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# Endoscopic diagnosis and treatment of inlet patch: Justification, techniques, and results

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ABSTRACT

Esophageal gastric inlet patches (EGIPs) comprise an island of heterotopic gastric columnar epithelium in the cervical esophagus with a reported prevalence of up to 10%. Usually the diagnosis is made by chance in the course of an upper gastrointestinal endoscopy. After histopathologic examination EGIPs can be classified as oxyntic (mucosal glands contain parietal cells), mucoid type (mucosa is composed solely of glands with mucous cells), or mixed type (presence of both: glands with parietal cells and glands of mucous cells). Despite their overall low incidence of clinically relevant conditions, EGIPs seem to be a significant entity. Few individuals with EGIPs report symptoms of globus sensations, dysphagia, hoarseness, or chronic cough that are often misinterpreted as an atypical manifestation of gastro-esophageal reflux disease. It is known that these symptoms significantly compromise the patients' quality of life. Therefore, therapy should be initiated. However, proton pump inhibitors' response seems to be poor in these patients. We were able to show that an interventional ablative endoscopic therapy by argon plasma coagulation can be a safe and effective procedure. However, further researches are required to better understand the clinical significance of EGIPs and their association to symptoms.



## 1. Introduction

Esophageal gastric inlet patches (EGIPs), also referred to as "heterotopic gastric mucosa of the esophagus," "inlet patch," or "cervical inlet patch," commonly comprise an island of heterotopic gastric columnar epithelium in the cervical esophagus. They have a reported prevalence of 1%-10% [1,2]. Although the first description of EGIPs was in the year 1805 [3], still many questions concerning their etiology, pathophysiology of consecutive symptoms, and the necessity of treatment remain unclear.

EGIPs are widely considered to be of congenital nature as they, in theory, originate from a misplacement or sequestration of the endoderm from the gastric anlage in the developing esophagus [4]. However, this theory never has been proven. Recently, it has also been proposed that EGIPs represent an acquired condition [5,6]. In most patients showing this condition, related symptoms are generally not perceived [7], but several patients report symptoms of globus sensations, dysphagia, hoarseness, or chronic cough that are often misinterpreted as atypical manifestations of gastro-esophageal reflux disease (GERD). In very few patients, complicated courses develop because of EGIPs and may lead to a wide clinical spectrum ranging from ulcers, strictures, perforation, or fistulas. Malignant progression of EGIPs is, compared with its high prevalence, an exceedingly rare incident [1]. Published case reports on associated symptoms or diseases that are linked to EGIPs are listed in a chronological order in the Table.

## 2. Diagnosis

The diagnosis of EGIPs is based on endoscopic findings and is confirmed by histopathologic examination. Generally, EGIPs appear as salmon-colored islands that are visible right below the upper esophageal sphincter. In most forms, they can be distinguished macroscopically from the normal gray-white squamous epithelium of the esophagus. However, the number, appearance, configuration, and size, as well as the histologic "composition" of gastric cells, can vary significantly. In Figure 1 endoscopic images of different forms of histopathologically proven EGIPs are shown. Of high interest is the fact that EGIPs are frequently overlooked. There is good evidence that EGIPs are more often identified by endoscopists who pay special attention examining for this disorder in comparison with endoscopists who routinely examine the upper gastrointestinal (GI) tract [8]. Therefore one has to assume that the reported prevalence of EGIPs is usually underestimated. General recommendations to overcome this common misinterpretation of an upper GI endoscopy do not exist but the following 3 courtesies for the endoscopist have to be kept in mind.

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**Table**
Published reports on symptoms or diseases associated with EGIPs in chronological order.

| References | Symptom or disease |
|---|---|
| Bosher and Taylor [35] | Ulceration or stricture |
| Frezza [36] | Adenocarcinoma |
| Libcke [37] | Aspiration |
| Kohler et al [38] | Esophagotracheal fistula |
| Payne-James et al [39] | Nausea |
| Borhan-Manesh and Farnum [40] | Hp infection |
| Buse et al [41] | Esophageal web |
| Bataller et al [27] | Upper GI bleeding |
| Mion et al [42] | High-grade dysplasia in an adenoma |
| Chatelain and Fléjou [43] | Hyperplastic polyp |
| Sánchez-Pernaute et al [44] | Esophageal perforation |
| Macha et al [45] | Extraesophageal GERD |
| Akbayir et al [46] | Laryngopharyngeal reflux |
| Silvers et al [26] | Vocal cord dysfunction |
| Lancaster et al [47] | Globus pharyngeus |
| Satoh et al [48] | Hypopharyngeal squamous cell carcinoma |
| Korkut et al [21] | Esophageal motility disorder |
| di Palmo et al [25] | Laryngospasm |

### 2.1. *Control the quality of every single endoscopist*

Similar to the "adenoma detection rate," which is known to be a key measure of quality in colonoscopy [9], the frequent revision of diagnosed EGIPs compared with the overall count of upper GI endoscopies should be performed. If endoscopists fail to diagnose EGIPs in less than 5%-10% of their upper GI endoscopies, their general performance has to be classified as too superficial and the following points have to be trained.

### 2.2. *Careful extraction of the endoscope*

Endoscopists should generally withdraw the scope slowly through the upper esophageal sphincter. As this procedure usually represents the last step of an upper GI tract endoscopy and propofol administration is mostly already interrupted at this stage, many endoscopists abdicate this step and quickly extract the scope because of patient discomfort. But, especially when investigating patients with atypical GERD symptoms (eg, globus sensations, chronic cough, and laryngitis), it is necessary to search the potential causative EGIP and to additionally inspect the arytenoids and vocal cords [10].

### 2.3. *Routinely use new imaging modalities such as narrow band imaging in the esophagus*

As stated earlier and seen in Figure 1, the macroscopic appearance of EGIPs can vary significantly. They can appear unifocal or multifocal, cystic or solid, round or oval, and they can extend longitudinally or circumferentially with a diameter ranging from 1-50 mm [11]. The surface can be flat, slightly elevated, or depressed. Several endoscopic tools were tested to improve the endoscopic detection rate of mucosal alterations of the esophagus (eg, early neoplastic lesions, Barrett, and EGIPs). One of the most well-known and evaluated features is "narrow band imaging" (NBI). NBI comprises the use of filters to illuminate the target in narrowed red, green, and blue bands of a spectrum. In the esophagus, this results in different images at distinct levels of the mucosa and increases the contrast between the squamous epithelial surface and the submucosal vascular layer. Herewith, the surface of even very small islands of intestinal mucosa appears much more visible to the surrounded gray-white squamous epithelium of the esophagus. This was already demonstrated in various endoscopic studies investigating this matter [12,13]. Another benefit of using NBI is that, in case of detected EGIP, NBI is superior in demonstrating a disorganization of vascular pattern and superficial neoplastic lesion harbored in intestinal metaplasia compared with white light endoscopy [14].

The confirmation of the diagnosis of EGIP is made by histopathology. The histologic appearance of an EGIP is related but not uniform to the mucosa of the gastric cardia, fundus, corpus, or antrum. Biopsies are generally stained with hematoxylin and eosin. Beside the occurrence of metaplasia and dysplasia, EGIPs should be classified as oxyntic when the mucosal glands contain parietal cells, as mucoid type when the mucosa solely comprises glands with mucous cells, or as mixed type where a composition of glands with parietal cells and glands of mucous cells is detected. In most reports, a mixed-type mucosa was found predominantly [7]; however, there are several studies where predominantly parietal cells were identified [15], as well as studies where predominantly mucous-producing cells were seen [16]. We assume, that these conflicts mainly might be explained by sampling errors or a certain interobserver variability of the pathologist. Prospective multicenter trials with blinded pathologist should highlight this issue in the future.

## 3. Symptoms

Almost every carrier of EGIP is asymptomatic and the diagnosis is made by chance in the course of an upper GI endoscopy. Nevertheless, EGIPs can be responsible for local mucosal alterations (eg, strictures, ulcers, fistula, and neoplasia), thereby causing local symptoms such as pain or dysphagia. There is also evidence that EGIPs without any further pathologic mucosal abnormality may result in exacerbation of symptoms like globus sensations, chronic cough, laryngitis, or other oropharyngeal symptoms [16-18]. Those symptoms are often thought to be related to extraesophageal manifestations of GERD. However, studies investigating this association or separation are conflicting. There is evidence that GERD (most likely nonerosive reflux disease) is responsible for globus sensations [19], but it has also been reported that antireflux therapy has only a limited effect on extraesophageal symptoms [20].

The pathophysiology of the onset of symptoms is unclear. It seems to be self-evident that potent gastric cells in the cervical esophagus may cause symptoms because of the production of acid, mucous, or both, depending on the composition of the different types of gastric cells. This theory was supported by studies applying functional testing of the esophagus, including manometry and pH-metry [21,22], but the question rises, why oropharyngeal symptoms, which are linked to EGIPs, occur only in comparably few patients. Another unclear matter is the question why the symptoms in EGIP carriers occur at different ages despite the fact that affected individuals might harbor EGIPs lifelong. We recently hypothesized that EGIPs may develop in a multistep process from occluded esophageal glands in the proximal esophagus, leading to esophageal retention cysts that are internally layered with columnar epithelium, which may finally burst and result in focal areas of heterotopic gastric mucosa [5]. Certainly, further studies investigating EGIP carriers are needed to understand the pathophysiology of the breakout of associated symptoms.

## 4. Therapy

Most EGIP carriers are free of symptoms. Hence, there is no need for further therapy. Furthermore, progression of EGIPs to severe disease (eg, ulceration, fistula, laryngospasm, adenocarcinoma, and perforation) is extremely rare; endoscopic surveillance of EGIPs is therefore not required.