**Background**

Eosinophilic esophagitis (EoE) is a chronic, allergy-related disease in which prolonged eosinophil-predominant inflammation can cause tissue remodeling. The remodeling results in serious complications including esophageal rings, strictures, and mucosal fragility, which can cause dysphagia, food impactions, and painful mucosal tears. A feature of the remodeling is the pattern of dense, subepithelial fibrosis in the lamina propria, and it is unclear whether this subepithelial fibrosis is unique to EoE.

**Aims**

The purpose of this study was to determine prevalence and thickness of subepithelial fibrosis in EoE and compare it to other esophageal conditions.

**Methods**

From the archives of a histopathology laboratory, we retrieved esophageal biopsy specimens from randomly selected patients, including 50 with EoE; 50 with esophageal strictures; 25 with reflux esophagitis; and 135 with a normal esophagus. A blinded pathologist reviewed all slides and measured the thickest portion of fibrosis underlying the squamous epithelium (Fig. 1A). Unadjusted odds ratios (OR) and ANOVA were used to compare differences of prevalence and thickness, respectively.

Pursuant to 45 CFR 46, section 101b (4) – the Miraca Life Sciences Research Institute IRB determined this study to be “analysis of deidentified existing records only” and, therefore, exempt from the requirement of informed consent.

**Results**

After excluding cases with technical issues that could affect the evaluation of subepithelial fibrosis, there remained 45 patients with EoE (median age 43 years; 67% male); 48 with esophageal strictures (median age 48 years, 33% male); 23 with reflux esophagitis (median age 53 years, 52% male); and 133 patients with a normal esophageal mucosa (median age 55 years, 41% male). Table 1 shows the OR for having any amount of subepithelial fibrosis in the four groups of patients. The median thickness of fibrosis was 70 microns in patients with EoE and 35 microns in each of the other three groups. There were four patients with fibrosis within the esophageal papillae, all with EoE.

**Conclusion**

Although some fibrosis was detected in specimens from patients with a normal esophagus and other inflammatory conditions, distinct fibrotic areas of greater thickness, in some cases creeping into the papillary pegs, were found in more than 2/3 of EoE patients. These findings, if confirmed in a larger study, suggest that fibrosis in esophageal biopsies might serve as an adjunct criterion for the histopathologic diagnosis of EoE.

**Study Highlights**

- Subepithelial fibrosis is a component of tissue remodeling that is potentially responsible for esophageal rings, furrows, strictures, and other mucosal alterations associated with EoE.
- Subepithelial fibrosis was identified in 68.9 percent of EoE cases studied, which is statistically significantly higher than the normal, gastroesophageal reflux, and stricture groups.
- Further studies of subepithelial fibrosis in these patients may uncover valuable diagnostic and/or prognostic implications in the management of EoE.

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**Table 1** – Esophageal fibrosis in patients with normal, gastroesophageal reflux, eosinophilic esophagitis, and esophageal strictures.

<table>
<thead>
<tr>
<th>Esophageal Biopsy Diagnosis</th>
<th>Total</th>
<th>Total with fibrosis (%)</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>133</td>
<td>23 (17.3)</td>
<td>1</td>
</tr>
<tr>
<td>Reflux</td>
<td>23</td>
<td>7 (30.4)</td>
<td>2.09 (0.77 – 5.66) n.s.</td>
</tr>
<tr>
<td>Stricture</td>
<td>48</td>
<td>12 (25.0)</td>
<td>1.59 (0.72 – 3.52) n.s.</td>
</tr>
<tr>
<td>EoE</td>
<td>45</td>
<td>31 (68.9)</td>
<td>10.59 (4.88 – 22.98) p&lt;.0001</td>
</tr>
</tbody>
</table>

**Figure 1** – Esophageal biopsy specimens with fibrosis. A. Subepithelial Fibrosis (SF) B. Subepithelial (SF) and papillary (*) fibrosis.