Complications following endoscopic submucosal dissection for gastric, esophageal, and colorectal cancer: a review of studies based on nationwide large-scale databases

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Abstract: Endoscopic submucosal dissection (ESD) is a relatively new procedure used for the treatment of early gastrointestinal cancers regardless of the lesion size and configuration, and it has gradually acquired popularity because of its minimally invasive nature. As compared to conventional endoscopic resection, ESD is a more complex procedure and requires a higher level of technical skill. Therefore, it is associated with a higher complication rate. Many previous studies that investigated the complication rates following ESD analyzed data from a limited number of specialized centers, possibly leading to an underestimation of the complication rates. Further, the relationship between hospital volume and complication rates is poorly understood. In the present study, we searched the MEDLINE and the Cochrane Library databases for studies that have reported on ESD-related complications and the relationship between hospital volume and ESD-related complication rates in a nationwide setting. The complication rates (including perforation, peritonitis, and bleeding) were 3.5% for gastric ESD, 3.3% for esophageal ESD, and 4.6% for colorectal ESD. The studies reviewed showed that ESD-related complication rates were permissibly low, and that there was a linear association between a higher hospital volume and a lower frequency of complications following ESD.

Keywords: Endoscopic submucosal dissection (ESD); complication rate; nationwide inpatient database

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Introduction

When it was first introduced, endoscopic submucosal dissection (ESD) was used for treating early gastric cancers in Japan (1), and it is now being used for the treatment of early esophageal cancers and early colorectal cancers. As compared to conventional endoscopic mucosal resection, ESD offers more advantages because it allows en-bloc removal for accurate histopathological evaluation regardless of the lesion size and configuration (2,3); however, ESD is a more difficult and complex procedure to perform and is therefore associated with a higher frequency of complications (4,5).

At first, the Japanese government had imposed restrictions, and ESD was only performed in specialized centers. After the effectiveness and safety of ESD were confirmed, the Japanese public healthcare insurance started to cover gastric ESD in April 2007, esophageal ESD in April 2008, and colorectal ESD in April 2012. Nowadays, ESD is performed in general hospitals as well in Japan.

Many previous studies that investigated the complication rates following ESD analyzed data from a limited number of specialized centers, possibly leading to an underestimation of the complication rates. Further, the relationship
between hospital volume and complication rates is poorly understood. Recently, several multicenter large-scale studies have analyzed the complication rates by using data from nationwide databases. Herein, we review previous studies that reported on ESD complication rates based on data obtained from nationwide databases.

**Literature search**

We searched the Medline and the Cochrane Library databases for studies that analyzed post-ESD complications in a nationwide clinical setting from 1 January 1990 to 31 October 2016. The following search terms were used: ESD and database.

The search yielded a total of 42 articles. After reviewing all the titles and abstracts, we identified 7 articles that were based on data derived from nationwide large-scale databases: 5 articles used the Diagnosis Procedure Combination (DPC) database in Japan (6-10), 1 used the Health Insurance Review and Assessment Service database in Korea (11), and 1 used the Surveillance, Epidemiology, and End Results database in the United States (12). Of these 7 articles, only 4 articles investigated complications after ESD, and all these 4 articles derived data from the Japanese DPC database.

**The DPC database**

The details of the DPC database have been described elsewhere (13). Briefly, this database includes administrative claims and hospital discharge abstract data for Japanese patients. Data were compiled from 1 July to 31 December each year from 2007 to 2010, and during the entire year for each year since 2011. In 2012, the DPC database included data for approximately 50% of all inpatient admissions to acute care hospitals. The following data are included: the hospital unique identifier; type of hospital (academic or non-academic); patient’s age and sex; diagnoses, comorbidities, and complications; surgical procedures; and discharge status. Postadmission adverse events are clearly differentiated from preadmission comorbidities. The DPC system is linked to the hospital payment system, and submission of data is mandatory in order to obtain the relevant public health insurance funding.

**Gastric ESD**

Two previous studies analyzed national data on complications after gastric ESD in Japan (6,7). Of these, the study published in 2014 reported that 27,385 gastric ESD procedures were performed in 867 hospitals between 2009 and 2011 (6). In this study, hospital volume was categorized into tertiles depending on the number of cases handled during the study period: low-volume (<50 cases), middle-volume (50–100 cases), and high-volume (>100 cases). Each hospital volume had approximately equal numbers of patients. The study showed that the total rate of ESD-related complications, including perforation, peritonitis, and bleeding, was 3.5%, and the complication rates did not differ significantly among the different hospital volume tertiles (low-volume: 3.8%, middle-volume: 3.5%, and high-volume: 3.3%; P=0.135). However, for ESD for upper gastric cancer, which requires a higher skill level, the complication rates were inversely associated with hospital volume (low-volume: 6.5%, middle-volume: 5.2%, and high-volume: 3.4%; P=0.017).

Multivariable logistic regression analysis revealed a significant association between high hospital volume and a lower complication rate after ESD for upper gastric cancers (odds ratio, 0.51; 95% CI, 0.31–0.83; P=0.007). However, no significant differences were observed in cases of middle and lower gastric cancers (6).

With regard to the time trend of ESD-related complications, a previous study that analyzed 32,943 gastric ESD cases reported that complication rates were stable between 2009 and 2011 (3.2% in 2009 vs. 3.5% in 2010 vs. 3.3% in 2011; P=0.496) (7).

**Esophageal ESD**

One study analyzed nationwide data on complications after esophageal ESD in Japan (14). Among 12,899 esophageal ESD procedures performed in 699 hospitals from 1 July 2007 to 31 March 2013, 422 (3.3%) patients had perforation and perforation-related complications after esophageal ESD (14). Among these 422 patients, 7 (1.7%) underwent open thoracotomy to treat the esophageal perforation. Hospital volume was categorized into quartiles depending on the number of cases of esophageal ESD per year: very low volume (≤8 cases), low volume (9–17 cases), high volume (18–38 cases), and very high volume (≥39 cases), and the numbers of patients in each group were almost equal.

There was a linear association between lower hospital volume and a higher rate of perforation and perforation-related complications following esophageal ESD (very low volume: 4.8%, low volume: 4.5%, high volume: 2.5%, and very high volume: 1.3%; P<0.001). Although not significant,
the frequency of blood transfusion after esophageal ESD was higher in low volume hospitals than in high volume hospitals.

Multivariable logistic regression analysis showed that a lower hospital volume and the female sex were factors associated with a higher occurrence of complications, including perforation and perforation-related disorders, in-hospital death, or the need for blood transfusion within 1 week after esophageal ESD (14).

**Colorectal ESD**

One previous study analyzed national data on complications after colorectal ESD in Japan (9). Among 7,567 colorectal ESD procedures performed in 421 hospitals during the period from 1 April 2012 to 31 March 2013, postoperative bleeding occurred in 331 (4.4%) patients (9). Hospital volumes were categorized into quartiles depending on the number of cases handled per year: very low volume (≤18 cases), low volume (19–35 cases), high volume (36–58 cases), and very high volume (≥59 cases), and the numbers of patients in each group were almost equal.

There was a linear association between low hospital volume and a higher rate of postoperative bleeding (very low volume: 6.0%, low volume: 4.2%, high volume: 3.9%, and very high volume: 3.2%; P=0.002). Perforation occurred in 13 (0.2%) patients. Although not significant, the rate of perforation occurrence was higher in low volume hospitals than in high volume hospitals (0.3% in very low volume hospitals, 0.1% in low volume hospitals, 0.2% in high volume hospitals, and 0.1% in very high volume hospitals; P=0.14).

With regard to the timing of endoscopic hemostasis after colorectal ESD, approximately 30% of the hemostatic procedures were performed on postoperative day 1, and approximately 83% were carried out within 1 week after colorectal ESD (9).

The factors associated with a higher rate of postoperative bleeding were lower hospital volume, male sex, liver cirrhosis, renal failure, and the use of antithrombotic agents. The likelihood of bleeding after colorectal ESD was 2-fold higher in patients using antithrombotic agents (9).

**Limitations of the DPC database**

We reviewed 4 observational studies that retrospectively analyzed ESD-related complications based on data obtained from the DPC database in Japan. The DPC database had several limitations. The database lacked the following information on the clinicopathological features related to ESD: lesion location, size, configuration, lesion depth, submucosal invasion, submucosal adhesion, and the presence of scar tissue. In addition, the database did not record the experience level of the endoscopists who performed the ESD procedure, types of knives used, type of insufflation gas used, and procedure duration. Further, the database did not have important information on the clinical outcomes after ESD, such as the local recurrence rate and long-term mortality. Finally, the diagnoses recorded in inpatient databases are generally less well validated as compared to those recorded in planned prospective registries.

**Conclusions**

Several studies have investigated ESD-related complications by analyzing data from nationwide large-scale inpatient databases. The studies reviewed in the present study all analyzed data from the DPC database and indicated that the ESD-related complication rates for gastric cancers, esophageal cancers, and colorectal cancers were permissibly low. In addition, they reported a linear association between a higher hospital volume and a lower complication rate following ESD.

The introduction of ESD has dramatically impacted treatment strategies for early gastrointestinal cancers, and it has gained popularity because of its minimally invasive nature. However, only a few studies have investigated complication rates following ESD by analyzing data from a multicenter nationwide large-scale database. Therefore, further studies are needed to confirm the safety of ESD for treating early gastrointestinal cancers in Japan and across the globe.

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**Footnote**

Conflicts of Interest: The authors have no conflicts of interest to declare.

**References**


