Moreover, female patients scored significantly lower on the PCS compared to males in our EoE cohort ( $52.5 \pm 6.5$  vs  $47.3 \pm 10.4$ ;  $P < 0.001$ ) (Fig. 1A). Total levels of the MCS were significantly lower in EoE patients compared to the general population ( $47.9 \pm 10.4$  vs  $50.1 \pm 1.5$ ;  $P = 0.01$ ). Although MCS scores of females were similar (EoE vs general population;  $P = 0.112$ ), males scored

significantly lower on the MCS (EoE vs general population;  $P = 0.040$ ). However, no differences between male vs female patients on MCS scores were found in our EoE cohort ( $49.1 \pm 9.4$  vs  $46.0 \pm 11.6$ ;  $P = 0.076$ ) (Fig. 1B).

**Table 2.** Factors Associated With Disease Specific Quality of Life in Eosinophilic Esophagitis Patients

| Disease specific quality of life<br>(EoE-QOL-A)<br>N = 147    | Univariate analysis |         |                  |                      | Multivariable analysis |         |                  |                      |
|---|---------------------|---------|------------------|----------------------|------------------------|---------|------------------|----------------------|
|   | B                   | $\beta$ | 95% CI (B)       | P-value              | B                      | $\beta$ | 95% CI (B)       | P-value              |
| <b>Eating/diet impact</b>                                     |                     |         |                  |                      |                        |         |                  |                      |
| Female gender   | -0.589              | -0.257  | -0.953 to -0.225 | 0.002 <sup>a</sup>   | -0.374                 | -0.163  | -0.715 to -0.034 | 0.031 <sup>a</sup>   |
| Age   | 0.025               | 0.313   | 0.013 to 0.038   | < 0.001 <sup>a</sup> | 0.018                  | 0.229   | 0.007 to 0.030   | 0.002 <sup>a</sup>   |
| Severe clinical disease activity                              | -1.301              | -0.330  | -1.911 to -0.691 | < 0.001 <sup>a</sup> | -1.053                 | -0.267  | -1.625 to -0.481 | < 0.001 <sup>a</sup> |
| Dietary restrictions  | -0.696              | -0.294  | -1.069 to -0.324 | < 0.001 <sup>a</sup> | -0.496                 | -0.209  | -0.850 to -0.142 | 0.006 <sup>a</sup>   |
| Disease duration <sup>c</sup>                                 | 0.075               | 0.269   | 0.031 to 0.119   | 0.001 <sup>a</sup>   | NS                     |         |                  |                      |
| Adapted eating behavior                                       | -0.497              | -0.213  | -0.871 to -0.124 | 0.009 <sup>a</sup>   | NS                     |         |                  |                      |
| <b>Social impact</b>  |                     |         |                  |                      |                        |         |                  |                      |
| Age   | 0.01                | 0.142   | -0.001 to 0.02   | 0.086 <sup>b</sup>   |                        |         |                  | NS                   |
| Severe clinical disease activity                              | -1.067              | -0.323  | -1.580 to -0.553 | < 0.001 <sup>a</sup> | -1.062                 | -0.321  | -1.571 to -0.553 | < 0.001 <sup>a</sup> |
| Disease duration <sup>c</sup>                                 | 0.031               | 0.131   | -0.007 to 0.069  | 0.114 <sup>b</sup>   |                        |         |                  | NS                   |
| Number of endoscopic interventions with food bolus extraction | -0.072              | -0.154  | -0.148 to 0.004  | 0.062 <sup>b</sup>   |                        |         |                  | NS                   |
| Adapted eating behavior                                       | -0.218              | -0.111  | -0.537 to 0.101  | 0.179 <sup>b</sup>   |                        |         |                  | NS                   |
| <b>Emotional impact</b>                                       |                     |         |                  |                      |                        |         |                  |                      |
| Female gender   | -0.504              | -0.275  | -0.793 to -0.214 | 0.001 <sup>a</sup>   | -0.446                 | -0.212  | -0.769 to -0.122 | 0.007 <sup>a</sup>   |
| Age   | 0.018               | 0.283   | 0.008 to 0.028   | 0.001 <sup>a</sup>   | 0.016                  | 0.236   | 0.005 to 0.025   | 0.003 <sup>a</sup>   |
| Severe clinical disease activity                              | -0.828              | -0.263  | -1.326 to -0.330 | 0.001 <sup>a</sup>   | -0.604                 | -0.199  | -1.103 to -0.146 | 0.011 <sup>a</sup>   |
| Disease duration <sup>c</sup>                                 | 0.055               | 0.248   | 0.02 to 0.090    | 0.002 <sup>a</sup>   |                        |         |                  | NS                   |
| Adapted eating behavior                                       | -0.232              | -0.125  | -0.535 to 0.071  | 0.132 <sup>b</sup>   |                        |         |                  | NS                   |
| <b>Disease anxiety</b>  |                     |         |                  |                      |                        |         |                  |                      |
| Female gender   | -0.478              | -0.228  | -0.814 to -0.143 | 0.006 <sup>a</sup>   | -0.446                 | -0.212  | -0.769 to -0.122 | 0.007 <sup>a</sup>   |
| Age   | 0.019               | 0.256   | 0.007 to 0.030   | 0.002 <sup>a</sup>   | 0.015                  | 0.204   | 0.003 to 0.027   | 0.001 <sup>a</sup>   |
| Severe clinical disease activity                              | -0.422              | -0.117  | -1.009 to 0.166  | 0.158 <sup>b</sup>   |                        |         |                  | NS                   |
| Disease duration <sup>c</sup>                                 | 0.061               | 0.239   | 0.02 to 0.101    | 0.004 <sup>a</sup>   | 0.044                  | 0.172   | 0.001 to 0.086   | 0.043 <sup>a</sup>   |
| Number of endoscopic interventions with food bolus extraction | -0.060              | -0.117  | -0.143 to 0.023  | 0.157 <sup>b</sup>   | -0.100                 | -0.196  | -0.179 to -0.021 | 0.014 <sup>a</sup>   |
| <b>Swallowing anxiety</b>                                     |                     |         |                  |                      |                        |         |                  |                      |
| Age   | 0.018               | 0.244   | 0.006 to 0.03    | 0.003 <sup>a</sup>   | 0.015                  | 0.186   | 0.002 to 0.025   | 0.02 <sup>a</sup>    |
| Severe clinical disease activity                              | -1.095              | -0.304  | -1.660 to -0.531 | < 0.001 <sup>a</sup> | -0.913                 | -0.253  | -1.477 to -0.350 | 0.002 <sup>a</sup>   |
| Disease duration <sup>c</sup>                                 | 0.038               | 0.148   | -0.004 to 0.079  | 0.074 <sup>b</sup>   |                        |         |                  | NS                   |
| Adapted eating behavior                                       | -0.397              | -0.186  | -0.741 to -0.052 | 0.024 <sup>a</sup>   |                        |         |                  | NS                   |

<sup>a</sup>P-value of < 0.05, indicating a significant outcome.

<sup>b</sup>P-value < 0.2, indicating a possible trend.

<sup>c</sup>Disease duration = measured from year of diagnosis.

EoE-QOL-A, adult eosinophilic esophagitis quality of life questionnaire; B, unstandardized regression coefficient, where 1 point increase in the predictor variable (eg, female gender) is associated with B point(s) increase in the dependent variable (EoE-QOL-A subscale score);  $\beta$ , standardized regression coefficient, where 1 standard deviation increase in the predictor variable (eg, female gender) is associated with  $\beta$  point(s) increase in the dependent variable (EoE-QOL-A subscale score); NS, not significant.

### Disease Specific Health-related Quality of Life and Associated Factors

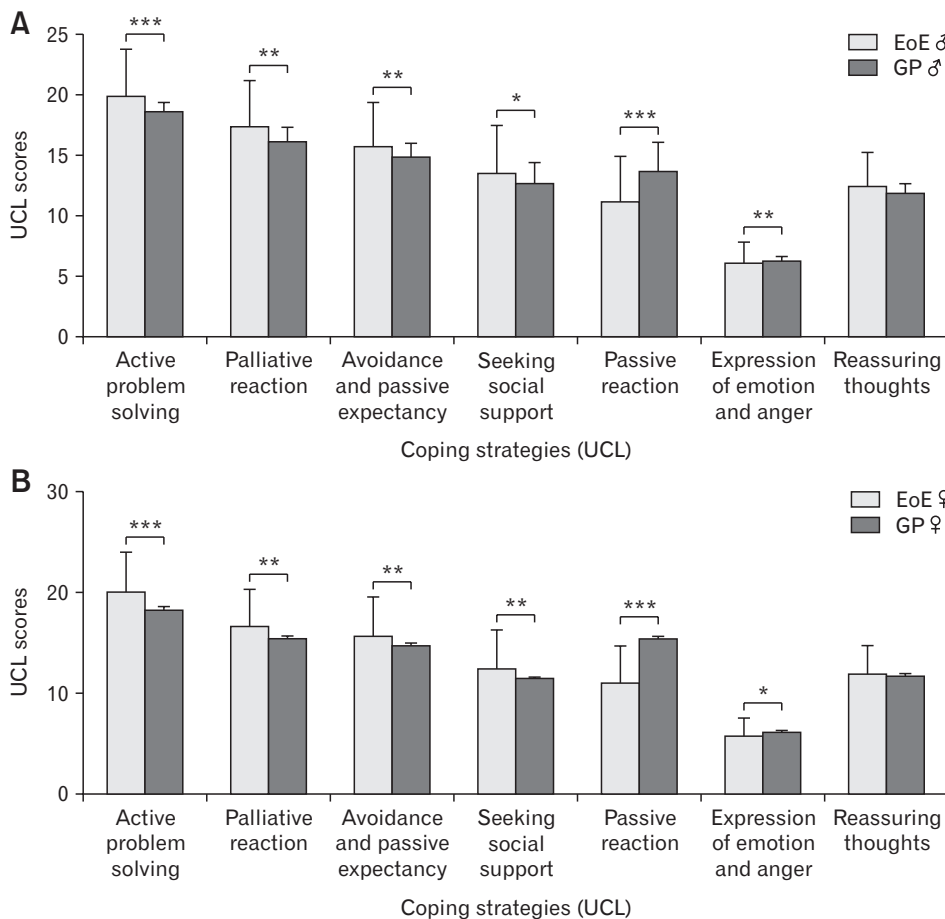
Evaluation of the disease specific impact on psychosocial functioning (EoE-QOL-A) showed an average weighted score of  $2.77 \pm 0.81$  (range, 0.75-4.00) in our EoE cohort, with significant lower levels in females (vs males;  $P = 0.002$ ) (Supplementary Table 3). Lowest subdomain scores in our sample were observed on disease anxiety ( $2.46 \pm 1.03$  [range, 0.20-4.00]) and eating/diet impact ( $2.47 \pm 1.12$  [range, 0.00-4.00]), with lower levels in females on both domains (vs males, all;  $P < 0.01$ ). While emotional impact scores were also significantly lower in females (vs males;  $P = 0.001$ ), subdomain scores of social impact and swallowing anxiety were similar (male vs female, all;  $P > 0.05$ ) (Supplementary Table 3).

Multiple linear regression analysis indicated factors including: female gender, younger age, severe clinical disease activity (ie, current symptoms of daily dysphagia and food impaction), and dietary restrictions to be independently associated with impairment of EoE-HRQOL on the “eating/diet” subdomain (Table 2).

Moreover, severe clinical disease activity was only found to be significantly related to low levels of the EoE-HRQOL “social impact” scores. Factors including female gender, younger age, and severe clinical disease activity were all independently associated with lower scores on the EoE-HRQOL “emotional impact” subdomain. In addition, low scores of the EoE-HRQOL “disease anxiety” subdomain were significantly associated with independent predictors, such as: female gender, younger age, more recent EoE-diagnosis, and a higher number of endoscopic food bolus extractions. Finally, younger age and severe clinical disease activity were both indicated as significant determinants for low scores on the EoE-HRQOL “swallowing anxiety” subdomain. More details on univariate and multivariable linear regression analysis of determinant factors for EoE-HRQOL are presented in Table 2.

### Coping Strategies

Coping styles (UCL) of EoE patients showed significantly more active problem solving, palliative reaction, avoidance and passive expectancy as well as seeking social support compared to passive expectancy as well as seeking social support compared to



**Figure 2.** Coping styles of patients with eosinophilic esophagitis (EoE) compared to the Dutch general population (GP), stratified for gender. (A) EoE males vs GP males. (B) EoE females vs GP females. UCL, Utrechtse Coping Lijst. \* $P$ -value of  $< 0.05$ , indicating a significant outcome, \*\* $P$ -value of  $< 0.01$ , \*\*\* $P$ -value of  $< 0.001$ .



the general population (all;  $P < 0.05$ ). Moreover, passive reaction and expression of emotion and anger were significantly less reported in EoE patients (vs general population; all;  $P < 0.01$ ) (Fig. 2A). Male EoE patients showed significantly more active problem solving, palliative reaction, avoidance as well as seeking social support compared to males of the general population (all;  $P < 0.05$ ). Moreover, passive reaction and emotion expressing were significantly less reported in male EoE patients (vs general population; all;  $P < 0.01$ ) (Fig. 2B). Female EoE patients showed more palliative reaction compared to females of the general population ( $P = 0.035$ ), whereas no difference was found for other coping strategies (vs general population; all;  $P > 0.05$ ) (Fig. 2C). Females in our EoE sample showed significantly more palliative reaction and seeking for social support compared to males (all;  $P < 0.01$ ) (Fig. 2C).

### Different Coping Styles in Males and Females Correlated to Perception of High-related Quality of Life

Considering the general differences in coping behaviors between males and females, the relationship between coping strategies and HRQOL were determined for both genders.<sup>23,24</sup> Less effective coping styles, such as; palliative reaction, avoidance, and passive reaction significantly correlated with higher impairment of the MCS of the HRQOL (SF-36), whereas active problem solving was related with better perception of mental HRQOL (SF-36) in male EoE patients (all;  $P < 0.05$ ) (Supplementary Table 4A). A passive coping style was significantly correlated with lower levels of the MCS in female EoE patients, whereas active problem solving also correlated with improvement of mental HRQOL.

**Table 3A.** Correlations Between Coping Styles and Disease Specific Health Related Quality of Life in Male Eosinophilic Esophagitis Patients

| Coping strategies (UCL)<br>N = 89 | Disease specific quality of life (EoE-HRQOL-A) |                      |               |                      |                  |                      |                 |                      |                    |                      |
|-----------------------------------|--|----------------------|---------------|----------------------|------------------|----------------------|-----------------|----------------------|--------------------|----------------------|
|                                   | Eating/diet impact                             |                      | Social impact |                      | Emotional impact |                      | Disease anxiety |                      | Swallowing anxiety |                      |
|                                   | r  | P-value <sup>a</sup> | r             | P-value <sup>a</sup> | r                | P-value <sup>a</sup> | r               | P-value <sup>a</sup> | r                  | P-value <sup>a</sup> |
| Active problem solving            | 0.086  | 0.421                | 0.084         | 0.434                | 0.056            | 0.605                | -0.043          | 0.689                | 0.200              | 0.060                |
| Palliative reaction               | -0.376   | < 0.001 <sup>b</sup> | -0.262        | < 0.01 <sup>c</sup>  | -0.455           | < 0.001 <sup>b</sup> | -0.451          | < 0.001 <sup>b</sup> | -0.332             | < 0.001 <sup>b</sup> |
| Avoidance and passive expectancy  | -0.117   | 0.275                | -0.221        | 0.037                | -0.148           | 0.167                | -0.133          | 0.214                | -0.152             | 0.155                |
| Seeking social support            | -0.026   | 0.806                | 0.023         | 0.832                | -0.071           | 0.509                | -0.102          | 0.341                | 0.000              | 1.000                |
| Passive reaction                  | -0.468   | < 0.001 <sup>b</sup> | -0.264        | < 0.01 <sup>c</sup>  | -0.355           | < 0.001 <sup>b</sup> | -0.372          | < 0.001 <sup>b</sup> | -0.464             | < 0.001 <sup>b</sup> |
| Expression of emotion and anger   | -0.182   | 0.087                | -0.126        | 0.239                | -0.184           | 0.085                | -0.188          | 0.078                | -0.213             | 0.045                |
| Reassuring thoughts               | -0.089   | 0.407                | -0.097        | 0.365                | -0.216           | 0.042                | -0.254          | 0.016                | -0.130             | 0.223                |

<sup>a</sup>P-value correlation between Utrecht Coping List (UCL) domains and adult eosinophilic esophagitis health-related quality of life questionnaire (EoE-HRQOL-A) domains (Pearson's or Spearman's rank correlation coefficients, as appropriate).

<sup>b</sup>P-value < 0.001.

<sup>c</sup>P-value of < 0.01, indicating a significant outcome.

**Table 3B.** Correlations Between Coping Styles and Disease Specific Health Related Quality of Life in Female Eosinophilic Esophagitis Patients

| Coping strategies (UCL)<br>N = 56 | Disease specific quality of life (EoE-HRQOL-A) |                      |               |                      |                  |                      |                 |                      |                    |                      |
|-----------------------------------|--|----------------------|---------------|----------------------|------------------|----------------------|-----------------|----------------------|--------------------|----------------------|
|                                   | Eating/diet impact                             |                      | Social impact |                      | Emotional impact |                      | Disease anxiety |                      | Swallowing anxiety |                      |
|                                   | r  | P-value <sup>a</sup> | r             | P-value <sup>a</sup> | r                | P-value <sup>a</sup> | r               | P-value <sup>a</sup> | r                  | P-value <sup>a</sup> |
| Active problem solving            | 0.079  | 0.561                | 0.02          | 0.884                | 0.205            | 0.130                | 0.146           | 0.283                | -0.017             | 0.899                |
| Palliative reaction               | -0.080   | 0.559                | -0.187        | 0.167                | -0.228           | 0.092                | -0.127          | 0.352                | -0.188             | 0.165                |
| Avoidance and passive expectancy  | -0.012   | 0.931                | -0.240        | 0.075                | -0.092           | 0.500                | -0.108          | 0.428                | -0.225             | 0.095                |
| Seeking social support            | 0.022  | 0.872                | -0.016        | 0.906                | -0.110           | 0.418                | -0.210          | 0.120                | -0.092             | 0.501                |
| Passive reaction                  | -0.286   | 0.033                | -0.312        | 0.019                | -0.498           | < 0.001 <sup>b</sup> | -0.491          | < 0.001 <sup>b</sup> | -0.288             | 0.031                |
| Expression of emotion and anger   | -0.086   | 0.529                | -0.051        | 0.710                | -0.225           | 0.096                | -0.281          | 0.036                | -0.124             | 0.361                |
| Reassuring thoughts               | -0.137   | 0.314                | -0.158        | 0.244                | -0.255           | 0.058                | -0.207          | 0.126                | -0.243             | 0.071                |

<sup>a</sup>P-value correlation between Utrecht Coping List (UCL) domains and adult eosinophilic esophagitis health-related quality of life questionnaire (EoE-HRQOL-A) domains (Pearson's or Spearman's rank correlation coefficients, as appropriate).

<sup>b</sup>P-value < 0.001.

(SF-36) (all;  $P < 0.05$ ) (Supplementary Table 4B). With regards to disease specific HRQOL (EoE-QOL-A), both palliative and passive coping styles were associated with a significant impact on each individual EoE-HRQOL subdomain in male EoE patients (all;  $P < 0.01$ ) (Table 3A). Additionally, passive reaction significantly correlated with more impairment of the subdomains “emotional impact” and “disease anxiety” in female EoE patients (all;  $P < 0.05$ ) (Table 3B).

## Discussion

This is the first study evaluating coping strategies and the degree to which different coping styles are related to (disease specific) HRQOL in adult EoE patients. Mental (SF-36) HRQOL was significantly affected in our EoE cohort in comparison to the general population norms. These observations are in line with a study by van Hewett et al,<sup>39</sup> also reporting lower MCS scores in EoE patients compared to sex and age matched controls. Moreover, disease specific HRQOL (EoE-QOL-A) subdomains; “disease anxiety” and “eating/diet impact” were mostly affected. Our data show that less effective coping styles, such as passive and palliative reactions were associated with a significant impact on each individual EoE-HRQOL subdomain as well as lower scores of the MCS in male EoE patients. Passive reaction in female EoE patients correlated with impairment of the EoE-HRQOL domains “emotional impact” and “disease anxiety.” Active problem solving was significantly related to better perception of mental HRQOL in both genders. Overall, determinants such as severe clinical disease activity (ie, daily dysphagia and food impaction), younger age, and female gender were associated with impairment of EoE-HRQOL on most of the subdomains.

The subdomain “eating/diet impact” of the EoE-HRQOL being mostly affected within our cohort supports also the former illustrated impact of dietary restrictions on patients’ disease specific HRQOL.<sup>18</sup> We observed that total EoE-HRQOL and most subdomain scores were significantly lower in females compared to males (Supplementary Table 3). HRQOL related gender disparities are well-described in literature, with female gender being associated with poor HRQOL outcomes in multiple chronic health populations (eg, rheumatoid arthritis and Asthma).<sup>40-42</sup> Within our sample, the subdomains “social impact” and “swallowing anxiety” did not differ between both genders. Factors such as severe clinical disease activity and younger age were independently associated with impaired EoE-HRQOL in these 2 domains. This may be further supported by previous findings in adult EoE patients of males be-

ing more prone to stricture development, strong correlates between clinical disease activity and anxiety symptoms as well as a 3-fold risk of significant anxiety symptoms in young adulthood (18-35 years).<sup>13,43</sup> In fact, EoE patients generally display avoidance behaviors in social situations due to symptoms of food impaction with subsequent swallowing anxiety and fear of giving others the impression of a state of illness.<sup>44</sup> Hence, social situations leads to stress, anxiety symptoms and embarrassment. Of note, also MCS scores were significantly lower only in EoE male patients compared to males of the general population (with no difference for females) (Fig. 1B). Taken together, particularly (young) males that are diagnosed with EoE may be more at risk of impaired HRQOL, specifically related to food impaction. In addition to this, a recent study by Taft et al<sup>45</sup> observed that many EoE patients have elevated hypervigilance (ie, heightened focus on physical symptoms) and symptom specific anxiety such as swallowing anxiety, both being associated with worst reported EoE symptoms and poor HRQOL. These observations in mental health research emphasizes the importance of understanding the psychosocial issues being faced by EoE patients in clinical practice.

The subdomain “disease anxiety” was the most affected in our cohort, with stress and anxiety related to “having a chronic condition” being independently associated with factors such as female gender, younger age, severe clinical disease activity, higher number of endoscopic interventions with food bolus extraction, and a more recent EoE-diagnosis (Table 3). In particular, a more recent diagnosis of EoE being predictive of poor EoE-HRQOL seems to be in line with findings in the broader fields of IBD-research, with recently diagnosed patients’ having lower perception of disease specific HRQOL and greatest need of education and support.<sup>46,47</sup> Moreover, disease-related knowledge levels in IBD-patients are known to affect self-management (ie, managing oneself) and the ability to adapt mechanisms to manage the burden of having a chronic illness (ie, coping strategies).<sup>48</sup> Therefore, specifically, patients’ education needs to be indicated as highly relevant for EoE-practice, since this relatively new disease still yields a scarcity of patients’ information-resources.

According to the well-described Common-Sense Model (CSM) of self-regulation and health, HRQOL is suggested to be affected by 2 major determinants: illness perception and coping strategies.<sup>49</sup> The CSM postulates that coping strategies affects adjustment to an illness as indicated, eg, by physical, mental, and social well-being.<sup>50</sup> Females are known to differently cope compared to males.<sup>21</sup> In general, females tend to use coping strategies that are aimed to change their emotional response to a stressful situation,



whereas males use more problem-focused methods for stress management.<sup>23,24</sup> Apart from the well-described association between female gender and seeking more social support as coping style, we observed also females using more palliative coping compared to males in our EoE cohort (Fig. 2C). Interestingly, the use of less effective coping styles, such as passive and palliative reaction in male EoE patients was significantly associated with impaired perception of EoE-HRQOL on all 5 subdomains as well as lower perception of mental HRQOL. Additionally, passive reaction in females also significantly correlated with impairment of the EoE-HRQOL domains “emotional impact” and “disease anxiety” and lower scores of the MCS (Table 3 and Supplementary Table 4). As illustrated by the CSM, it may be suggested that adapting these negative behavioral strategies into more effective coping mechanisms will effectively influence patients’ perception of EoE-HRQOL. This is also further supported by our observation on active problem solving being significantly related to better perception of mental HRQOL in both genders (Supplementary Table 4). Hence awareness (ie, recognition and understanding) amongst gastroenterologists and allergists on the use of less effective coping strategies in adult EoE patients should be increased in daily practice. More importantly, when inadequate styles are identified, referral to a medical psychologist/psychotherapist for cognitive behavioral therapy in order to support self-management may be helpful to adapt these coping strategies and improve EoE patients’ perception of HRQOL.<sup>51</sup>

The study design has a few limitations that should be addressed. First, our observations are extracted from a large EoE sample of patients visiting the outpatient clinic of a tertiary health-care center, thus limiting its generalizability. However, it should be noted that our cohort, although not population-based actually reflects a diversified population, including different stages of disease severity and treatment. Secondly, we did not assess patients’ illness perception (ie, individual’s beliefs and feelings about their disease). According to the CSM, cognitive and emotional illness perception also impacts directly or indirectly through influence on coping mechanisms on patients’ HRQOL.<sup>50</sup> In a previous validation study of the EoE-QOL-A measure, HRQOL was linked to illness perception in adult EoE patients.<sup>52</sup> Therefore, the evaluation of illness beliefs amongst adult EoE patients, specifically related to HRQOL and coping styles may be implicated for future research. Nevertheless, we believe that this is the first study with specific interest of determining coping strategies in adult EoE patients and the degree to which different coping styles are related to (disease specific) HRQOL. Aside from the large sample size, also the use

of multiple (validated) health outcome measures may be considered as another strength of our design.

In summary, our study confirms that EoE has a significant negative impact on mental HRQOL in adult EoE patients. Less effective coping strategies are related to poor perception of general and disease specific HRQOL, particularly in males. This study emphasizes the importance of HRQOL being a key health outcome in daily EoE practice and research evaluation effect of interventions. Therefore, a pro-active approach towards coping mechanisms and provision of sufficient mental care is needed to support adjustment to living with a chronic illness, and ultimately enhance EoE patients HRQOL.

## Supplementary Materials

Note: To access the supplementary tables mentioned in this article, visit the online version of *Journal of Neurogastroenterology and Motility* at <http://www.jnmjournal.org/>, and at <https://doi.org/10.5056/jnm21143>.

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