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5 **Dilation modifies association between symptoms and esophageal eosinophilia in adult**

6 **patients with eosinophilic esophagitis**

7 **Short title:** modifying effect of dilation on association between symptoms and esophageal

8 eosinophilia

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35   **Abbreviations:** Adj., adjusted; CI, confidence interval; DSQ, dysphagia symptom score;

36   EEsAI, eosinophilic esophagitis activity index; eos/hpf, peak esophageal eosinophil counts

37   per high-power filed; EREFS, endoscopic reference score; IQR, interquartile range; PRO

38   patient-reported outcomes.

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59   8, 9.

60   **ABSTRACT**

61   **Background and aims:** We investigated whether dilation modifies the association between

62   symptoms and esophageal eosinophilia (eos/hpf) in eosinophilic esophagitis (EoE) patients

63   enrolled into randomized trial comparing efficacy of budesonide and fluticasone.

64   **Methods:** Baseline DSQ and EEsAI were available in 102 and 73 patients, respectively, of

65   whom 56 and 39 underwent dilation at screening endoscopy before symptom assessment.

66   The pair-wise relationship between DSQ, EEsAI, and eos/hpf was analyzed with

67   nonparametric correlations.

68   **Results:** In non-dilated patients, the association between baseline eos/hpf and symptoms

69   was moderate and significant, whilst it was abolished in dilated patients.

70   **Conclusion:** Dilation modifies association between symptoms and eos/hpf. (clinicaltrials.gov

71   NCT02019758)

72   Word count: 100

73   **Key words:** eosinophilic esophagitis; dysphagia, dysphagia symptom questionnaire;

74   eosinophilic esophagitis activity index; esophageal eosinophilia; correlation.

75

76 **INTRODUCTION**

77 Esophageal dilation is used to manage adults with eosinophilic esophagitis (EoE).[1,2,3,4] Using

78 a non-validated dysphagia measure in patients managed with dilation alone, Schoepfer *et al.*

79 observed a median post-dilation dysphagia improvement lasting ≥12 months.[5] To date,

80 dilation effect on symptoms has not been evaluated by patient-reported outcomes (PROs),

81 including Dysphagia Symptom Questionnaire (DSQ) and Eosinophilic Esophagitis Activity

82 Index (EEsAI).

83 We investigated whether dilation modifies the association between symptoms assessed

84 using validated PROs and esophageal eosinophilia in EoE adults enrolled into a randomized

85 trial comparing budesonide and fluticasone (NCT02019758).[6]

86

87 **METHODS**

88 Dilation was allowed during the screening endoscopy before symptom assessment at

89 baseline. The pair-wise relationship between DSQ (0 to 84; 24-hour recall), EEsAI (0 to 100;

90 7-day recall), EoE Endoscopic Reference Score (EREFS), and peak esophageal

91 eosinophils/high-power field (eos/hpf) was analyzed with nonparametric correlations.[7,8,9,10,11]

92 We used linear regression with eos/hpf as the outcome, EEsAI and DSQ as predictors, and

93 an interaction for dilation and symptoms (see Supplementary Materials).

94

95 **RESULTS**

96 Of the 111 trial patients, 102 patients completed DSQ ≥4 days over 7-day period at baseline

97 and 73 patients completed EEsAI (**Suppl.Figure 1**). At baseline, DSQ, EREFS, and eos/hpf

98 were similar between the two groups (**Suppl.Table 1**).

99 When assessing the relationship between DSQ, DSQ subscales, maximum dysphagia

100 days/week, and eos/hpf at baseline (n=102) (**Figure 1**, **Suppl.Table 2**), we observed weak

101 associations between eos/hpf and dysphagia symptoms. We observed moderate

102 associations between the eos/hpf and dysphagia symptoms in non-dilated patients and no

103 association between these in dilated patients. When examining the association between

104   changes from baseline to end of treatment (EOT) in eos/hpf and DSQ (n=79), trends were

105   similar.

106   When analyzing subjects completing DSQ and EEsAI at baseline (n=73) (**Figure 2**,

107   **Suppl.Table 2**, **Suppl.Figure 2**), we observed moderate to strong associations between

108   DSQ and EEsAI scores regardless of dilation status. Irrespective of PRO used, we observed

109   moderate correlations between symptoms and eos/hpf in non-dilated patients and no

110   association in dilated patients.

111   For a 10-unit DSQ increase in non-dilated patients, the predicted log-transformed eos/hpf

112   increased by 27.1% (p-value=0.016) (**Suppl.Table 3**). For a 10-unit DSQ increase in dilated

113   patients, the predicted eos/hpf decreased by 7.7% (p-value=0.398). When assessing the

114   association between change in symptoms and eos/hpf from baseline to EOT (**Suppl.Table 4;**

115   positive coefficient indicates PRO improvement or inflammation reduction), we found that

116   predicted eos/hpf improves by 21 cells per 10-point DSQ improvement in non-dilated patients

117   (p-value=0.016). In dilated patients, predicted eos/hpf decreased by 4 cells per 10-point DSQ

118   improvement (p-value=0.511). The trends for DSQ subcomponents were similar.

119   The relationship between baseline dysphagia and predicted eos/hpf, and between change

120   from baseline to EOT in dysphagia and predicted eos/hpf, is illustrated in **Figure 3**. Single

121   variable linear regression analyses for non-dilated patients (46/102) at baseline and (32/79)

122   at EOT are in **Suppl.Table 5**.

123   We observed no associations between PROs and EREFS at baseline and for changes in

124   EREFS and PRO from baseline to EOT regardless of dilation status.

125

126   **DISCUSSION**

127   Dilation performed before symptom assessment modifies the associations between baseline

128   eos/hpf and symptom severity and between the change from baseline to EOT in these

129   parameters. In non-dilated patients, the association between esophageal eosinophilia and

130   symptom severity is moderate, and it is abolished in dilated patients.

131   The dilation effects likely last ~12 months.[5] These findings are corroborated in a

132   multicenter observational adult cohort, in which no association between symptom and

133   eos/hpf in dilated patients and a moderate association in non-dilated patients was found.[12]

134   These are *post-hoc* analyses; hence, our findings should be regarded as observational.

135   The interaction term between EEsAI-assessed symptoms and dilation was not significant in

136   the 73-patient subset. The study limitations are countered by sound methodology and the

137   fact that data come from a small, rigorously conducted RCT, during which validated

138   endpoints were used.

139   Dilation modifies the association between eos/hpf and symptom severity. Consideration

140   should be given to stratified randomization on dilation status at baseline in studies assessing

141   efficacy of anti-inflammatory therapies in EoE patients, and monitoring symptoms only as a

142   treatment outcome should be discouraged after dilation in the clinical setting.[13,14]

143

144 **SUPPLEMENTARY TABLES**

145 **Supplementary Table 1:** Patient characteristics at baseline.

Characteristics	Median, IQR, range or Frequency (%) n=102 (DSQ group)	Median, IQR, range or Frequency (%) n=73 (DSQ + EEsAI group)
Age	39 (IQR [26, 51], range 16– 73)	41 (IQR [28, 52], range 17– 73)
Male	68 (67)	53 (73)
White	98 (96)	71 (97)
Any atopic conditions	77 (75)	55 (75)
Length of dysphagia prior to diagnosis (years)	8 (IQR [4, 14], range 0-49)	8 (IQR [4, 15], range 0-38)
Maximum dysphagia days	3 (IQR [1.0, 5.6], range 0 – 7)	3 (IQR [0, 5.6], range 0 – 7)
DSQ score	6.00 (IQR [1.08, 14], range 0 - 42)	5.83 (IQR [1, 16], range 0 - 42)
EEsAI PRO	39 (IQR [15, 50], range 0 - 83) (n=73)	39 (IQR [15, 50], range 0 - 83)
Eos/hpf	60 (IQR [35, 100], range 15 – 320)	60 (IQR [35, 100], range 15 – 230)
EREFS	5 (IQR [3, 6], range 0 – 8)	5 (IQR [3, 6], range 0 – 8)
Dilation required at baseline	56 (55%)	39(53%)

146 **Abbreviations:** DSQ, dysphagia symptom questionnaire; EEsAI, eosinophilic esophagitis activity index; esophageal
147 eosinophilia per high-power field (eos/hpf); EREFS, endoscopic reference score; IQR, interquartile range.

148

149 **Supplementary Table 2.** The Spearman's correlations (Rho) between dysphagia assessed using
150 DSQ and esophageal eosinophilia at baseline, between changes from baseline to end of treatment in
151 dysphagia assessed in DSQ and esophageal eosinophilia, dysphagia assessed using EEsAI PRO and
152 DSQ, as well as between dysphagia measures and esophageal eosinophilia at baseline. We applied
153 the following definitions to interpret the Spearman's correlation coefficient: ≤0.3, weak; >0.3-<0.7
154 moderate; ≥0.7, strong relationship.

DSQ only	All		Non-dilated		Dilated	
Baseline	**Rho**	**p-value**	**Rho**	**p-value**	**Rho**	**p-value**
Eos/hpf vs. PRO	**n=102**		**n=46**		**n=56**	
Eos/hpf vs. dysphagia days	0.216	0.030	0.477	0.001	0.029	0.831
Eos/hpf vs. DSQ score	0.167	0.094	0.448	0.002	-0.035	0.797
Eos/hpf vs. Dysphagia frequency	0.185	0.062	0.432	0.003	0.005	0.969
Eos/hpf vs. Strategy of dealing with dysphagia	0.160	0.109	0.433	0.003	-0.021	0.876
Change from baseline to end of treatment	**Rho**	**p-value**	**Rho**	**p-value**	**Rho**	**p-value**
ΔEos/hpf vs. ΔPRO	**n=79**		**n=32**		**n=47**	
ΔEos/hpf vs. Δdysphagia days (n=72/28/44)	0.060	0.617	0.231	0.237	0.001	0.997
ΔEos/hpf vs. ΔDSQ score	0.095	0.406	0.380	0.032	-0.039	0.793
ΔEos/hpf vs. ΔDysphagia frequency	0.071	0.533	0.362	0.042	-0.078	0.602
ΔEos/hpf vs. ΔStrategy of dealing with dysphagia	0.081	0.478	0.337	0.059	-0.074	0.623
DSQ and EEsAI Baseline	**Rho**	**p-value**	**Rho**	**p-value**	**Rho**	**p-value**
EEsAI vs. DSQ	**n=73**		**n=34**		**n=39**	
Dysphagia frequency DSQ vs. dysphagia days	0.963	<0.001	0.954	<0.001	0.965	<0.001
EEsAI PRO score vs. DSQ score	0.704	<0.001	0.608	<0.001	0.815	<0.001
Dysphagia frequency EEsAI PRO vs. dysphagia frequency DSQ	0.703	<0.001	0.568	<0.001	0.827	<0.001
EEsAI PRO score vs. dysphagia days	0.667	<0.001	0.5057	0.0023	0.820	<0.001
Dysphagia frequency EEsAI PRO vs. dysphagia days	0.660	<0.001	0.5045	0.0023	0.803	<0.001
DSQ and EEsAI Baseline	**Rho**	**p-value**	**Rho**	**p-value**	**Rho**	**p-value**
Eos/hpf vs. PRO	**n=73**		**n=34**		**n=39**	
Eos/hpf vs. dysphagia days	0.262	0.025	0.486	0.004	0.050	0.763
Eos/hpf vs. DSQ score	0.234	0.046	0.423	0.013	0.045	0.784
Eos/hpf vs. EEsAI PRO score	0.205	0.082	0.320	0.066	0.122	0.459

155   **Abbreviations:** DSQ, dysphagia symptom questionnaire; EEsAI, eosinophilic esophagitis activity index; esophageal
156   eosinophilia per high-power field (eos/hpf).

157

158   **Supplementary Table 3.** Linear regression coefficients, 95% confidence intervals, and p-
159   values for four models of natural log-transformed esophageal eosinophilia as outcome in 102
160   patients, in whom the baseline data on all subcomponents of DSQ were available.

	Coefficient [95% CI]	p-value	R[2d]	Constant[c] [95% CI]	% change in eos/hpf for every unit ↑ in symptoms
Model 1: Dysphagia days × Dilation as predictors					
[a]**Dysphagia days (normalized to over 7 days)**	0.119 [0.037, 0.202]	0.005	0.073 [a]	3.780 [3.437, 4.123]	In non-dilated, ↑12.6%
Dilation within 3 months of baseline	0.144 [-0.302, 0.591]	0.522			
Dilation within 3 months of baseline x Dysphagia days	-0.111 [-0.218, 0.003]	0.044			
([b]**Adjusted coefficient for dysphagia days in dilated patients)**	0.009 [0.060, 0.077]	0.796			In dilated, ↑0.9%
Model 2: DSQ score × Dilation as predictors					
[a]**DSQ (per 10-point)**	0.240 [0.045, 0.435]	0.016	0.060 [a]	3.948 [3.671, 4.225]	In non-dilated ↑27.1%
Dilation within 3 months of baseline	0.080 [-0.296, 0.455]	0.674			
Dilation within 3 months of baseline x DSQ	-0.320 [-0.590, 0.050]	0.021			
([b]**Adjusted coefficient for DSQ in dilated patients)**	-0.080 [-0.267, 0.107]	0.398			In dilated, ↓7.7%
Model 3: Dysphagia frequency based on DSQ × Dilation as predictors					
[a]**Dysphagia frequency (DSQ)**	0.065 [0.014, 0.117]	0.014	0.059 [a]	3.887 [3.578, 4.195]	In non-dilated ↑6.7%
Dilation within 3 months of baseline	0.120 [-0.283, 0.524]	0.555			
Dilation within 3 months of baseline x Dysphagia frequency (DSQ)	-0.078 [-0.146, -0.010]	0.025			
([b]**Adjusted coefficient for dysphagia frequency in dilated patients)**	-0.013 [-0.058, 0.031]	0.562			In dilated, ↓1.3%
Model 4: Strategy of dealing with dysphagia (DSQ) × Dilation as predictors					
[a]**Strategy of dealing with dysphagia (DSQ)**	0.043 [0.004, 0.082]	0.032	0.048 [a]	4.019 [3.766, 4.271]	In non-dilated ↑4.4%
Dilation within 3 months of baseline	-0.002 [-0.347, 0.342]	0.990			

Dilation within 3 months of baseline x Strategy of dealing with dysphagia (DSQ)	-0.060 [-0.115, -0.005]	0.033			
(ᵇAdjusted coefficient for Strategy of dealing with dysphagia (DSQ) in dilated patients)	-0.017 [-0.055, 0.022]	0.386			In dilated, ↓1.7%

[a] The coefficient represents the change in the value of the predicted change in natural log-transformed eos/hpf for each category change of the independent variable. For example, for a 10-point increase in the baseline value of DSQ score, the predicted esophageal eosinophilia improved (dropped) by 27.1% in non-dilated patients (e to the power of the coefficient, $e^{0.24}$=1.271, means increase of 27.1%).

[b] Adjusted coefficient for estimating increase in symptom score in dilated patients. For example, for a 10-point improvement in the baseline value of DSQ score, the predicted esophageal eosinophilia deteriorated (increased) by 7.7% in dilated patients (e to the power of the coefficient, $e^{-0.08}$=0.923, 1-0.923, means decrease of 7.7%).

[c] The constant represents the value of the predicted change from baseline to end of treatment in esophageal eosinophilia when all values of independent variables are set to zero or reference category.

[d] The coefficient of determination, R^2 is a measure of the extent to which the regression model describes the observed data. The closer the R^2 is to 1, the more precise the regression model is. Because R^2 can be made artificially high by including a large number of independent variables that have an apparent effect purely by chance, adjusted R^2 for the number of terms included into the model is provided.

[e] The underlying assumption for including continuous variables, such as esophageal eosinophilia, in the linear regression is that the residuals are linear. By log-transforming peak esophageal eosinophilia at baseline, the residuals were more linear and the fit of the model was improved. This kind of transformation is often performed for cell counts in blood.

Abbreviations: Adj., adjusted; CI, confidence interval; DSQ, dysphagia symptom score; EEsAI, eosinophilic esophagitis activity index.

184 **Supplementary Table 4.** Linear regression coefficients, 95% confidence intervals, and p-values for
185 the models of change in esophageal eosinophilia from baseline to end of treatment as outcome in 79
186 patients, in whom the baseline and end of treatment data on all subcomponents of DSQ were
187 available.

	Coeff. [95% CI]	p-value	R[2d]	Constant[c] [95% CI]
Model 1: ΔDysphagia days × Dilation as predictors				
[a]**ΔDysphagia days (normalized to over 7 days) (n=72)**	4.842 [-3.063, 12.749]	0.226	0.041	61.467 [43.828, 79.107]
Dilation within 3 months of baseline	-5.397 [-32.571, 21.777]	0.693		
Dilation within 3 months of baseline x ΔDysphagia days	-5.043 [-14.962, 4.876]	0.314		
([b]Adjusted coefficient for Δdysphagia days in dilated patients)	-0.201 [-6.191, 5.789]	0.947		
Model 2: ΔDSQ score × Dilation as predictors				
[a]**ΔDSQ (per 10 points)**	20.856 [4.069, 37.644]	0.016	0.060	52.733 [34.833, 70.633]
Dilation within 3 months of baseline	4.111 [-21.242, 29.467]	0.748		
Dilation within 3 months of baseline x ΔDSQ	-24.835 [-45.470, -4.200]	0.019		
([b]Adjusted coefficient for ΔDSQ in dilated patients)	-3.979 [-15.978, 8.020]	0.511		
Model 3: ΔDysphagia frequency based on DSQ × Dilation as predictors				
[a]**ΔDysphagia frequency (DSQ)**	4.794 [0.585, 9.004]	0.026	0.059	51.909 [33.577, 70.261]
Dilation within 3 months of baseline	6.433 [-20.606, 33.472]	0.637		
Dilation x ΔDysphagia frequency (DSQ)	-6.034 [-11.272, -0.795]	0.025		
([b]Adjusted coefficient for Δdysphagia frequency in dilated patients)	-1.239 [-4.358, 1.879]	0.431		
Model 4: ΔStrategy of dealing with dysphagia (DSQ) × Dilation as predictors				
[a]**ΔStrategy of dealing with dysphagia (DSQ)**	3.409 [0.465, 6.353]	0.024	0.051	55.932 [38.004, 73.861]
Dilation within 3 months of baseline	1.120 [-23.878, 26.117]	0.929		
Dilation x ΔStrategy of dealing with dysphagia (DSQ)	-4.314 [-7.975, -0.653]	0.022		
([b]Adjusted coefficient for Δstrategy of dealing with dysphagia (DSQ) in dilated	-0.905 [-3.081, 1.271]	0.410		

patients)				

188 [a] The coefficient represents the change in the value of the predicted change in eos/hpf for each
189 category change of the independent variable. For example, for a 10-point improvement in the DSQ
190 score from baseline to end of treatment, the predicted esophageal eosinophilia improved (dropped) by
191 21 cells in non-dilated patients.
192 [b] Adjusted coefficient for estimating increase in symptom score in dilated patients. For example, for a
193 10-point improvement in the DSQ score from baseline to end of treatment, the predicted esophageal
194 eosinophilia deteriorated (increased) by 4 cells in dilated patients.
195 [c] The constant represents the value of the predicted change from baseline to end of treatment in
196 esophageal eosinophilia when all values of independent variables are set to zero or reference
197 category.
198 [d] The coefficient of determination, R^2 is a measure of the extent to which the regression model
199 describes the observed data. The closer the R^2 is to 1, the more precise the regression model is.
200 **Abbreviations:** CI, confidence interval; Coeff., coefficient; Δ, change; DSQ, dysphagia symptom
201 score; EEsAI, eosinophilic esophagitis activity index.

202 **Supplementary Table 5.** Single variable linear regression coefficients, 95% confidence intervals, and p-values for the models of esophageal
203 eosinophilia as outcome in non-dilated patients, in whom data on DSQ (n=46) and on DSQ and EEsAI (n=34) was available and for the models of
204 change in esophageal eosinophilia as outcome in 32 non-dilated patients, in whom all the baseline and end of treatment DSQ data were available.

	Coefficient	95% CI	p-value	R^2	Constant [95% CI]	% change in eos/hpf for every unit ↑ in symptoms
N=46						
Dysphagia days (normalized to over 7 days)	0.120	[0.052, 0.187]	0.001	0.224	3.78 [3.50, 4.06]	12.7%
Per 10-points DSQ score	0.240	[0.077, 0.404]	0.005	0.166	3.95 [3.72, 4.18]	27.1%
Dysphagia frequency (DSQ)	0.065	[0.022, 0.108]	0.004	0.175	3.89 [3.63, 4.14]	6.7%
Strategy of dealing with dysphagia (DSQ)	0.043	[0.010, 0.076]	0.013	0.132	4.02 [3.80, 4.23]	4.4%
n=34						
Per 10-points DSQ score	0.224	[-0.042, 0.407]	0.018	0.164	3.93 [3.66, 4.24]	25.1%
Per 10-points EEsAI (7 days)	0.101	[-0.009, 0.193]	0.033	0.134	3.86 [3.49, 4.24]	10.6%
n=32						
ΔDysphagia days (normalized to over 7 days) (n=28)	4.842	[-3.371, 13.056]	0.236	0.079	61.47 [43.14, 79.79]	NA
ΔDSQ (per 10 points)	20.856	[3.537, 38.175]	0.020	0.135	52.73 [34.27, 71.20]	NA
ΔDysphagia frequency (DSQ)	4.794	[0.451, 9.137]	0.032	0.124	51.91 [32.98, 70.84]	NA

| ΔStrategy of dealing with dysphagia (DSQ) | 3.409 | [0.371, 6.446] | 0.029 | 0.105 | 55.93 [37.44, 74.43] | NA |

205　**Abbreviations:** CI, confidence interval; DSQ, dysphagia symptom score; EEsAI, eosinophilic esophagitis activity index; NA, not applicable.

206   **FIGURES**

207   **Figure 1.** Relationship between baseline DSQ and esophageal eosinophilia in all patients

208   (n=102) (**A**), in patients that did not undergo dilation (n=46) (**B**), and in patients that were

209   dilated (n=56) (**C**) at study baseline. Relationship between change from baseline to end of

210   treatment in DSQ and esophageal eosinophilia in all patients (n=79) (**D**), in patients that did

211   not undergo dilation (n=32) (**E**), and in patients that were dilated (n=47) (**F**) at screening

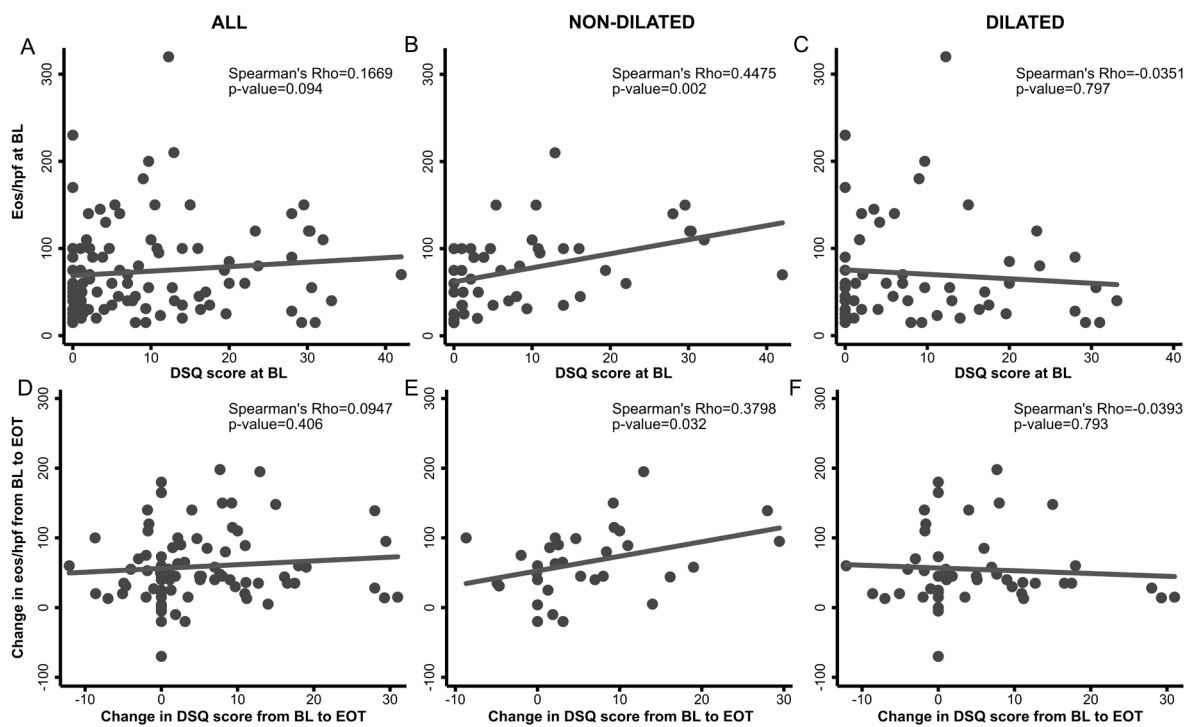212   endoscopy. **Abbreviations:** BL, baseline; DSQ, dysphagia symptom score; EOT (end of

213   treatment).

214

215

216   **Figure 2.** Relationship between baseline DSQ and EEsAI PRO in all patients (n=73) (**A**), in
217   patients that did not undergo dilation (n=34) (**B**), and in patients that were dilated (n=39) (**C**)
218   at study baseline. Relationship between baseline DSQ and esophageal eosinophilia in all
219   patients (**D**), in patients that did not undergo dilation (**E**), and in patients that were dilated (**F**)
220   at screening endoscopy. Relationship between baseline EEsAI PRO and esophageal
221   eosinophilia in all patients (**G**), in patients that did not undergo dilation (**H**), and in patients
222   that were dilated (**I**) at study baseline. **Abbreviations:** DSQ, dysphagia symptom score;
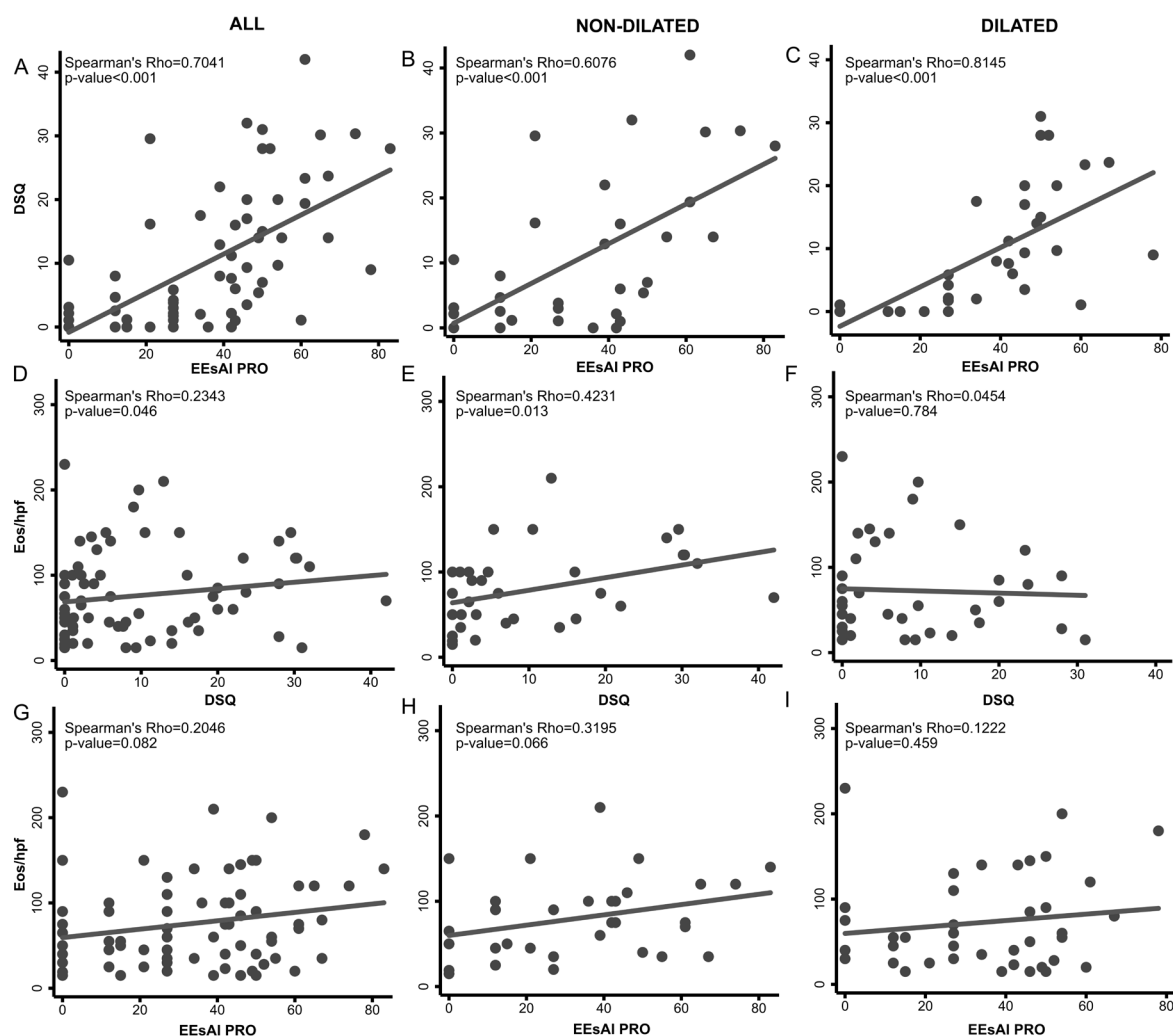223   EEsAI PRO, eosinophilic esophagitis activity index patient-reported outcomes instrument.

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225

226   **Figure 3.** The margin plot of expected esophageal eosinophilia stratified on dilation (n=102)

227   by DSQ (**A**), dysphagia frequency component of DSQ (**B**), and maximum number of

228   dysphagia days per week (**C**) at study baseline. The predictive margins of change from

229   baseline to end of treatment in esophageal eosinophilia stratified on dilation (n=79) by

230   change in DSQ (**D**), by change in dysphagia frequency component of DSQ (**E**), and by

231   change in maximum number of dysphagia days per week (**F**). **Abbreviations:** BL, baseline;

232   DSQ, dysphagia symptom score EOT (end of treatment).

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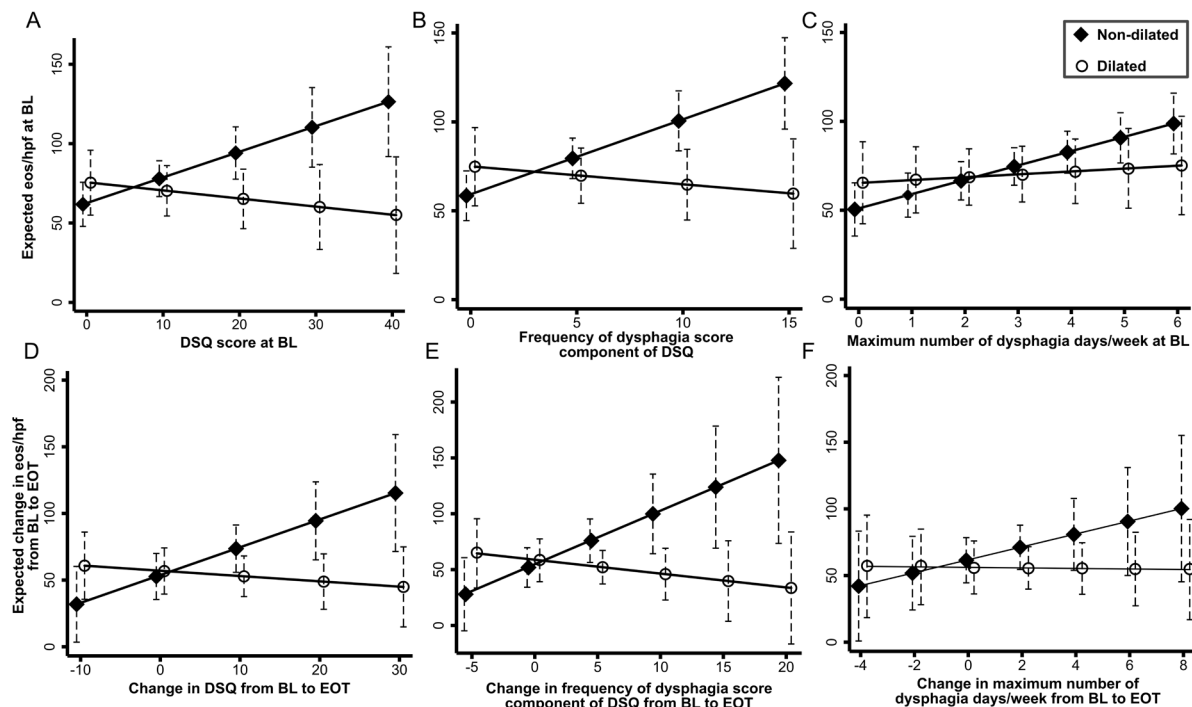
234   [a] (**A**) in non-dilated patients with the DSQ score of 10 and 30 points, predicted values of 77

235   eos/hpf and 110 eos/hpf, respectively, are observed (**A**). In dilated patients with the DSQ

236   score of 10 and 30 points, predicted values of 70 eos/hpf and 60 eos/hpf, respectively, are

237   observed.

238   [b] (**B**) in non-dilated patients with maximum dysphagia days of 2, 4, and 6, predicted values of

239   67, 83, and 99 eos/hpf, respectively, are observed. In dilated patients with maximum

240   dysphagia days of 2, 4, and 6, predicted values of 69, 72, and 75 eos/hpf, respectively, are

241   observed.

242

243   **Supplementary Figure 1.** Flow chart of patient populations. All the patients with complete
244   DSQ (completed for at least 4 days in a seven-day period) and EEsAI PRO subdomains data
245   at baseline and all the patients with complete DSQ at end of treatment were analyzed for the
246   purposes of this study.

247

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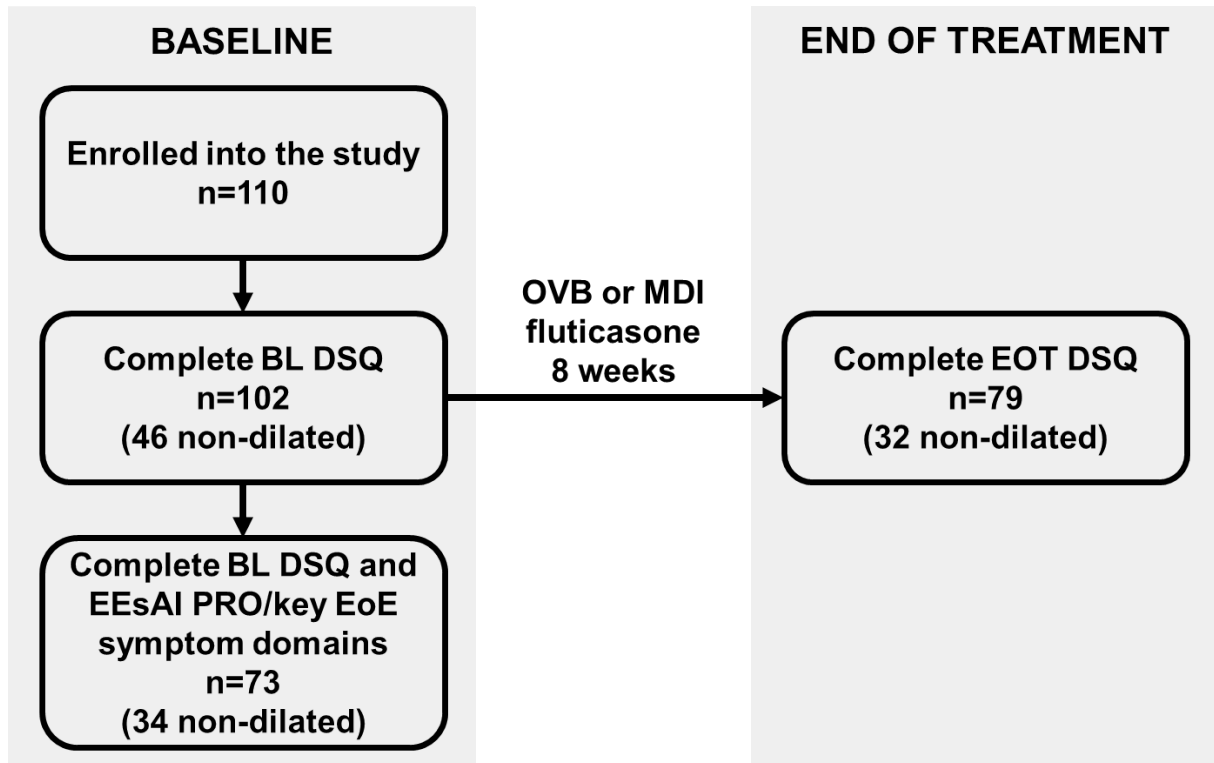
249   **Supplementary Figure 2.** Relationship between maximum dysphagia days (based on DSQ)

250   and the frequency of the trouble swallowing (EEsAI PRO) (**A-C**), as well as between

251   dysphagia frequency score (DSQ) and the frequency of the trouble swallowing (EEsAI PRO)

252   (**D-F**) features. For each distribution, the box spans the values between the quartiles 1 and 3

253   (interquartile range), and the median is marked by horizontal line inside the box. The

254   whiskers extend to the maximum of 1.5× the interquartile range beyond the box boundaries.

255   Data beyond the range of whiskers are outliers and presented as points. In the trend test for

256   each panel, p-values ≥ 0.004 or smaller were observed. **Abbreviations:** DSQ, dysphagia

257   symptom score; EEsAI PRO, eosinophilic esophagitis activity index patient-reported

258   outcomes instrument.

259

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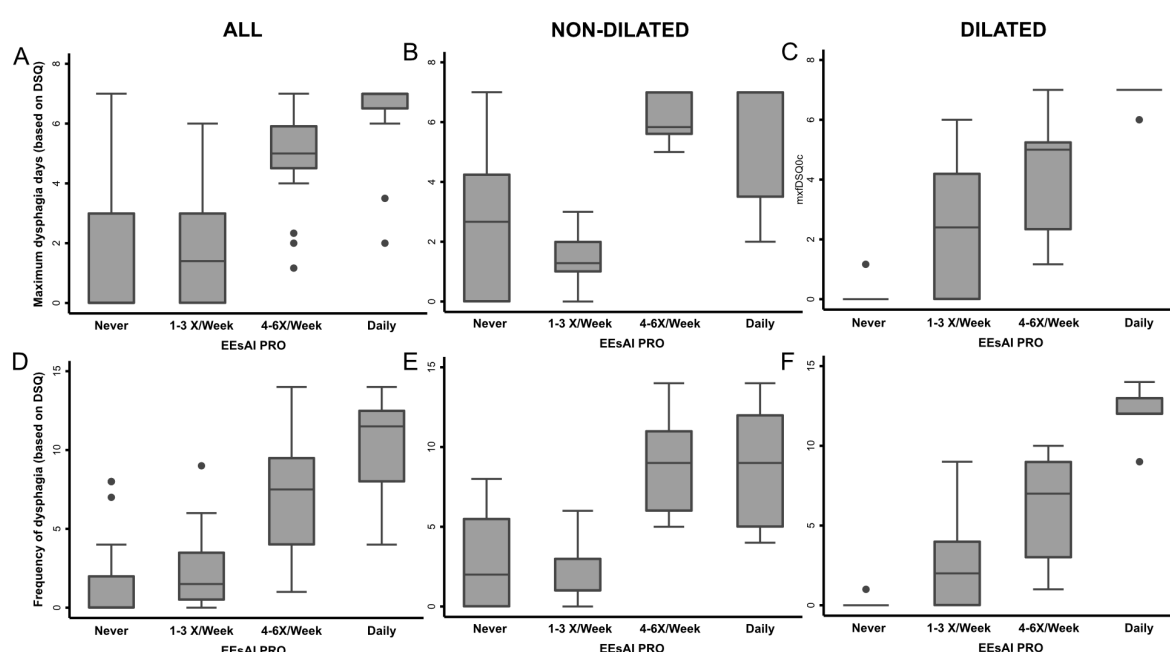
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