Abstract. Bronchogenic cyst is a relatively rare congenital malformation that is often identified in the mediastinum. The occurrence of bronchogenic cysts in the intramural esophagus and gastroesophageal junction is rare. The present report describes three cases of intramural bronchogenic cysts of the esophagus and gastroesophageal junction and reviews the clinicopathological features of these lesions. A 35-year-old Japanese male (Case 1), a 50-year-old Japanese woman (Case 2) and a 34-year-old Japanese man (Case 3) presented with dysphagia, pharyngeal pain and heartburn, respectively. Upper endoscopic examination revealed submucosal tumors in the esophagus (Case 1 and 2) and gastroesophageal junction (Case 3). Subsequent endoscopic examination revealed perforation of the cyst into the surface of the esophageal mucosa (Case 2). Surgical resection was performed in all cases. Histopathological examinations revealed that the submucosal cysts were covered by respiratory-type ciliated epithelium without atypia. Cartilage and bronchial glands were not observed in any of the cases. The present review of the clinicopathological characteristics of bronchogenic cysts of the esophagus and gastroesophageal junction revealed that males and females were equally affected. The median age of the patients was 34.5 years with a wide age distribution. The most common main complaint was dysphagia. A pre-operative diagnosis of bronchogenic cyst is difficult because no specific imaging features are present. As surgical resection is recommended for this lesion, recognition of the clinicopathological features of bronchogenic cysts is important for an accurate pre-operative diagnosis.

Introduction
Bronchogenic cyst is a relatively rare congenital malformation that develops from abnormal budding of the ventral foregut during the early stage of gestation (1). Histologically, the cyst wall is covered by respiratory-type ciliated epithelium that may include cartilage and bronchial glands (2). The location of the cyst is dependent on the stage of embryogenesis at which budding of the foregut occurs (1). The most common location of bronchogenic cysts is the middle and superior mediastinum, following the lung parenchyma (1.2). Unusual locations of bronchogenic cysts include the thymus, pericardium, diaphragm, esophagus, stomach, and retroperitoneum (3-10).

Intramural esophageal bronchogenic cysts are rare, and only 25 cases have been reported in the English literature since 2000 (7,8,11-25). However, some cases of bronchogenic cysts in the mediastinum perforating into the esophagus have been described (26). Intramural bronchogenic cysts in the gastroesophageal junction are extremely rare (only 6 cases have been reported in the English literature) (27-32), and because of the rarity of intramural bronchogenic cysts in the esophagus and gastroesophageal junction, their unique clinicopathological features have not been well recognized. The treatment strategy for bronchogenic cyst is complete excision to avoid recurrence and rare malignant transformation (33,34). Therefore, accurate pre-operative diagnosis is very important for treatment.

In this study, we report three new cases of intramural bronchogenic cysts in the esophagus and gastroesophageal junction and review the clinicopathological characteristics of these rare lesions.

Case report
Case 1. A 35-year-old Japanese man presented with dysphagia. Upper endoscopic examination revealed an esophageal submucosal tumor. Pre-operative computed tomography (CT) was not available in our hospital. Subsequently, thorascopic enucleation of the tumor was performed. Histopathological examination indicated that a cyst (4.5x4x3.5 cm in diameter) was located in the muscularis propria and contained exudative fluid (Fig. 1). The cyst wall was covered by respiratory
type ciliated epithelium without atypia (Fig. 1 inset). Neither cartilage nor bronchial glands were observed in the cyst wall. On the basis of these results, the patient was diagnosed with an intramural esophageal bronchogenic cyst. The post-operative course was uneventful, and the cyst did not reoccur by CT over 3 years of medical follow-up.

**Case 2.** A 50-year-old Japanese woman presented with pharyngeal pain and dysphagia. Upper endoscopic examination revealed a submucosal tumor in the esophagus, and no surface mucosal abnormality was noted. CT demonstrated a submucosal tumor in the esophagus (Fig. 2A). Subsequent endoscopic examination showed that the submucosal tumor was perforating into the esophageal lumen. Therefore, she underwent thoracoscopic subtotal esophagectomy. Histopathological examination revealed that the cyst (3.5x2 cm in diameter) was located in the muscularis propria of the esophagus, and perforated into the surface squamous mucosa of the esophagus, accompanied by lymphoplasmacytic infiltration around the cyst (Fig. 2B). The cyst wall was covered by respiratory-type ciliated epithelium without atypia, and a few goblet cells were occasionally observed (Fig. 2B, inset). Neither cartilage nor bronchial glands were observed in the cyst wall. On the basis of these clinical findings, the patient was diagnosed with an intramural bronchogenic cyst perforating into the esophagus. The post-operative course was uneventful, and the patient was free from recurrence by CT during the 3 months of medical follow-up.

**Case 3.** A 34-year-old Japanese man presented with heartburn. Upper endoscopic examination demonstrated that a submucosal tumor (4.5x3.3 cm in diameter) was located immediately under the gastroesophageal junction without a remarkable change on the surface of the gastric mucosa. Pre-operative computed tomography (CT) was not available in our hospital. Subsequently, enucleation of the tumor was performed. Histopathological analysis showed that a large cyst was present under the mucosa of the gastroesophageal junction (Fig. 3A and B) and its wall was covered by respiratory-type ciliated epithelium without atypia (Fig. 3B, inset). Neither cartilage nor bronchial glands were observed in the cyst wall. Accordingly, the patient was diagnosed as intramural bronchogenic cyst in the gastroesophageal junction. The post-operative course was uneventful, and the patient was free from recurrence by CT for 1 year of medical follow-up.

**Discussion**

In this article, we describe the clinicopathological features of three cases of intramural bronchogenic cysts in the esophagus and gastroesophageal junction. Table I summarizes the clinicopathological features of intramural bronchogenic cysts of the esophagus and gastroesophageal junction that have been reported since 2000.

Among the 34 patients, men and women were equally affected. The median age of the patients was 34.5 years with a wide age distribution (from 3 days to 71 years) (Table I). The most common chief complaint was dysphagia with discomfort and pain, and no specific complaint for this lesion is present (Tables I and II). These symptoms may appear only when the cysts become larger, leading to compression of the esophagus and gastrointestinal junction. As most patients have small
Table I. Clinicopathological features of intramural bronchogenic cysts occurring in the esophagus and gastroesophageal junction.

**A. Esophagus**

| Author, year | Case no. | Age      | Sex   | Size, cm | Chief complaint                   | Location       | Procedure     | Histological features                                      | Outcome          | (Refs.) |
|-------------|---------|----------|-------|----------|-----------------------------------|----------------|---------------|------------------------------------------------------------|------------------|---------|
| Cheng et al, 2018 | 1      | 30 years | Male  | 8x7x4    | Dysphagia, abdominal pain          | Distal esophagus | Myotomy       | Ciliated epithelium, cartilage, bronchial glands           | FFR, 3 months    | 7       |
| Lin et al, 2017  | 2      | 20 months | Male  | 1.2x1x0.4 | Recurrent vomiting                 | Distal esophagus | Laparoscopic resection | Ciliated epithelium, cartilage, bronchial glands          | FFR 7, months    | 11      |
| Han et al, 2016  | 3      | 31 years | Male  | 14.5x2.3 | Chest pain, dysphagia abdominal pain | Para-esophagus    | Thoracotomy   | Ciliated epithelium                                        | FFR 3 months     | 12      |
| Altieri et al, 2015  | 4     | 40 years | Female | 3        | Dysphagia, abdominal pain          | Lower esophagus   | Laparoscopic resection | Ciliated epithelium                                        | FFR 2 weeks      | 8       |
| Suda et al, 2015  | 5      | 3 days   | Male  | 2x1      | Inspiratory stridor                | Cervical esophagus | Myotomy       | Ciliated epithelium                                        | FFR 9 months     | 13      |
| Tang et al, 2014  | 6      | 23 years | Male  | 2.5x2    | Chest dyscomfort, dyspnea          | Distal esophagus  | Endoscopic submucosal tunnel dissection | Ciliated epithelium, cartilage, bronchial glands  | FFR              | 14      |
| Vannucci et al, 2013  | 7     | 39 years | Female | 25       | Dyspnea, palpable epigastric mass   | Thoracoabdominal  | Thoracotomy   | NA                                                        | FFR 36 months    | 15      |
| Ghibakhhlou et al, 2012  | 8     | 23 years | Female | 3x3      | Dysphagia, abdominal pain          | Distal esophagus  | Thoracotomy   | Ciliated epithelium                                        | FFR              | 16      |
| Wang et al, 2012   | 9      | 56 years | Female | 8x7x7    | Chest pain, dysphagia              | Lower paraesophagus | Thoracotomy   | Ciliated epithelium, cartilage                             | FFR 2 years      | 17      |
| Barbetakis et al, 2011  | 10    | 46 years | Male  | NA       | Dysphagia                          | Distal esophagus  | VATS          | NA                                                        | FFR              | 18      |
| Chafik et al, 2011  | 11     | 51 years | Male  | 3.6x3.1  | Dysphagia, pain                    | Lower esophagus   | Thoracotomy   | Ciliated epithelium, bronchial glands                     | FFR              | 19      |
| Turkyilmaz et al, 2007  | 12    | 48 years | Male  | 3x2x1.5  | Dysphagia                          | Distal esophagus  | Thoracotomy   | Ciliated epithelium, cartilage                             | FFR 6 months     | 20      |
| Akutsu et al, 2006  | 13     | 26 years | Male  | NA       | Dysphagia                          | Lower esophagus   | Thoracotomy   | Ciliated epithelium, cartilage                             | FFR              | 21      |
| Ko et al, 2006      | 14     | 21 years | Male  | 4        | Dysphagia, pain                    | Mid esophagus     | VATS          | Ciliated epithelium, cartilage (1/7 case)                 | FFR 2 years      | 22      |
| Ko et al, 2006      | 15     | 31 years | Female | 3.8      | Dysphagia, pain                    | Mid esophagus     | Thoracotomy   | FFR 6 years                                               |                 |         |
| Ko et al, 2006      | 16     | 19 years | Female | 3.2      | Dysphagia, pain                    | Mid esophagus     | Thoracotomy   | FFR 8 years                                               |                 |         |
| Ko et al, 2006      | 17     | 20 years | Female | 3        | Dysphagia, chest discomfort         | Mid esophagus     | Thoracotomy   | FFR 4 years                                               |                 |         |
Table I. Continued.

A. Esophagus

| Author, year | Case no. | Age   | Sex     | Size, cm | Chief complaint                     | Location         | Procedure       | Histological features | Outcome          | (Refs.) |
|--------------|----------|-------|---------|----------|-------------------------------------|------------------|------------------|-----------------------|-------------------|---------|
| Ko et al, 2006 | 18       | 34 years | Female  | 3.9      | Dysphagia, chest discomfort         | Mid esophagus    | Thoracotomy      | FFR, 7 years          | 22                |         |
| Ko et al, 2006 | 19       | 24 years | Female  | 3.6      | Dysphagia                           | Lower esophagus  | VATS             | FFR, 1 year           | 22                |         |
| Ko et al, 2006 | 20       | 60 years | Female  | 3.4      | No symptom                          | Lower esophagus  | Thoracotomy      | FFR, 14 years         | 22                |         |
| Westerterp et al, 2004 | 21 | 67 years | Male    | 6.6      | Odynophagia                         | Thoracic esophagus | Esophagectomy   | Ciliated epithelium   | FFR              | 23      |
| Westerterp et al, 2004 | 22 | 49 years | Female  | 3.1      | Dysphagia                           | Mid esophagus    | Endoscopic mucosal resection | Ciliated epithelium | FFR, 1 year | 23      |
| Westerterp et al, 2004 | 23 | 49 years | Female  | 3.3      | No symptom                          | Esophagus        | Local enucleation | Ciliated epithelium   | FFR, 1 year | 23      |
| Hallani et al, 2004 | 24 | 64 years | Male    | NA       | Chest pain                          | Distal esophagus | Thoracotomy      | NA                    | FFR              | 24      |
| Sashiyama et al, 2002 | 25 | 34 years | Female  | 5        | Dysphagia                           | Mid esophagus    | Endoscopic mucosal resection | Ciliated epithelium | FFR              | 25      |
| Present study | 26       | 35 years | Male    | 4.5x4x3.5 | Dysphagia                           | Lower esophagus  | Enucleation mucosal resection | Ciliated epithelium | FFR, 3 years | -       |
| Present study | 27       | 50 years | Female  | 3.5x2    | Pharyngeal pain and dysphagia       | Mid esophagus    | Thoracoscopic esophagectomy | Ciliated epithelium | FFR, 3 months | -       |

B. Gastroesophageal junction

| Author, year     | Case no. | Age   | Sex     | Size, cm | Chief complaint                  | Procedure                     | Histological features | Outcome          | (Refs.) |
|------------------|----------|-------|---------|----------|----------------------------------|-------------------------------|-----------------------|-------------------|---------|
| Tonouchi et al, 2016 | 1   | 32 years | Female  | 6        | No symptom                       | Laparoscopic extirpation      | Ciliated epithelium   | FFR, 3 months | 27      |
| Kurokawa et al, 2013 | 2  | 71 years | Male    | 3        | Throat discomfort                 | Laparoscopic resection        | Ciliated epithelium   | FFR, 1 year    | 28      |
| Ballehaninja et al, 2013 | 3  | 40 years | Female  | 5x3.5    | Dysphagia                        | Laparoscopic resection        | Ciliated epithelium   | FFR, 6 months | 29      |
| Fernández et al, 2011 | 4  | 33 years | Male    | 4.5x1.7  | Epigastric and right upper pain   | Laparoscopic resection        | Ciliated epithelium   | NA               | 30      |
| Díaz Nieto et al, 2010 | 5  | 67 years | Male    | 6        | Back pain                        | Laparoscopic resection        | Ciliated epithelium   | NA               | 31      |
| Melo et al, 2005  | 6       | 39 years | Female  | 4x2.5x1  | No symptom                       | Laparoscopic resection        | Ciliated epithelium   | FFR              | 32      |
| Present study    | 7       | 34 years | Male    | 4.5x3.3  | Heartburn                        | Enucleation                  | Ciliated epithelium   | FFR, 1 year    | -       |

FFR, free from recurrence; NA, not available; VATS, video-assisted thoracoscopic surgery.
asymptomatic cysts (7), the accurate morbidity of these lesions is unclear. Histopathologically, the respiratory-type ciliated epithelium was observed in all cases, and cartilage and bronchial glands were occasionally found in the cyst wall.

Accurate pre-operative diagnosis of bronchogenic cyst is very important for its appropriate treatment. The diagnosis of these lesions is challenging because they do not have specific imaging characteristics. Ko et al (22) reported the imaging characteristics of 7 cases of esophageal bronchogenic cysts. In the report, computed tomography (CT) revealed that well-defined thin-wall cystic lesions were present within the esophageal wall. Furthermore, varied cyst densities were observed (because of the content of the cyst) without enhancement after administration of a contrast agent, and no intracystic solid content or abnormal air was identified (22). However, it may be difficult to distinguish intramural bronchogenic cysts from mediastinal masses, including lymphadenopathy or mediastinal tumors, compressed against the esophageal wall (7,22). Furthermore, magnetic resonance imaging (MRI) showed variable signal intensities on T1-weighted images and a homogenous, high signal intensity on T2-weighted images (25).

Recently, endoscopic ultrasound (EUS) examination has been recognized as a useful tool for the diagnosis of bronchogenic cysts (7). EUS can identify whether the lesions of the esophagus and gastroesophageal junction are cystic or solid. Moreover, fine-needle aspiration (FNA) cytological examination using EUS can provide an even more accurate diagnosis because by this method it is possible to obtain a sample from the cyst wall. However, EUS-FNA may not be recommended for all patients with bronchogenic cysts because it can induce an infection, which would complicate the operation (7). The treatment strategy for bronchogenic cysts in the esophagus and gastroesophageal junction is complete resection (7). Therefore, a combination of the above-mentioned imaging techniques is required for an accurate pre-operative diagnosis of bronchogenic cyst.

The interesting finding of the present study is that one of bronchogenic cysts perforated into the esophageal lumen (Case 2). Only the second endoscopic examination detected the connection between the cyst and the surface mucosa of the esophagus. Therefore, secondary inflammation (probably due to infection) may have led to perforation of the cyst into the esophageal surface mucosa. Previous studies have already described an esophageal bronchogenic cyst with a connection to the surface squamous mucosa (17) and a mediastinal bronchogenic cyst perforated into the esophageal wall (26).

In conclusion, we reviewed the clinicopathological features of bronchogenic cysts in the esophagus and gastroesophageal junction. No specific symptoms or pre-operative imaging characteristics were present in this lesion, therefore, bronchogenic cyst must be added a list of differential diagnosis of the submucosal tumor of the esophagus and gastroesophageal junction. As surgical resection is recommended for this lesion, recognition of the clinicopathological features of bronchogenic cysts is important for accurate pre-operative diagnosis of this lesion.
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Availability of data and materials
All data generated or analyzed during this study are included in this published article.

Authors' contributions
HM, MI and CM conceived and designed the present study. HM, MI, CM, TM, KI, MS and KT collected and analyzed data. HM and MI drafted the manuscript and figures. All authors read and approved the final manuscript.

Ethics approval and consent to participate
The present study was conducted in accordance with the Declaration of Helsinki, and the study protocol was approved by the Institutional Review Board of Kansai Medical University Hospital (approval no. 2019050). Opt-out consent was obtained from each participant of this study.

Patient consent for publication
The need for informed consent was waived due to the retrospective design of the study, and opt-out consent was obtained from each participant of the present study.

Competing interests
The authors declare that they have no competing interests.

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