Endoscopic Upper GI Screening

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Keywords

Screening · Endoscopy · Cancer

Abstract

The rationale behind endoscopic screening of the upper gastrointestinal tract (GIT) in the West is different from Asian countries with a high prevalence of gastric cancer. If epidemiological data on upper GIT cancer in the Western world is considered, then endoscopic screening of the upper GIT must target premalignant conditions as well and, furthermore, lay emphasis on the assessment of the entire upper GIT in high-risk individuals from the mouth till the duodenum. Although data on the incidence, prevalence, and further development of premalignant conditions in the upper GIT is lacking, a risk-based approach to endoscopic screening will be more cost-effective than a general screening approach. Finally, endoscopists need to be educated and trained in the assessment of the upper GIT during screening endoscopy.

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Introduction

The endoscopic screening of the upper gastrointestinal tract (GIT) is a controversial topic partly because supporting data is lacking for the Western world, but more importantly because it has been difficult to prove its beneficial effect on mortality. Unlike in the colorectum, it is somewhat unclear what the target screening lesion in the upper GIT should be. The most common opinion would be to screen primarily the stomach for gastric cancer. However, limiting upper GIT screening to the stomach will probably not be cost-effective especially from the perspective of countries with a low gastric cancer prevalence. Far more

efficient may be to involve the entire upper GIT in search of premalignant or early malignant lesions of the mouth, tongue, and hypopharynx as well as the esophagus, stomach, and duodenum including the ampulla of Vater.

In this paper, we will discuss the rationale behind endoscopic upper GIT screening and its possible benefits especially in high-risk groups.

Epidemiology

Although the incidence of stomach cancers is falling, the incidence of malignant lesions in the entire upper GIT including the esophagus, mouth, and larynx has shown a measurable increase in the past decade in Germany (Table 1) [1]. The reason may be partly due to improvements in the diagnostic ability of endoscopists and endoscopic equipment but may also be a real numerical increase in cancer incidence.

Adenocarcinomas of the stomach and the esophagogastric junction belong to tumor entities with the highest cancer-related mortality rates worldwide [2]. Adenocarcinomas of the stomach and the esophagogastric junction have shown an exponential increase in incidence and prevalence rates [3]. Data from the USA demonstrated a 463% rise in the incidence rate of esophageal adenocarcinoma in white male patients. A continuous increase in the incidence rates of esophageal adenocarcinoma is expected till the year 2030 [4]. Furthermore, a shift in tumor location from the distal stomach to more proximal locations in the upper stomach and cardia region has been observed [5, 6].

Upper GIT cancers often become symptomatic in later stages of disease. In Germany, for instance, far less than 10% of the stomach cancers are diagnosed in an early stage of disease (stage I), leading to an overall 5-year sur-

Table 1. Prevalence of cancer in the upper GIT in Germany [1]

	2006	2012
Mouth/hypopharynx	10,860	11,400
Larynx	3,890	4,110
Esophagus	5,190	6,540
Stomach	17,850	15,640
Total upper GIT cancers	37,790	40,220

vival rate for gastric cancer of only 33% [3, 7]. A similar situation holds true for esophageal cancer where only 1 out of 7 cancers is diagnosed in a T1-stage [3]. Therefore, most patients presenting with esophageal and stomach cancers will have a poor prognosis due to late-stage diagnosis [8].

Risk-Based Screening

Premalignant lesions in the stomach include not just adenomas or dysplastic polyps but also severe atrophic gastritis, intestinal metaplasia, as well as Barrett's esophagus. All these conditions can have a substantial risk of cancer development. In the West, a risk-based screening approach may make endoscopic upper GIT screening appear in a different – less controversial – light.

Identification of cohorts with a substantial risk of upper GIT cancer and then targeting such individuals for screening is a central point when discussing upper GIT screening. For example, the most common risk factors identified as having a strong association with gastric cancer include a positive family history, *Helicobacter pylori* infection, alcohol and nicotine consume, intestinal metaplasia, and severe atrophic gastritis [9]. In addition, the incidence of gastric cancer increases significantly between the ages of 55 and 60 years.

Precancerous and premalignant lesions of the stomach include conditions associated with chronic inflammation such as *H. pylori* infection. A recent study from Korea showed that *H. pylori* eradication significantly reduces the risk of de novo gastric cancer [10].

The most important risk factors for the development of esophageal squamous cell cancer are nicotine and alcohol consume, while esophageal adenocarcinoma is more commonly associated with long-standing reflux disease, obesity, and nicotine consume [11]. Furthermore, about 90% of the esophageal adenocarcinomas are associated with Barrett's esophagus, and the development of Barrett's esophagus seems to be directly correlated to the duration of reflux disease [12].

However, it remains unclear how environmental and patient-related factors interact during the development

of esophageal and stomach cancer [11]. For instance, it is unclear why certain patients develop Barrett's esophagus and others do not although both groups may have been exposed to similar environmental conditions. Detailed knowledge of biological and pathophysiological processes associated with carcinogenesis as well as risk factors that trigger these pathways is the prerequisite to improving the detection, screening, surveillance, and therapy of upper GIT cancers.

The so-called gastric precancerous cascade described by Correa includes chronic inflammation, atrophic change, intestinal metaplasia, dysplasia, and cancer [13]. Possible target lesions for upper GIT screening endoscopy could be precancerous lesions such as atrophy and intestinal metaplasia – and not only cancerous lesions as is usually the assumption when discussing upper GIT screening. However, epidemiologic data regarding the prevalence and incidence of precancerous upper GIT lesions is lacking. In one such study on participants who presented for screening colonoscopy and also underwent upper GIT endoscopy, about 9,3% had a premalignant condition such as severe atrophic gastritis or intestinal metaplasia [14]. Nevertheless, for accurate cost-effectivity models, more data on premalignant conditions in asymptomatic individuals need to be collected and assessed, including long-term follow-up data on surveillance examinations of such individuals.

Although recommendations for the surveillance of patients with premalignant changes such as Barrett's esophagus or severe corpus-dominant atrophy exist, [15] these surveillance measures can only be initiated after a diagnosis has been made. This seems contradictory, since the risk of cancer development is the reason for surveillance in high-risk patients. However, primary screening to identify such high-risk individuals is not recommended.

Endoscopy

Considering the low incidence of gastric cancer in the West, target lesions of upper GIT screening must include precancerous lesions in all sections of the upper GIT, including the mouth, hypopharynx, larynx, esophagus, cardia, stomach, duodenum, and ampulla of Vater. Technological advancements in endoscopic equipment could lead to an improved detection and diagnosis of premalignant and early malignant lesions. However, endoscopists performing upper GIT screening must be trained to observe and recognize premalignant and subtle early lesions (Fig. 1–4).

An endoscopic examination of the upper GI tract should always start in the oral cavity with special focus on the ventral side of the tongue, oropharynx, as well as hypopharynx regions. Special attention should be given to

Fig. 1. Endoscopic white-light view with widespread intestinal metaplasia and an early gastric cancer at the anterior wall of the gastric antrum.

Fig. 2. Acetic-acid staining with excellent demarcation of a small early gastric cancer lesion at the anterior wall of the gastric antrum.

Fig. 3. Indigocarmine chromoendoscopy with excellent demarcation of a small early gastric cancer lesion at the anterior wall of the gastric antrum.

Fig. 4. Endoscopic white-light magnification view of an early gastric cancer lesion.

patients with an increased risk for cancers of the head and neck region, especially those who smoke or have an increased alcohol consume.

In the oropharynx, image-enhanced endoscopy such as narrow-band imaging may facilitate the detection of small squamous cell cancers that appear brownish. In the hypopharynx, a simple Valsalva maneuver can be used to improve visualization of the posterior wall. However, this is only possible in unsedated patients. Finally, before the esophagus is intubated, careful attention should be directed to the vocal cords to assess them for irregularities.

In a meta-analysis by Menon and Trudgill [16], a pooled missed rate of upper GIT cancer of 11,3% was demonstrated; and even in Japan, Shimodate et al. [17] showed that 75% of the newly diagnosed gastric cancers were evident in retrospectively analyzed images of prior gastroscopies of the same patients. This means that even with technological advancements, endoscopists performing the examination remain the weakest link.

For a proper and detailed endoscopic assessment of the upper GIT, certain performance measures need to be considered. These performance measures have been de-

scribed in detail by the European Society of GI Endoscopy (ESGE) and include key performance measures as well as minor performance measures (Table 2). Even though time seems to play a crucial role in the quality of an upper GIT examination, standardization seems to be even more important in quality improvement. Such standards as accurate photodocumentation, accurate terminology and nomenclature, as well as correct documentation seem to be paramount in the achievement of a high-quality upper GIT endoscopic examination [18].

In countries with standardized upper GIT screening endoscopy such as Korea and Japan, more than 50% of the upper GIT cancers are diagnosed at an early stage, with a significant improvement of stomach cancer survival rates in these countries [14]. In Korea, the 5-year survival rates for gastric cancer increased from 43% in 1993 to about 69% in 2011 [19]. Furthermore, mass screening for gastric cancer in Japan was shown to be cost-effective [20, 21].

Of course, the question that comes to mind is whether the same would hold true for low-prevalence regions in the Western world. If individuals at a particular age and

Table 2. Description of the different performance measures recommended by the ESGE [18]

Key performance measures	Minor performance measures
Fasting instructions prior to UGI endoscopy	Minimum 7-min procedure time for first diagnostic UGI endoscopy and follow-up of gastric intestinal metaplasia
Documentation of procedure duration	Minimum 1-min inspection time per cm circumferential Barrett's epithelium
Accurate photodocumentation of anatomical landmarks and abnormal findings	Use of Lugol chromoendoscopy in patients with a curatively treated ENT or lung cancer to exclude a second primary esophageal cancer
Application of Seattle protocol in Barrett's surveillance	Application of validated biopsy protocol to detect gastric intestinal metaplasia (MAPS guidelines)
Accurate registration of complications after therapeutic UGI endoscopy	Prospective registration of Barrett's patients

UGI, upper gastrointestinal; ENT, ear, nose, and throat; MAPS, management of patients with precancerous conditions and lesions of the stomach.

with high-risk factors such as a positive family history or known *H. pylori* infection are considered, then a similar situation as in Asia could be achieved. In the West, a screening program targeting a smaller high-risk population will be more cost-effective than a general screening program, irrespective of age or risk factors [9].

Conclusion

Endoscopic screening of the upper GIT in the West needs to be analyzed from a different perspective than in high-prevalence countries such as Korea and Japan. Em-

phasis must be laid on precancerous lesions and premalignant conditions such as severe atrophy or intestinal metaplasia. Furthermore, the entire upper GIT from the oral cavity down to the duodenum/ampulla must be considered when discussing the pros and cons of upper GIT screening. Finally, a risk-based approach to endoscopic upper GIT screening may be more cost-effective than general screening of asymptomatic low-risk cohorts.

Disclosure Statement

The authors of this paper declare no competing interests.

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