Magnification chromoendoscopy in comparison to standard chromoendoscopy for detection of intestinal metaplasia in renal transplant recipients

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Abstract

Purpose: Renal transplantation is associated with frequent gastrointestinal complications. Intestinal metaplasia is a feature of atrophic gastritis whereas the diagnosis of Barrett's esophagus is based on histological demonstration of specialized metaplasia. Both conditions are associated with increased risk of adenocarcinoma. The aim of the present study was to assess whether magnification endoscopy improves the diagnostic accuracy of intestinal metaplasia in stomach and in esophagus.

Material and methods: In this non-randomized, feasibility study thirty one (12 women and 19 men) renal transplant recipients, with a mean age of 44.0 years were evaluated for the presence of intestinal metaplasia. Standard esophagogastroscopy with methylene blue staining was followed by magnification endoscopy. The presence of gastritis and intestinal metaplasia was classified according to modified updated Sydney classification.

Results: Of 31 patients, 16 patients had endoscopic and histopathological evidence of gastric intestinal metaplasia, and standard endoscopy with methylene blue staining was sufficient for diagnosis (15 from 16). Magnification endoscopy allowed identification of 6 patients with specialized intestinal metaplasia in Barrett's esophagus, which would be otherwise missed.

Conclusions: In this study diagnostic accuracy of standard endoscopy for identification of intestinal metaplasia in the stomach was not improved by the use of magnification endoscopy, but the latter was an accurate method of predicting specialized intestinal metaplasia in Barrett's esophagus. The use of magnification endoscopy in the clinical setting of renal transplantation needs further studies.

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Introduction

Although the worldwide incidence of gastric cancer has declined rapidly over the recent few decades [1] it is still the second leading cause of death from cancer worldwide [2]. The highest incidence rates are seen in Eastern Asia, the Andean regions of South America, and Central and Eastern Europe, wheras its incidence in USA is one of the lowest in the world [3].

In spite of these facts surprisingly little attention is paid to this form of cancer in the transplant recipients, and no specific guidelines for screening are given. This attitude is based on the premise of only modestly increased stomach and esophagus cancer rates in the USA [4]. However, there are some data suggesting that we might need to rethink such policy. One of the most provocative findings is that in USA 5-year survival of transplant recipients (for the entire transplant recipient group) diagnosed with gastric cancer was 29% as compared with a 5% to 15% 5-year survival in the general population, finding clearly attributable to early detection [5]. Amazingly, 53% of cases were discovered incidentally during endoscopy and additional 12% during computed tomography performed for other reasons [5]. There is also small study from Asian country suggesting possibility of increased incidence of gastric cancer in renal transplant recipients [6].

Intestinal metaplasia (IM) a universal feature of atrophic gastritis is the most dependable defining morphologic feature, and is also highly relevant to the pathogenesis of atrophic gastritis [7,8]. Intestinal metaplasia is defined by the replacement of the surface foveolar and glandular epithelium in the oxyntic or antral mucosa by intestinal epithelium, which is recognized by the presence of goblet cells [7,8]. Intestinal metaplasia takes several forms, type I shows fully formed small intestinal epithelium, type II and III are incomplete, consist of goblets cells interspersed among gastric-type mucin cells. Type III of

intestinal metaplasia seems to correlate with increased risk of gastric adenocarcinoma [7]. The recent data suggest that long-term metaplasia could induce invasive carcinoma [8]. Hence reliable diagnosis of intestinal metaplasia, which is demonstrable both endoscopically and in gastric biopsy specimens may be important for early diagnosis of gastric cancer. Little is known, however, about the frequency of intestinal metaplasia in renal transplant recipients.

Despite technological advances the ability of the classical endoscopy to detect dysplastic and early cancerous changes in the upper GI tract remains limited. In conditions such as Barrett's oesophagus, practice guidelines recommend periodic endoscopic surveillance with multiple biopsies, a methodology that is hindered by random sampling error, inconsistent histopathological interpretation, and delay in diagnosis. Early diagnosis may be improved by new diagnostic modalities such as chromoendoscopy and magnification endoscopy [9].

Staining is readily available and cheap, however, adds several steps and likely several minutes to routine endoscopy. A new technique – enhanced magnification endoscopy seems to be effective, readily available method and adds only an additional 5 to 10 minutes to standard endoscopic procedures. The value of this technique is still being explored, but it seems that it may improve the detection of mucosal changes by permitting better targeting of biopsies.

This has prompted us to undertake a feasibility study in order to evaluate the value of enhanced magnification chromoendoscopy as compared with chromoendoscopy and classic endoscopy in detecting intestinal metaplasia in the stomach and in the esophagus in renal transplant recipients.

Material and methods

This was an open, non-randomized clinical study. Thirty one subjects (12 females and 19 males, aged 44.0±10.8 years), attending transplantation clinic agreed to participate in the study. Inclusion criteria were: stable graft function and 1st or 2nd renal transplantation performed more than 6 months ago (mean 2.6 years; range 0.5-20 years). The indications for upper gastrointestinal endoscopy were as follows: upper abdominal pain or discomfort (n=15), ulcer disease in the past in an asymptomatic patient (n=2) and routine endoscopy screening (performed once a year) (n=14). All endoscopic examinations were performed by a single experienced endoscopist and recorded on a videotape. At first a routine esophagogastroscopy was performed using a Fujinon GIF EG-200HR videoendoscope. The intestinal metaplasia was identified by methylene blue staining (the stain is picked up by actively absorbing tissues such as areas of intestinal metaplasia in gastric and esophageal mucosa. It does not stain nonabsorptive epithelia such as gastric mucosa). The gastric biopsies were then obtained with biopsy forceps – two from antral area, two from stomach corpus and always from the area of macroscopic changes suggesting metaplasia in stomach, or from esophagus in case of suspected intestinal metaplasia in esophagus. Mucosal surface patterns were recorded in every patient. In the next step of the examination esophagogastroscopy was repeated using Fujinon EG 485 ZW magnifying videoendoscope. The mucosa was washed of any traces of blood and additional biopsies were taken from areas suggestive of metaplasia, and the results of both examinations were compared.

Table 1. **Indications for upper gastrointestinal endoscopy in renal transplant recipients**

Indication for endoscopy	No of patients
Upper abdominal pain or discomfort	15
Ulcer disease in the past	2
Routine (performed once a year)	14

Table 2. **Intestinal metaplasia in the stomach and in esophagus identified by chromoscopy followed by routine and magnifying endoscopy**

Site of metaplasia identification	No of patients with metaplasia identified by chromoendoscopy	No of patient with metaplasia identified by chromoscopy followed by enhanced magnification endoscopy	P
Antrum	13	13	ns
Gastric corpus	2	3	ns
Esophagus	0	6	p=0.024
Total	15	22	ns

The biopsy specimens were embedded in paraffin and typical sections were obtained. The sections were stained with hematoxilin-eosin and pathologist experienced in gastrointestinal histology examined the slides. Chronic gastritis was diagnosed by the presence of mononuclear cells within the lamina propria. The presence of gastritis and intestinal metaplasia was classified according to the updated Sydney classification [10]. Rarefaction and loss of gastric glands served to assess the occurrence of mucosal atrophy. Intestinal metaplasia was defined by the presence of goblet cells and/or specialized intestinal cells [7,8].

Results

A total of 31 renal transplant recipients were examined. 16 subjects had endoscopic and histopathologic evidence of gastric mucosal intestinal metaplasia (51.6%) in antrum or in stomach corpus (13 and 3 respectively). Seven subjects had no endoscopic and histological evidence of intestinal metaplasia (*Tab. 2*).

In 15 subjects (48.4%) endoscopic evidence was consistent with histological evaluation, and diagnosis was done by standard endoscopic examination after methylene blue staining. Diagnostic accuracy of intestinal metaplasia was not significantly improved by the use of magnification endoscopy. In this group we have found only one more focus of intestinal metaplasia in the corpus of the stomach with magnification endoscopy followed by chromoscopy (*Tab. 2*). Enhanced magnification endoscopy, however, allowed identifying all 6 patients (19.4%) with specialized intestinal metaplasia in esophagus (*Tab. 2*; p=0.024 vs standard endoscopy by Fisher's exact test). All these patients had low grade dysplasia in this area identified by enhanced

Figure 1. **Endoscopic images of gastric antrum in a kidney transplant recipients without staining (left panel) and after staining (right panel) with methylene blue. Area of heterogenous staining corresponding to metaplasia (confirmed by biopsy) is seen**

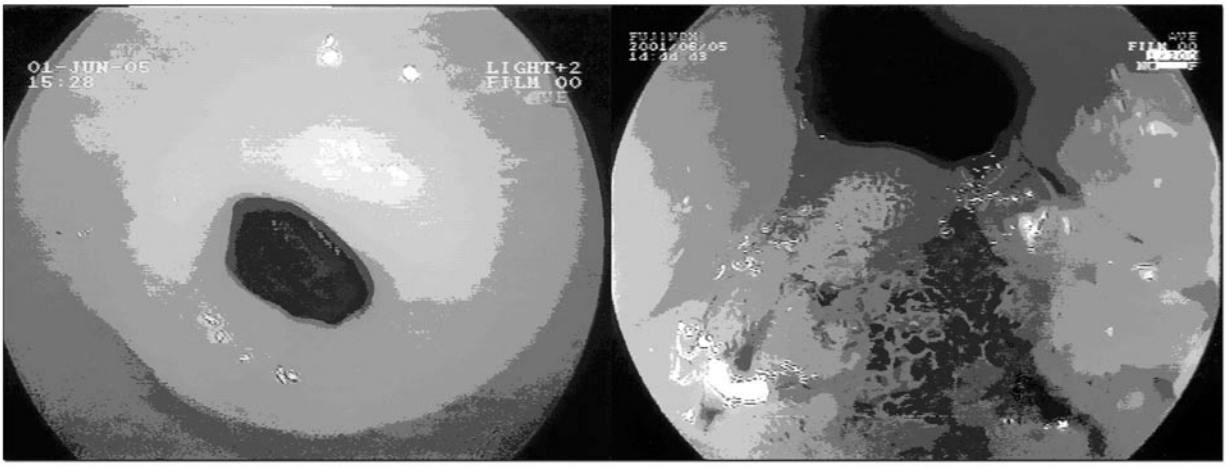
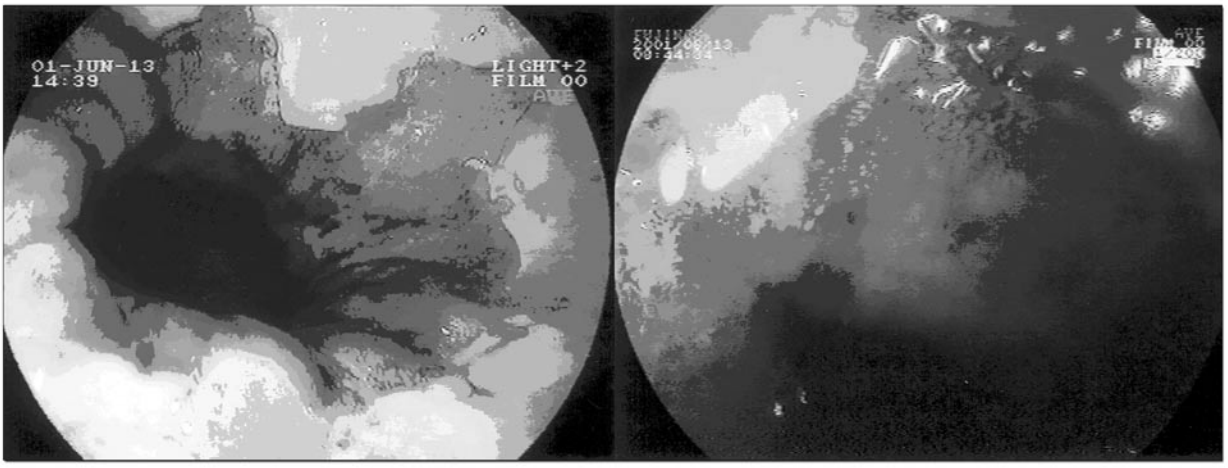


Figure 2. **Endoscopic image of specialized intestinal metaplasia in Barrett's esophagus in kidney transplant reciepients. Left panel – methylene blue chromoendoscopy. Right panel – magnification view with a tubular pit pattern**



magnification endoscopy, what has allowed diagnosing Barrett's esophagus.

Discussion

In the transplant recipient population, little is known about the clinical staging and outcome of gastric cancer and precancerous stages. The results of the present study show that in this population gastric intestinal metaplasia is a frequent finding. Its incidence in our study was similar to that reported for asymptomatic uremic patients under maintenance hemodialysis prior to kidney transplantation [11].

In this study magnification chromoendoscopy has not improved diagnostic accuracy for detection of gastric intestinal metaplasia. Standard endoscopy enhanced by methylene blue staining was sufficient. Magnification chromoendoscopy, however, significantly increased the chance of identification of specialized intestinal metaplasia in Barrett's esophagus. In fact in all cases diagnosis would be otherwise missed. This seems to have important clinical implications. It has to be borne in mind that Barrett's esophagus as a complication of gastroesophageal reflux disease (GERD) is an established precancerous condition which can lead to adenocarcinoma in the distal esophagus [12,13]. Currently, different dyes are used in conjunction with magnifying endoscopes to characterize specific surface patterns of Barrett's epithelium [13,14]. The real value of magnifying chromoendoscopy for clinical practice has not been yet determined and currently under investigation [15]. Our data suggest that these techniques have significant potential to improve diagnostic accuracy in patients with Barrett esophagus, however, were not better that routine chromoscopy in diagnosis of intestinal metaplasia in the stomach. Our results are in agreement with other investigators observations that magnification endoscopy is an accurate method predicting specialized intestinal metaplasia in Barrett's esophagus [15,16]. According to a recent paper

methylene blue staining does improve the detection of Barrett's mucosa, and areas of intestinal metaplasia are detected much more frequently than was previously recognized, even in people who were thought to have a normal esophagogastric junction on regular endoscopy [16]. According to our data the use of magnification chromoscopy is better than routine chromoscopy especially in the esophagus. This could be explained by difficulties in staining in esophagus, which is often patchy and uneven. Chromoendoscopy is a relatively new technique and depends on the skill and experience of endoscopist. Magnification in this case improves detecting of intestinal metaplasia in esophageal columnar-appearing mucosa. It seems that this technique might have impact on long-term outcome of renal transplant recipients by having a potential to improve diagnostic accuracy in patients with Barrett's esophagus, but this has yet to be proven.

In conclusion diagnostic accuracy of standard endoscopy for identification of intestinal metaplasia in the stomach is not improved by the use of magnification endoscopy, but our results suggest that this is an accurate method in renal transplant recipients for prediciting specialized intestinal metaplasia in Barrett's esophagus. Further research on the use of magnification endoscopy in renal transplant recipients in a well designed study is required to confirm our findings.

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