

Case Report**Chromoendoscopic findings in diagnostic esophagoscopy****Puspa Zuleika, Adeli, Eriza, Daniel Bramantyo**Department of Otorhinolaryngology–Head and Neck Surgery, Faculty of Medicine,
Universitas Sriwijaya/Dr. Mohammad Hoesin General Hospital, Palembang, Indonesia**ABSTRACT**

Background: Patients with head and neck squamous cell carcinoma (HNSCC) carry a significant risk for potential spread of malignancy to the aerodigestive tract. Lugol chromoendoscopy is a well-established image-enhanced technique that increases the sensitivity for detecting early synchronous esophageal squamous cell neoplasms (ESCNs) by selectively staining normal glycogen-rich epithelium brown, leaving dysplastic or malignant areas unstained. **Purpose:** To describe the findings of chromoendoscopy during diagnostic esophagoscopy in three patients diagnosed with laryngeal carcinoma, who were scheduled for total laryngectomy as a follow-up treatment. **Case reports:** We presented three cases of male patients diagnosed with Stage III laryngeal carcinoma. Case 1 and case 2 were scheduled for primary total laryngectomy. Case 3 was scheduled for total laryngectomy following post-chemoradiotherapy recurrence. All patients underwent diagnostic esophagoscopy to evaluate potential esophageal extension. **Clinical question:** “Is chromoendoscopy highly sensitive in detecting malignant spread in patients with head and neck squamous cell carcinoma in the esophageal area?” **Method:** Literature search was conducted using key word “chromoendoscopy” AND “esophagoscopy” AND “esophagus” AND “therapy” in PubMed and Google Scholars. Exclusion criteria included articles published before the year 2000. **Result:** A total 30 articles relevant to this topic, and nine could be used as references. **Conclusion:** Chromoendoscopy is a highly effective diagnostic tool in the preoperative workup of laryngeal carcinoma patients. It significantly enhances the detection of both synchronous esophageal lesions and malignant extensions, enabling more precise surgical planning and comprehensive management, before major interventions such as total laryngectomy.

Keywords: chromoendoscopy, esophagus, esophagoscopy, therapy**ABSTRAK**

Latar belakang: Pasien dengan kanker kepala dan leher (HNSCC) memiliki risiko tinggi terhadap potensi penyebaran sel kanker ke saluran pencernaan. Lugol chromoendoscopy merupakan teknik pencitraan tambahan untuk meningkatkan sensitivitas deteksi dini synchronous esophageal squamous cell neoplasms (ESCNs) dengan mewarnai epitel normal yang kaya glikogen menjadi coklat, sementara area displastik atau ganas tetap tidak terwarnai. **Tujuan:** Untuk mendeskripsikan temuan kromoendoskopi selama esofagoskopi diagnostik pada tiga pasien dengan diagnosis karsinoma laring, yang direncanakan untuk menjalani laringektomi total sebagai terapi lanjutan. **Laporan Kasus:** Kami menyajikan tiga kasus pasien laki-laki dengan diagnosis Karsinoma Laring Stadium III. Kasus 1 dan kasus 2 dijadwalkan untuk laringektomi total primer. Kasus 3 dijadwalkan untuk laringektomi total setelah rekurensi pasca kemoradioterapi. Seluruh pasien menjalani esofagoskopi diagnostik untuk mengevaluasi potensi perluasan ke esofagus. **Pertanyaan klinis:** “Apakah kromoendoskopi memiliki sensitivitas yang tinggi dalam mendeteksi penyebaran keganasan di area esofagus pada pasien dengan karsinoma sel skuamosa kepala dan leher?” **Metode:** Tinjauan literatur dengan kata kunci “kromoendoskopi” DAN “esofagoskopi” DAN “esofagus” Dan “terapi”. Pencarian dilakukan di PubMed dan Google Scholar. Kriteria eklsusi meliputi artikel yang diterbitkan sebelum tahun 2000. **Hasil:** Didapatkan 30 artikel yang relevan terhadap topik ini, dan sembilan artikel diantaranya dapat digunakan sebagai referensi. **Kesimpulan:** Kromoendoskopi merupakan alat diagnostik yang sangat efektif dalam pemeriksaan preoperatif pasien karsinoma laring. Teknik ini secara signifikan meningkatkan deteksi lesi esofagus sinkron maupun perluasan keganasan, sehingga

memungkinkan perencanaan bedah yang lebih tepat dan manajemen pasien yang komprehensif, sebelum intervensi besar seperti laringektomi total.

Kata kunci: kromoendoskopi, esofagus, esofagoskopi. terapi

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INTRODUCTION

Endoscopic screening using image-enhanced endoscopy has significantly improved outcomes for high-risk populations, such as patients with head and neck squamous cell carcinoma. Lugol chromo-endoscopy, one of the earliest image-enhanced endoscopy techniques for esophageal squamous cell neoplasms (ESCNs), selectively stains normal squamous epithelium brown, leaving dysplastic or cancerous areas unstained. This approach enhances the sensitivity of endoscopists in detecting early ESCNs.¹

One of the medical endoscopic tools used is the esophagoscope, where the part inserted into the esophagus is a rigid tube. Imaging techniques such as mucosal staining, magnification, high-definition endoscopy, electronic chromoendoscopy, spectroscopy, and endoscopic ultrasound play a significant role in detecting abnormalities and suspicious lesions in the esophagus.^{2,3}

Chromoendoscopy is a gastrointestinal endoscopic procedure that uses stains, pigments, or dyes to detect malignant lesions on the mucosal lining of the gastrointestinal tract, that are not visible with conventional endoscopy. Cancer cells react differently to dyes compared to normal cells. For example, normal cells turn dark green or brown when sprayed with Lugol solution, whereas squamous cancer cells do not absorb the dye.³ Frequently used dyes include Lugol solution,

methylene blue, and toluidine blue, which are readily available and have high sensitivity and specificity in diagnostic applications. In the field of ENT, chromoendoscopy is used to enhance the detection of various pathological processes during endoscopic evaluations, such as identifying Barrett's esophagus, and suspicious malignant lesions in the esophagus.⁴

The purpose of this case report was to describe the findings of chromoendoscopy during diagnostic esophagoscopy in patients diagnosed with laryngeal carcinoma, who were planned to undergo total laryngectomy as a follow-up treatment.

CASE REPORT

Case 1

A 48-year-old male was diagnosed with Stage III Laryngeal Carcinoma (T3N0M0) and had a tracheostomy. The patient underwent a tracheostomy in Jambi on January 5, 2024, due to upper airway obstruction caused by a laryngeal mass. A direct laryngoscopy with biopsy was performed at Moh. Hoesin Hospital on January 24, 2024, which resulted in a histopathological diagnosis of conventional squamous cell carcinoma of the larynx. The patient was planned to undergo a total laryngectomy by the Oncology Department at Moh. Hoesin Hospital. A consultation was made with the Bronchoesophagology Department for a diagnostic esophagoscopy

to evaluate the possibility of carcinoma spreading to the esophagus, before performing the total laryngectomy.

During anamnesis, the patient complained of worsening hoarseness that had persisted for six months. There were no complaints of dysphagia, and ear or nasal symptoms were denied. On initial examination, the patient was in good general condition, fully conscious with *compos mentis* status, blood pressure of 120/80 mmHg, heart rate of 79, respiratory rate of 20 per minute, and oxygen saturation of 99%. The patient had a tracheostomy cannula size 7.0 in place, with good airway patency and minimal secretions.

Diagnostic esophagoscopy with chromoendoscopy was performed on February 13, 2024. The examination revealed a smooth esophageal mucosa. A mucolytic agent, dimethylpolysiloxane, was sprayed

in a volume of 40 cc starting from a depth of 30 cm using a nasogastric tube (NGT) size 12. The esophagoscope was then withdrawn while rotating to the right and left, up to a depth of 16 cm, and left in place for 2 minutes before being cleared with suction. The esophagoscope was then reintroduced to a depth of 28 cm, followed by spraying 40 cc Lugol solution, using the same NGT while rotating the scope as before. After 2 minutes, the solution was suctioned out. Evaluation revealed multiple whitish plaques at a depth of 20-21 cm (anterior esophageal mucosa at 1 o'clock position), 24 cm (anterior and posterior esophageal mucosa at 1 and 6 o'clock positions), and 25 cm (posterior esophageal mucosa at 5 o'clock position). These plaques appeared inhomogeneous compared to the surrounding mucosa after Lugol staining, resembling features of malignant extension to the esophagus.

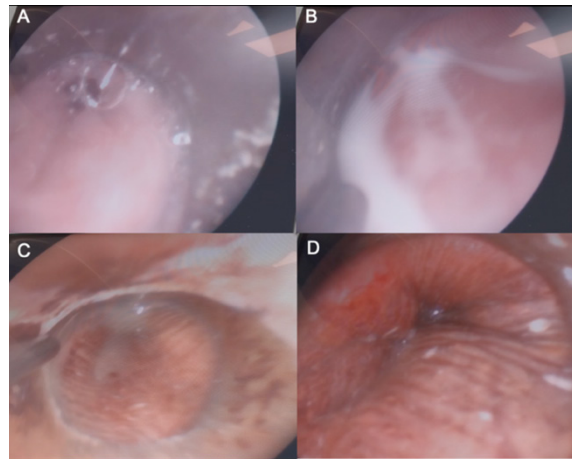


Figure 1. Chromoendoscopy of case 1. (A) Esophageal mucosa; (B) Application of dimethylpolysiloxane on the esophageal mucosa; (C) Application of Lugol solution on the esophagus (showing color change to brown on the esophageal mucosa); (D) Less intense staining observed on the esophageal mucosa.

Case 2

A 67-year-old male was diagnosed with Stage III Laryngeal Carcinoma (T3N0M0) and had undergone a tracheostomy. The patient underwent tracheostomy and direct laryngoscopy at the Larynx-Pharynx Division in November 2023 due to upper airway obstruction caused by a laryngeal mass. Histopathological examination revealed conventional moderately differentiated squamous cell carcinoma of the larynx. A total laryngectomy was planned by the Oncology Department at Moh. Hoesin Hospital. The patient was then referred to the Bronchoesophagology Division for diagnostic esophagoscopy to assess for potential carcinoma spread to the esophagus, before the total laryngectomy procedure.

During anamnesis, the patient reported progressive hoarseness and difficult in swallowing over the past two years, but he denied any ear or nasal complaints. On initial examination, the patient was fully conscious and alert with stable vital signs: blood pressure 116/74 mmHg, heart rate 89, respiratory rate 20, and oxygen saturation 99%. A non-fenestrated tracheostomy cannula

No. 7.0 was in place with good air passage and minimal secretions.

Diagnostic esophagoscopy with chromoendoscopy was performed on March 21, 2024. Examination revealed smooth esophageal mucosa. A mucolytic agent, dimethylpolysiloxane (40 cc), was sprayed from a depth of 30 cm using an NGT No. 12 tube, while retracting the esophagoscope with rotation to the right and left, up to a depth of 16 cm. The solution was left for 2 minutes before being cleared by suction. The esophagoscope was then advanced back to a depth of 30 cm, and Lugol solution (40 cc) was sprayed using the same technique, followed by a 2-minute wait and suctioning.

Evaluation revealed multiple whitish plaques at depths of 19 cm, 20 cm, 23 cm, 25 cm, and 27 cm, that appeared inhomogeneous compared to the surrounding mucosa after Lugol staining. At a depth of 21 cm on the anterior esophageal mucosa, an area showed a lack of Lugol absorption, suggesting possible malignant spread to the esophagus.

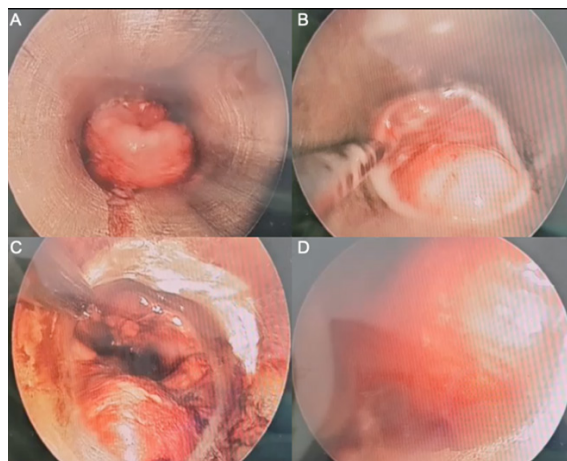


Figure 2. Chromoendoscopy of case 2.
(A) Esophageal mucosa; (B) Application of dimethylpolysiloxane on the esophageal mucosa; (C) Application of Lugol solution on the esophagus (showing a color change to brown on the esophageal mucosa); (D) Area of the esophageal mucosa showing a lack of staining.

Case 3

A 66-year-old male was diagnosed with Stage III Laryngeal Carcinoma (T3N0M0) post-chemoradiotherapy and tracheostomy status. The patient underwent tracheostomy and direct laryngoscopy in the Larynx-Pharynx Division in November 2022 due to upper airway obstruction caused by a laryngeal mass. Histopathological examination revealed moderately differentiated conventional squamous cell carcinoma of the glottis. The patient subsequently received one cycle of chemotherapy, completed in April 2023, and 33 sessions of radiotherapy, completed in September 2023. A follow-up direct laryngoscopy biopsy on January 30, 2024, revealed well-differentiated conventional squamous cell carcinoma on the right vocal cord. The patient was scheduled for total laryngectomy by the Oncology Department at Moh. Hoesin Hospital and was referred to the Bronchoesophagology Division for diagnostic esophagoscopy to assess the possibility of carcinoma spread to the esophagus, before undergoing total laryngectomy.

During the anamnesis, the patient reported worsening hoarseness over the

past 3 years, accompanied by coughing and throat phlegm, but denied any ear or nasal symptoms. On initial examination, the patient's general condition was good, fully conscious, and alert (*compos mentis*), with blood pressure of 124/72, pulse rate of 88, respiratory rate of 20, and SpO₂ of 99%. The patient had a non-fenestrated tracheostomy cannula size 7.0, with good airway passage and minimal secretions.

Diagnostic esophagoscopy with chromoendoscopy was performed on March 25, 2024. The examination revealed a smooth esophageal mucosa. A mucolytic agent, dimethylpolysiloxane was sprayed at a depth of 30 cm using an NGT no.12, while rotating the esophagoscope right and left, up to a depth of 16 cm. The agent was left in place for 2 minutes before being suctioned out. The esophagoscope was then advanced to a depth of 35 cm, and Lugol solution was sprayed similarly. After 2 minutes, the area was suctioned. Evaluation revealed that the esophageal mucosa absorbed the Lugol solution evenly, and no signs of carcinoma spread were observed on the esophageal mucosa.

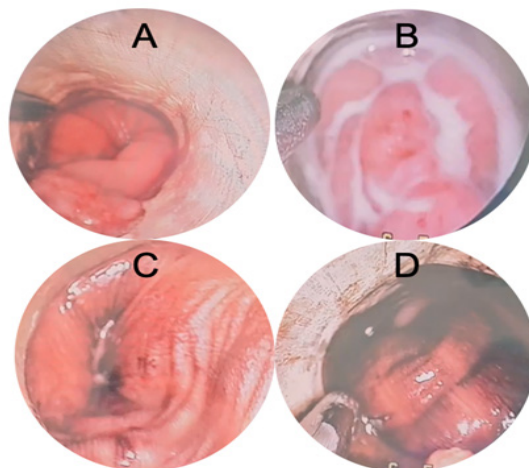


Figure 3. Chromoendoscopy of case 3. (A) Esophageal mucosa; (B) Application of dimethylpolysiloxane on the esophageal mucosa; (C) Application of Lugol's solution on the esophagus (showing brown discoloration on the esophageal mucosa); (D) Hyperstaining of the esophageal mucosa observed.

CLINICAL QUESTION

The clinical question based on the case reports above: Is chromoendoscopy highly sensitive in detecting malignant spread in patients with head and neck squamous cell carcinoma in the esophageal area?

P (Patient/Population): Patients diagnosed with head and neck squamous cell carcinoma (HNSCC).

I (Intervention): Lugol chromoendoscopy (an image-enhanced technique using Lugol's solution) and esophagoscopy.

C (Comparison): The conventional method.

O (Outcome): Sensitivity and detection rate of early-stage esophageal squamous cell neoplasms (ESCNs).

METHOD

Literature review was conducted on January 2025, using PubMed and ResearchGate with the keywords: Chromoendoscopy AND Esophagoscopy AND Esophagus AND Therapy.

The search was limited with inclusion criteria of full-text availability and articles in English. Exclusion criteria included articles published before the year 2000.

Since this examination was highly useful for diagnostic purposes, all study designs from the highest level of validity (systematic review) to the lowest (case reports), were included.

RESULT

The search obtained 46 literatures published in the last 15 years, and found 30 articles relevant to this topic. Based on the literature review, it could be concluded that chromoendoscopy was highly effective in detecting malignant spread in patients with head and neck squamous cell carcinoma, particularly in the esophageal area.

DISCUSSION

In this case report, all subjects were diagnosed with squamous cell carcinoma of the larynx. Muto et al.⁵ reported that the risk of a second primary tumor in the esophagus ranged from 16% to 36%, as the aggressive nature of squamous cell carcinoma generally led to poor prognosis in head and neck cancer. In this case, all subjects underwent esophagoscopy with chromoendoscopy to evaluate the potential spread of squamous cell carcinoma to the esophagus. A study by Fukuhara et al.⁶ showed that patients with head and neck squamous cell carcinoma tended to have metastatic lesions spreading to the aerodigestive tract. Regular pigment endoscopy combined with mucosal targeted biopsy and pathological examination is the most effective method to find precancerous lesions and early esophageal squamous cell carcinoma (ESCC).⁷

Case 1

Esophagoscopy revealed multiple whitish plaques at 20-21 cm (anterior esophageal mucosa at 1 o'clock), 24 cm (anterior and posterior esophageal mucosa at 1 and 6 o'clock), and 25 cm (posterior esophageal mucosa at 5 o'clock), which appeared inhomogeneous after Lugol staining, indicating potential malignant spread to the esophagus. Inhomogeneous appearance, areas that do not stain brown, appearing unstained or lightly stained, indicates a lack of glycogen in those cells, which is characteristic of squamous cell dysplasia, or carcinoma.²

This underscored the need to examine the upper aerodigestive tract in staging head and neck squamous cell carcinoma, even in asymptomatic patients, particularly those at high risk, such as laryngeal squamous cell carcinoma patients.⁶

Case 2

Esophagoscopy revealed an unstained area at 21 cm on the anterior esophageal mucosa, resembling malignant esophageal lesions. Muto et al.⁵ reported that 55% of patients with squamous cell carcinoma with multiple irregular Lugol-voiding lesion (LVL), had esophageal squamous cell carcinoma. Fukuhara et al.⁶ also reported that 85.7% of patients with metachronous esophageal squamous cell carcinoma showed multiple irregular LVL. Head and neck squamous cell carcinoma patients are at high risk for synchronous esophageal squamous cell carcinoma, so esophagoscopy with chromoendoscopy should be performed to detect this possibility.⁸

Case 3

This patient had previously undergone one cycle of chemoradiotherapy, and 33 radiation sessions. A follow-up biopsy revealed persistent laryngeal squamous cell carcinoma. Esophagoscopy showed good Lugol uptake (hyperstaining) with no signs of malignant spread to the esophageal mucosa. Muto et al.⁵ categorized Lugol staining patterns into four types: (1) Grade I: hyperstaining, (2) Grade II: normal brown-green staining, (3) Grade III: less intense staining, and (4) Grade IV: no staining. Lugol solution primarily evaluates the gastroesophageal junction because its iodine component binds to glycogen in normal squamous mucosa. Inflammation, dysplasia, metaplasia, and squamous cell carcinoma in the esophagus will not absorb Lugol solution due to low glycogen content.⁸

Chromoendoscopy with Lugol in these three cases of laryngeal squamous cell carcinoma showed varied findings, illustrating malignant spread patterns, and the effectiveness of this technique in detecting esophageal mucosal lesions. This technique provided clearer visualization of mucosal areas undergoing dysplastic or neoplastic transformation, particularly

in high-risk patients for malignant spread to the upper aerodigestive tract.⁸

Generally, chromoendoscopy with Lugol dye works by detecting glycogen content in squamous epithelial cells. Normal glycogen-rich cells absorb Lugol dye, appearing dark brown, while dysplastic or carcinomatous cells lack glycogen and do not absorb the dye, appearing as pale or bright areas.⁵ This examination is crucial for distinguishing normal from abnormal tissue, detecting early lesions that might be missed with conventional endoscopy, and guiding accurate biopsy sampling. It also evaluates treatment response, as seen in the third case, where post-chemoradiotherapy staining indicated healthy mucosa.⁶

Komínek et al. conducted a study on 132 head and neck squamous cell carcinoma patients (117 males and 15 females). Chromoendoscopy with Lugol revealed multiple LVL in 24 patients, leading to biopsies. Two patients were diagnosed with synchronous esophageal squamous cell carcinoma, both with stage IV head and neck squamous cell carcinoma. Although only two patients with synchronous primary carcinoma were found among newly diagnosed head and neck squamous cell carcinoma patients in this study, esophagoscopy and advanced endoscopic methods should be recommended to rule out secondary esophageal carcinoma or dysplasia. Lugol staining of the esophagus is a simple and cost-effective method that can be performed in most hospitals.^{9,10}

In conclusion, based on these three cases, chromoendoscopy was highly effective in detecting malignant spread in patients with head and neck squamous cell carcinoma, especially in the esophagus. This technique not only could detect lesions that were not visible through conventional endoscopy, but also enabled more precise biopsy sampling, thus enhancing diagnostic accuracy and improving further management effectiveness.

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