# **VIDEO CASE SERIES**

# Soft palate findings associated with a high risk of esophageal squamous cell carcinoma using an endoscopic system with enhanced depth-of-field imaging



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**Background and Aims:** We previously reported that 3 endoscopic findings of melanosis, whitish epithelium, and vasodilation in the soft palate are associated with a high risk of esophageal squamous cell carcinoma (ESCC). Conventional endoscopic systems require observation under magnification to evaluate vasodilation. This case series aims to present the evaluation of vasodilation without magnification using an endoscopic system with enhanced depth-of-field (EDOF) imaging.

**Methods:** We observed the soft palate of 3 patients with early ESCC using an endoscopic system with EDOF (GIF-EZ1500 and EVIS X1 CV-1500, Olympus Co, Tokyo, Japan).

**Results:** The patient in case 1 had marked melanosis, whitish epithelium, and vasodilation (focal type) in the soft palate. The patient in case 2 had melanosis and vasodilation (diffuse type) in the soft palate. The vasodilation in cases 1 and 2 could be evaluated sufficiently without magnification. The patient in case 3 had melanosis and whitish epithelium in the soft palate. The color tone of melanosis became sharpened using texture and color enhancement imaging.

**Conclusions:** The endoscopic system with EDOF enabled us to evaluate all 3 soft palate findings associated with a high risk of ESCC, without magnification. (VideoGIE 2021;6:380-6.)

Esophageal cancer is the sixth most common cause of cancer-related mortality in the world, <sup>1</sup> and esophageal squamous cell carcinoma (ESCC) is the most common esophageal cancer in Asia. <sup>2</sup> To improve the prognosis of patients with ESCC, it is important to detect the lesion early and perform endoscopic resection (ER). <sup>3-7</sup> The early detection of ESCC requires the identification of patients at high risk of ESCC using meticulous observation of the esophagus with image-enhanced endoscopy (narrowband imaging [NBI]/blue laser imaging) or Lugol chromoendoscopy.

The soft palate is one of the most accessible and easily observed mucosal regions of the aerodigestive tract. We previously reported that 3 endoscopic findings of melanosis—whitish epithelium, and vasodilation in the soft palate—are associated with a high risk of ESCC. These 3 endoscopic findings have high positive likelihood ratios (range: 2.80-7.23) and are considered useful as indicators of ESCC.

Conventional endoscopic systems required magnified observation to evaluate vasodilation in the soft palate. However, an endoscopic system with enhanced depth-of-field (EDOF) imaging technology (GIF-EZ1500 and EVIS X1 CV-1500, Olympus Co, Tokyo, Japan) enabled us to

evaluate vasodilation in the soft palate without magnification. In addition, new image enhancement technology referred to as texture and color enhancement imaging (TXI) has the potential to improve the visibility of melanosis in the soft palate. In this case series, we present observations of the soft palate in 3 patients with early ESCC using an endoscopic system with EDOF imaging.

#### **METHODS**

Three patients with suspected ESCC underwent endoscopic examination of the soft palate using the GIF-EZ1500 endoscope (Olympus Co) and EVIS X1 CV-1500 video processor (Olympus Co).

The 3 soft palate endoscopic findings associated with the risk of ESCC are shown in Figures 1 to 3. Melanosis was defined as a dark pigmented area in the mucosa. The most common site of melanosis is the transition zone between the soft and hard palates. Whitish epithelium was defined as a white epithelium with a shaggy surface, because this finding was endoscopically similar to esophageal epidermalization, we considered it to histologically reflect hyperkeratosis or hyperparakeratosis. Vasodilation was

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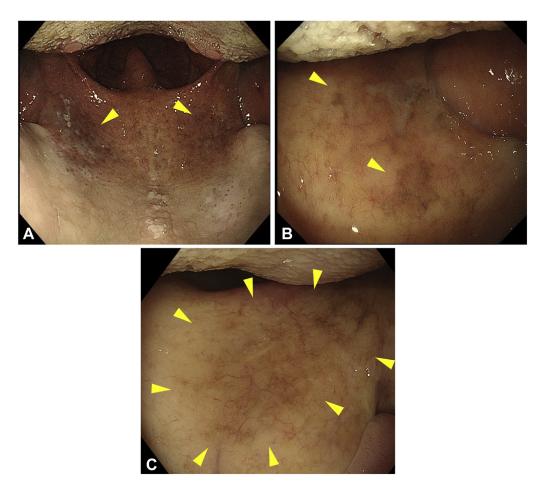


Figure 1. Endoscopic images of melanosis (yellow arrowhead) in the soft palate mucosa under white-light imaging (A-C).

defined as proliferated and dilated intrapapillary capillary loops<sup>8</sup> and was classified as diffuse or focal.

We obtained written consent for endoscopic procedures and opt-out agreement on the use of images from all patients.

## **RESULTS**

#### Case 1

A 71-year-old man underwent upper GI endoscopy in a previous clinic to investigate loss of appetite. Early ESCC was detected, and he was referred to our institute for ER of the lesion. He was a current heavy drinker (about 930 g of ethanol/week for 50 years) and heavy smoker (30 cigarettes/day for 50 years) and had a positive alcohol flushing response.

Pretreatment endoscopy at our institute revealed marked melanosis, whitish epithelium, and focal vasodilation in his soft palate (Fig. 4A, B, and C). There was a slightly depressed lesion with a diameter of 20 mm in the posterior wall of the middle thoracic esophagus (Fig. 4D). Magnifying endoscopy with NBI revealed that the lesion contained

type B1 vessels, in accordance with the magnifying endoscopic classification of the Japan Esophageal Society. <sup>12</sup> En bloc resection of the lesion was achieved by endoscopic submucosal dissection. Histologic examination revealed that the resected specimen was squamous cell carcinoma with invasion to the lamina propria, no lymphovascular invasion, and cancer-free margins.

#### Case 2

A 57-year-old woman with a history of ER for early ESCC underwent surveillance upper GI endoscopy, which detected a new ESCC. She had a history of heavy drinking (about 490 g ethanol/week for 5 years) and smoking (10 cigarettes/day for 30 years). In addition, she had a positive alcohol flushing response. Endoscopy revealed melanosis and diffuse vasodilation in her soft palate (Fig. 5A and B). We were able to evaluate the vasodilation without magnified endoscopy. In the middle thoracic esophagus, there was a flat lesion with a diameter of 30 mm covering more than half the esophageal circumference (Fig. 5C). The lesion was histologically diagnosed as a squamous cell carcinoma on biopsy examination.

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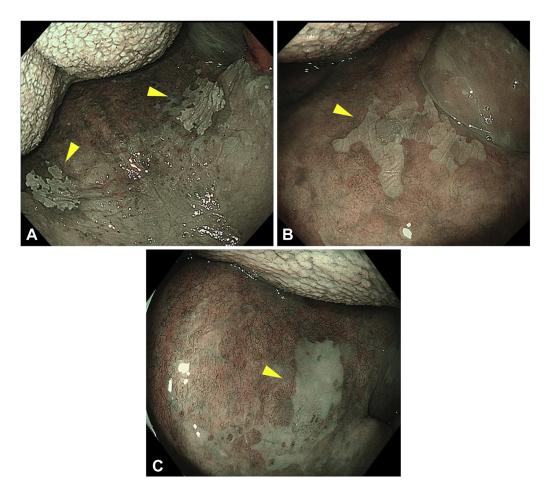


Figure 2. Endoscopic images of whitish epithelium (yellow arrowhead) in the soft palate mucosa under narrow-band imaging (A-C).

#### Case 3

A 57-year-old woman with a history of 4 ER procedures for early ESCC underwent surveillance upper GI endoscopy, which detected a new ESCC. She was a regular drinker (about 45 g ethanol/week for 36 years) and past smoker (20 cigarettes/day for 25 years). In addition, she had a positive alcohol flushing response. Endoscopy revealed melanosis and whitish epithelium in her soft palate (Fig. 6A, B, and C). The color tone of melanosis became sharpened using the TXI mode. In the middle thoracic esophagus, there was a flat lesion with a diameter of 20 mm in the anterior wall (Fig. 6D). The lesion was histologically diagnosed as a squamous cell carcinoma on biopsy examination.

#### **DISCUSSION**

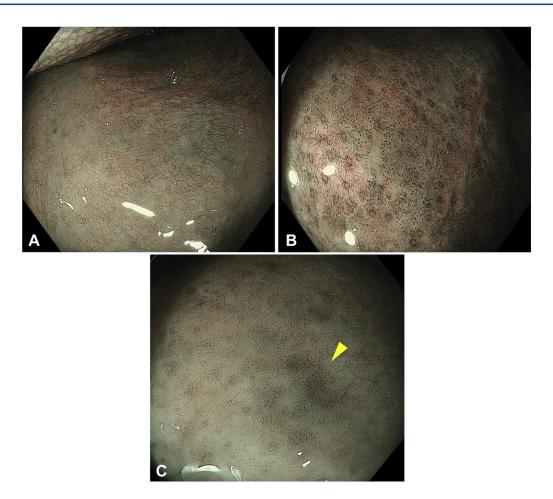
The effective detection of ESCC requires the identification of patients at high risk of ESCC and a detailed inspection of the esophagus. Heavy alcohol consumption and heavy cigarette smoking are reported as risk factors for ESCC. <sup>13</sup> However, these habits are self-reported by patients; thus, it is sometimes difficult to objectively assess

in detail the risk of ESCC associated with drinking or smoking in clinical practice. Our previous study reported 3 soft palate endoscopic findings that are useful for the objective identification of patients at high risk of ESCC and are considered indicators of ESCC.<sup>8</sup>

In the present cases, the new endoscopic system provided clearer images than the conventional system and enabled us to evaluate vasodilation in the soft palate without magnification. The endoscopic system uses EDOF technology, which combines 2 images at different focus distances into 1 image and enables the clinician to observe through continuous broad focus in real time. <sup>14</sup> EDOF technology enables the evaluation of intrapapillary capillary loops in the soft palate without magnification.

TXI is a new technology that improves color, structure, and brightness by using a white-light imaging effect. Although TXI has the potential to enhance the detection of some lesions, to our knowledge, no study has yet reported the use of TXI. We believe that TXI is useful for observation of the soft palate because it enhances the color tone of melanosis and improves visibility. However, further clinical trials are required to demonstrate the usefulness of TXI for observation of the soft palate.

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**Figure 3.** Endoscopic images of vasodilation in the soft palate mucosa under narrow-band imaging. **A,** Soft palate mucosa with no vasodilation (for comparison). **B,** Vasodilation (diffuse type). **C,** Vasodilation (focal type) (*yellow arrowbead*).

The soft palate is one of the most accessible and easily observed mucosal regions. The soft palate can be evaluated in about 10 to 20 seconds at the beginning of endoscopy. In the present 3 cases, we administered local anesthesia (2% lidocaine) and pethidine hydrochloride to enable us to observe the pharynx in detail. However, no anesthesia is required for the observation of only the soft palate.

We believe the 3 endoscopic soft palate findings suggestive of ESCC can be applied in clinical practice. Endoscopy can be used to perform an initial check of the soft palate to identify patients at high risk of ESCC. If the ESCC indicators are present, the esophagus is meticulously observed with NBI/blue laser imaging or Lugol chromoendoscopy. We believe that more endoscopists and facilities will be able to use this method because the endoscopic system with EDOF enabled us to evaluate all 3 soft palate findings without magnification. In addition, these soft palate findings are applicable during health screening or dental examinations, as the soft palate can be observed easily via visual inspection.

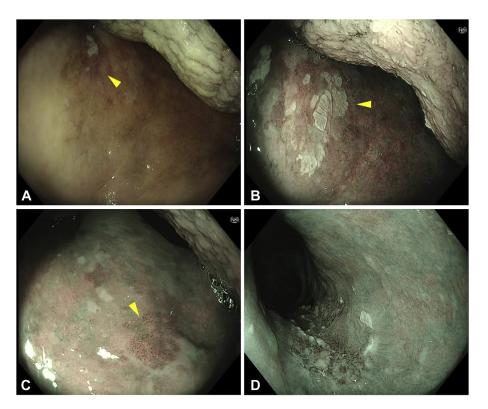
In conclusion, the endoscopic system with EDOF enabled us to evaluate for all 3 soft palate findings (melanosis, whitish epithelium, and vasodilation) associated with a high risk of ESCC, without the need for magnification. These findings have the potential to enhance the early detection of ESCC by identifying individuals at high risk of ESCC (Video 1, available online at www.giejournal.org).

## **ACKNOWLEDGMENTS**

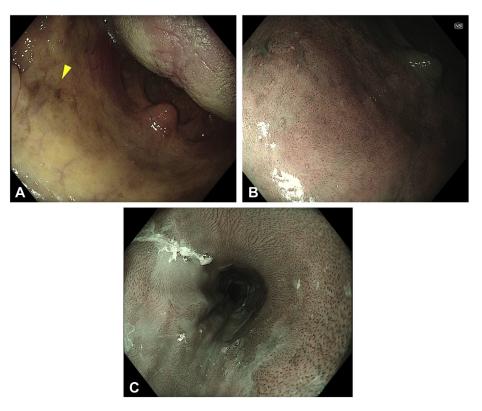
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#### **DISCLOSURE**

Dr Ishihara receives lecture fees from Olympus Co., Tokyo, Japan. All other authors disclosed no financial relationships. Video Case Series Waki et al

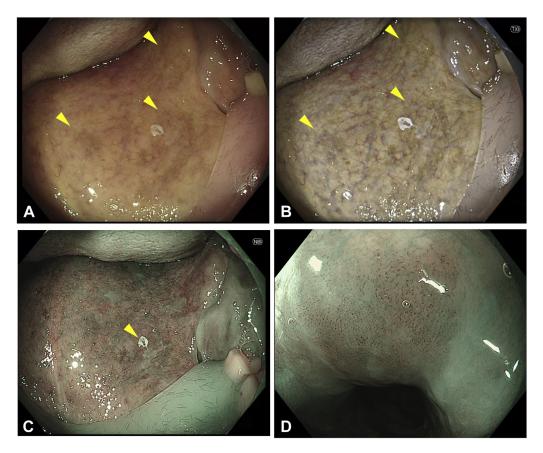


**Figure 4.** Endoscopic images of case 1 on pretreatment endoscopy for an esophageal lesion. **A,** Melanosis (*yellow arrowhead*) in the left soft palate under white-light imaging. **B,** Whitish epithelium (*yellow arrowhead*) in the left soft palate under narrow-band imaging. **C,** Vasodilation (focal type) (*yellow arrowhead*) in the right soft palate. **D,** A 20-mm early esophageal squamous cell carcinoma in the posterior wall of the middle thoracic esophagus.



**Figure 5.** Endoscopic images of case 2 on surveillance upper GI endoscopy. **A,** Melanosis (*yellow arrowhead*) in the left soft palate. **B,** Vasodilation (diffuse type); this finding could be evaluated without magnified endoscopy. **C,** A 30-mm early esophageal squamous cell carcinoma covering more than half the circumference of the middle thoracic esophagus.

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**Figure 6.** Endoscopic images of case 3 on surveillance upper GI endoscopy. **A,** Melanosis (*yellow arrowbead*) in the right soft palate under white-light imaging. **B,** Melanosis (*yellow arrowbead*) in the right soft palate under texture and color enhancement imaging. The color tone of melanosis was sharpened using texture and color enhancement imaging. **C,** Whitish epithelium (*yellow arrowbead*) in the right soft palate. **D,** A 20-mm early esophageal squamous cell carcinoma in the anterior wall of the middle thoracic esophagus.

Abbreviations: EDOF, enhanced depth-of-field; ER, endoscopic resection; ESCC, esophageal squamous cell carcinoma; NBI, narrow-band imaging; TXI, texture and color enhancement imaging.

#### REFERENCES

- Bray F, Ferlay J, Soerjomataram I, et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2018;68:394-424.
- Rustgi AK, El-Serag HB. Esophageal carcinoma. N Engl J Med 2014;371: 2499-509.
- Kodama M, Kakegawa T. Treatment of superficial cancer of the esophagus: a summary of responses to a questionnaire on superficial cancer of the esophagus in Japan. Surgery 1998;123:432-9.
- 4. Shimizu Y, Tsukagoshi H, Fujita M, et al. Long-term outcome after endoscopic mucosal resection in patients with esophageal squamous cell carcinoma invading the muscularis mucosae or deeper. Gastrointest Endosc 2002;56:387-90.
- Katada C, Muto M, Momma K, et al. Clinical outcome after endoscopic mucosal resection for esophageal squamous cell carcinoma invading the muscularis mucosae–a multicenter retrospective cohort study. Endoscopy 2007;39:779-83.
- Yamamoto S, Ishihara R, Motoori M, et al. Comparison between definitive chemoradiotherapy and esophagectomy in patients with clinical

- stage I esophageal squamous cell carcinoma. Am J Gastroenterol 2011;106:1048-54.
- Yamashina T, Ishihara R, Nagai K, et al. Long-term outcome and metastatic risk after endoscopic resection of superficial esophageal squamous cell carcinoma. Am J Gastroenterol 2013;108: 544-51
- Waki K, Ishihara R, Maekawa A, et al. Endoscopic findings in the soft palatal mucosa are associated with the risk of esophageal squamous cell carcinoma. J Gastroenterol Hepatol. Epub 2020 Oct 10.
- Ezoe Y, Fujii S, Muto M, et al. Epidermoid metaplasia of the esophagus: endoscopic feature and differential diagnosis. Hepatogastroenterology 2011;58:809-13.
- Yamanouchi S, Sako Y, Suemitsu S, et al. Early esophageal cancer with epidermization diagnosed and treated with endoscopic resection. Clin J Gastroenterol 2018;11:29-33.
- Fukui T, Sakurai T, Miyamoto S, et al. Education and imaging. Gastrointestinal: epidermal metaplasia of the esophagus. J Gastroenterol Hepatol 2006;21:1627.
- Oyama T, Inoue H, Arima M, et al. Prediction of the invasion depth of superficial squamous cell carcinoma based on microvessel morphology: magnifying endoscopic classification of the Japan Esophageal Society. Esophagus 2017;14:105-12.
- Ishiguro S, Sasazuki S, Inoue M, et al. Effect of alcohol consumption, cigarette smoking and flushing response on esophageal cancer risk: a population-based cohort study (JPHC study). Cancer Lett 2009;275: 240-6.

Video Case Series Waki et al

- OLYMPUS On-Demand Library. Available at: https://www.olympusprofed. com/gi/uppergi/24845/. Accessed January 18, 2021.
- OLYMPUS On-Demand Library. Available at: https://www.olympusprofed. com/gi/uppergi/24839/. Accessed January 18, 2021.

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