Fujinon intelligent color enhancement for the diagnosis of early esophageal squamous cell carcinoma and precancerous lesion

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ABSTRACT

Background/Aims: Esophageal squamous cell carcinoma is a common malignant tumor in recent years, and the key for improving the survival rate is early diagnosis and treatment. Computed virtual chromoendoscopy with the Fujinon intelligent color enhancement (FICE) system was reported to improve visualization of neoplastic and non-neoplastic lesions in gastroscopy and colonoscopy. The purpose of this study was to evaluate the value of FICE in the diagnosis of early esophageal squamous cell carcinoma and precancerous lesions.

Materials and Methods: Two hundred fifty-seven patients with suspicious lesions of the esophagus were examined successively by FICE, magnifying FICE, Lugol chromoendoscopy, and magnifying Lugol chromoendoscopy in the hospital. The lesions and the intrapapillary capillary loop (IPCL, microvessels at the surface of esophageal carcinoma) were observed and compared with the pathologic diagnosis that was regarded as the golden standard.

Results: The positive rates of early esophageal squamous cell carcinoma were 92.6% and 88.9% as examined by FICE and Lugol chromoendoscopy (p>0.05), and 96.3% and 92.6% as examined by magnifying FICE and magnifying Lugol chromoendoscopy (p>0.05), respectively. The magnifying FICE could observe the IPCL of the esophagus clearly. Early esophageal squamous cell carcinoma and high-grade intraepithelial neoplasia were mainly type IV and type V. Low-grade intraepithelial neoplasia and esophagitis were type II and type III, and normal esophagus was type I; however, the observation of the IPCL by magnifying Lugol chromoendoscopy was not clear.

Conclusion: Fujinon intelligent color enhancement and magnifying FICE are complements to Lugol chromoendoscopy and magnifying Lugol chromoendoscopy in the diagnosis of early esophageal lesions.

Keywords: Fujinon intelligent color enhancement, intrapapillary capillary loop, early esophageal squamous cell carcinoma

INTRODUCTION

Esophageal carcinoma is the eighth most common carcinoma in the world, and the mortality is the sixth highest (1,2). In China, the morbidity and mortality are higher than anywhere in the world and more than 90% of esophageal carcinomas are squamous cell carcinomas (3). As the symptoms are usually inconspicuous, most patients have been at advanced stages when they come to the hospital. Many researchers have proven that 5-year survival rate of early esophageal squamous cell carcinoma patients who are treated by endoscopies may be more than 84% (4-6). So, it is important for the patients to be diagnosed at the early stage.

With the rapid renewal of endoscopies, the detection rate and the diagnostic accuracy of early esophageal lesions were greatly improved. The Fujinon intelligent color enhancement (FICE) is a new diagnostic method to determine tumor margins and depth by observing the intrapapillary capillary loop (IPCL, microvessels at the surface of esophageal carcinoma) through using a magnifying mode (7). In this study, we compared FICE with Lugol chromoendoscopy and magnifying FICE with magnifying Lugol chromoendoscopy in the diagnosis of early esophageal squamous cell carcinoma and precancerous lesions in order to investigate the diagnostic value of FICE.
Li et al. FICE and early esophageal carcinoma

MATERIALS AND METHODS

Patients and conceptual knowledge
All the patients had been informed before endoscopy examination and they agreed to participate in the examination. Ethical approval was agreed by the Medical Ethics Committee of Renmin Hospital of Wuhan University. Between January 2010 and January 2011, the patients who were diagnosed by conventional endoscopies in our hospital with suspicious lesions of the esophagus were selected for the study. Esophageal squamous epithelium with severe dysplasia and carcinoma in situ was defined as precancerous lesions. Mucosal cancer and submucosal cancer without lymph node metastasis of early esophageal cancer were defined as early esophageal squamous cell carcinomas (8). According to the World Health Organization and Vienna classification, we classified severe dysplasia and carcinoma in situ as high-grade intraepithelial neoplasia and classified mild to moderate dysplasia as low-grade intraepithelial neoplasia (9,10).

Endoscopy equipment and reagent
In this study, we used a magnifying endoscope (EG-590ZW, Fujinon, Inc, Saitama, Japan), which was in combination with a light source (XL-4400, Fujinon, Inc, Saitama, Japan) and an image processor (VP-4400, Fujinon, Inc, Saitama, Japan). Of the 10 factory default modes in this endoscopy, we selected the three most appropriate ones in this study. Besides the endoscope, we also needed a reagent, 2% Lugol iodine solution.

Procedure
This study was conducted by a senior doctor who was familiar with endoscopic operations and had rich experience using the FICE system in endoscopic procedures for more than 2 years. Firstly, we checked esophageal mucosa by conventional endoscopy under a white light and then converted it to the FICE mode in the same endoscopic procedure by a simple push of a button for further observation. When lesions were found, we would observe them more clearly in FICE modes A, B, and C, respectively. Until the lesions were shown most clearly, we recorded and saved the best wavelength combinations. Secondly, we changed the mode to magnifying FICE, which could observe the IPCL of the esophageal mucosa. All images of each lesion were taken in single view to evaluate the same IPCL as far as possible. Thirdly, after the FICE and magnifying FICE, we would stain the lesions by 2% Lugol iodine solution, which was sensitive for early esophageal squamous cell carcinoma (11). Then, the lesions were observed by Lugol chromoendoscopy and magnifying Lugol chromoendoscopy. Lastly, the lesions were resected by biopsy and diagnosed by pathological examination, which was the gold standard for esophageal squamous cell carcinoma.

Diagnostic criteria
For detecting early-stage esophageal squamous cell carcinoma by Lugol chromoendoscopy, the unstained areas, which might be the abnormal esophagus, were discriminated (12). But, the lesions that were stained by different wavelength combinations of FICE were positive results, and the unstained ones were negative results. On this condition, the positive results might be abnormal esophagus. Then, the suspicious abnormal esophagus would be diagnosed by pathologic diagnosis. The various IPCL changes were classified as follows: dilatation, tortuosity, caliber change, and variety of shapes (13). The IPCL types in this study were based on our personal observation in our unit and from the published literature (13-15).

Type I (normal epithelial): normal IPCL with regular shape and size
Type II (like esophagitis): slight dilatation or elongation
Type III (mild dysplasia): slightly irregular or abnormal branch
Type IV (severe dysplasia): no more than three of the four kinds of changes as mentioned above
Type V (carcinoma): all of the four changes as mentioned above

Statistical analysis
Statistical analyses were performed using Statistical Package for the Social Sciences (SPSS) 17.0 (SPSS Inc, Chicago, IL, USA). The chi-square test was used to compare the lesion detections between different endoscopy images and pathologic diagnoses. A p value of less than 0.05 was accepted as statistically significant.

RESULTS

General results
A total of 257 patients with suspicious lesions of the esophagus had been selected for this study, including 155 males and 102 females, aged from 32 to 84 years, with a mean of 58 years. Pathologic diagnoses were as follows: 27 early esophageal squamous cell carcinomas (10.4%), 22 high-grade intraepithelial neoplasia (8.6%), 40 low-grade intraepithelial neoplasia (15.6%), 156 esophagitis (60.7%), and 12 normal esophagus (4.7%).

Positive rates and pathological results
The positive rate of FICE in the diagnosis of early esophageal squamous cell carcinoma was 92.6% (25/27), and the positive rate of Lugol chromoendoscopy was 88.9% (24/27). There was no significant difference between these two methods (P=0.642). The positive rate of magnifying FICE was 96.3% (26/27), and the positive rate of magnifying Lugol chromoendoscopy was 92.6% (25/27). There was no significant difference between these two methods, either (p=0.556) (Table 1).

Magnifying endoscopy images and pathological results
The pit patterns of early esophageal squamous cell carcinoma and high-grade intraepithelial neoplasia as examined by mag-
nifying FICE were mainly type IV and type V, and the percent-
ages were 96.3% (26/27) and 95.5% (21/22), respectively. How-
ever, the pit patterns of low-grade intraepithelial neoplasia and
esophagitis were mainly type II and type III (97.5%, 98.7%), and
normal esophagus was type I (100%). On the contrary, the pit
patterns could not be seen clearly by magnifying Lugol chro-
moeendoscopy.

Side effects
There were no side effects by FICE and magnifying FICE; however,
the total side effect rate of Lugol chromoendoscopy and magni-
fying Lugol chromoendoscopy was 12.8% (33/257). Among the
33 patients, there were 24 cases with retrosternal discomfort, 6
cases with bucking, and 3 cases with vomiting. The reasons why
patients got side effects may be the irritation and toxicity of the
esophagus caused by the oxide components of iodine as well as
the sensitivity of patients and the symptoms of the disease itself
(16,17). However, the side effects of the 33 patients all deviated
within 12 hours without special treatment.

DISCUSSION
Esophageal carcinoma, mainly divided into esophageal adeno-
carcinoma and esophageal squamous cell carcinoma, is one of
the common malignant tumors in the world. For Europe
and the United States, esophageal adenocarcinoma accounts
for 50% or more of esophageal carcinoma (18); however, the
prevalence of esophageal squamous cell carcinoma is higher
in Asia, such as China and Japan, which accounts for 90% of
esophageal carcinoma (19-21). The prognosis of esophageal
squamous cell carcinoma, if detected at an advanced stage,
is poor and worse than that of esophageal adenocarcinoma
(22,23). But, the 5-year survival rate of early esophageal squa-
mous cell carcinoma that is at an early stage is more than 90%
after early aggressive treatment, while the rates of advanced
esophageal carcinomas are significantly reduced; so, the key
for improving the prognosis is early diagnosis and treatment
(24). Precise endoscopic assessment of esophageal mucosal
features is important to detect neoplastic lesions at an early
stage. Currently, the diagnosis of early esophageal carcinoma
can only rely on endoscopy and endoscopic biopsy, but the
diagnosis rate by conventional endoscopy is very low. Al-
though the invention of Lugol chromoendoscopy can help
to diagnose early esophageal squamous cell carcinoma and
precancerous lesion, the side effects are too serious, including
vomiting, cough, bucking, retrosternal pain, and so on (25,26).
Moreover, after spraying 2% Lugol iodine solution, peristalsis
of the esophagus will be strengthened, and Lugol chromo-
endoscopy requires taking 1 or 2 minutes to color the whole
mucosa (27). The procedure is inconvenient for endoscopists
to observe the lesions. Sometimes, uneven dyeing will lead to
misdiagnosis or leak diagnosis.

With the development of endoscopic techniques and equip-
ment, the FICE system is a new dyeless imaging technique that
enhances mucosal visibility, which can improve visualization
of neoplastic and non-neoplastic lesions by gastroscopy and
colonoscopy (28). This computed virtual chromoendoscopy
technique, based on narrowing the bandwidth of the conven-
tional endoscopic image arithmetically, can estimate the spec-
trum reflectance from a white-light endoscopic image and re-
Li et al. FICE and early esophageal carcinoma

constitute a color image from the wavelength. Moreover, the single-wavelength images are freely selected and assigned to red (R), green (G), and blue (B), respectively, to build and display a FICE-enhanced color image. Based on the various lesions, different spectral images will be selected (29), which can achieve the purpose of electronic virtual chromoendoscopy. Some researchers have used FICE to diagnose gastrointestinal lesions and received satisfactory results in the world (30-32). In this study, the best wavelength combinations that we selected were as follows: R=540 nm, G=490 nm, B=420 nm and R=550 nm, G=500 nm, B=470 nm, which could clearly show the lesions.

In addition, the IPCL is commonly observed in squamous cell carcinoma derived from the squamous epithelium with little or no glandular structure (33,34). So, magnifying endoscopes can be used to observe the IPCL of esophageal squamous cell carcinoma but not esophageal adenocarcinoma. As a result, we also compared magnifying FICE with magnifying Lugol chromoendoscopy in the observation of the IPCL in this study.

According to these results, the positive rate of Lugol chromoendoscopy was 88.9% in the diagnosis of early esophageal squamous cell carcinoma, which was lower than that of FICE, while the statistics showed that there was no significant difference between these two methods (p=0.642). At the same time, the positive rate of magnifying FICE was 96.3%, which was a little higher than that of magnifying Lugol chromoendoscopy, and there was no significant difference between these two methods, either (p=0.556). Moreover, the study also showed that the characteristic changes of the IPCL from the submucosal vein could be clearly observed by magnifying FICE, while magnifying Lugol chromoendoscopy failed in observing the IPCL. According to the results of the characteristic changes of the IPCL and pathologic diagnosis, we concluded that the IPCL of esophageal carcinomas and high-grade intraepithelial neoplasia might be mainly type IV and type V, and low-grade intraepithelial neoplasia and esophagitis were mainly type II and type III, but all patterns of normal esophagus were type I.

In summary, FICE and magnifying FICE could determine the pathological types and enhance the diagnosis of early esophageal squamous cell carcinoma accurately through observing the IPCL. Furthermore, the use of FICE avoids side effects observed by Lugol’s solution and shortens the time of the endoscopic procedure. In other words, FICE and magnifying FICE are excellent complementary methods to Lugol chromoendoscopy and magnifying Lugol chromoendoscopy in diagnosing early esophageal squamous cell carcinoma and precancerous lesions.

Ethics Committee Approval: Ethics committee approval was received for this study from Medical Ethics Committee of Renmin Hospital of Wuhan University.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.


Acknowledgements: The authors would like to thank the anonymous reviewers for their helpful comments and the pathologists for their hard work and the pathological diagnoses.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

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