

## Circumstance of endoscopic and laparoscopic treatments for gastric cancer in Japan: A review of epidemiological studies using a national administrative database

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### Abstract

Currently, endoscopic submucosal dissection (ESD) and laparoscopic gastrectomy (LG) have become widely accepted and increasingly play important roles in the treatment of gastric cancer. Data from an administrative database associated with the diagnosis procedure combination (DPC) system have revealed some circumstances of ESD and LG in Japan. Some studies

demonstrated that medical costs or length of stay of patients receiving ESD for gastric cancer had become significantly reduced while length of hospitalization and costs were significantly increased in older patients. With respect to LG, some recent reports have shown that this has been a cost-beneficial treatment for patients compared with open gastrectomy while simultaneous LG and cholecystectomy is a safe procedure for patients with both gastric cancer and gallbladder stones. These epidemiological studies using the administrative database in the DPC system closely reflect clinical circumstances of endoscopic and surgical treatment for gastric cancer in Japan. However, DPC database does not contain detailed clinical data such as histological types and lesion size of gastric cancer. The link between the DPC database and another detailed clinical database may be vital for future research into endoscopic and laparoscopic treatments for gastric cancer.

**Key words:** Gastric cancer; Endoscopic submucosal dissection; Laparoscopic gastrectomy; Diagnosis Procedure Combination; Administrative database; Epidemiological studies

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**Core tip:** Currently, endoscopic submucosal dissection (ESD) and laparoscopic gastrectomy (LG) have become accepted for treatment of gastric cancer and increasingly played important roles on the treatments of gastric cancer in Japan. Using the database on national administrative database associated with the diagnosis procedure combination (DPC) system, the various studies with regards to ESD and LG for gastric cancer have been revealed. We herein describe the circumstance of ESD and LG for gastric cancer in Japan based on reports using Japanese administrative database associated in the DPC system in this review.

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## INTRODUCTION

Gastric cancer is one of the most frequent cancers and causes of cancer-related deaths<sup>[1,2]</sup>. Although a trend of declining incidence has been observed, gastric cancer still causes a great health care burden<sup>[3]</sup>. According to the report by the Ministry of Health, Labour and Welfare of Japan (MHLW), roughly 50000 Japanese people die due to gastric cancer annually, representing 15% of cancer-related deaths<sup>[2]</sup>. Therefore, health care policies for gastric cancer are increasingly focused on detection and treatment in the early stage because the 5-year cancer survival in the early stage of gastric cancer has been reported to be greater than 90%<sup>[4,5]</sup>. Almost half of gastric cancers have been discovered at an early stage because of early detection measures<sup>[6]</sup>.

Regarding the endoscopic treatments for early gastric cancer, endoscopic mucosal resection (EMR) was standard practice<sup>[6]</sup>. However, significant progress in endoscopic treatment has contributed to more effective resection of early gastric cancer. Endoscopic submucosal dissection (ESD) has achieved a high rate of histologically curative en bloc resection for early gastric cancer regardless of size, permitting the resection of previously non-resectable tumors. The ESD technique has spread rapidly owing to its excellent eradication rate compared with EMR<sup>[6-8]</sup>. ESD is recognized as an established endoscopic therapy for the treatment of early gastric cancer<sup>[8-10]</sup>.

Although almost early gastric cancers can be treated by ESD, the number of surgical operation for gastric cancer still remains high. Also in the field of surgical treatments, recent advances have allowed more effective and safe procedure for gastric cancer. Laparoscopic gastrectomy (LG) is significantly less invasive than open gastrectomy (OG), with lower mortality and morbidity rates<sup>[11-13]</sup>. Furthermore, LG is now performed not only as distal gastrectomy but also as proximal and total gastrectomy<sup>[11-13]</sup>. Currently, LG has been accepted for the treatment of gastric cancer, with the number of patients requiring this surgical procedure increasing in Japan, as well as other developed countries<sup>[13-15]</sup>.

Currently, endoscopic and laparoscopic treatments such as ESD and LG are increasingly playing important roles for the treatment of gastric cancer. In this review, we report the circumstances of ESD and LG for gastric cancer in Japan, based on reports using

Japanese administrative database associated with the diagnosis procedure combination (DPC) system.

## ADMINISTRATIVE DATABASE ASSOCIATED WITH THE DPC SYSTEM

### *History of the DPC system*

The health care system of Japan has severe problems owing to the expense of new medical technology and extended hospitalizations of patients<sup>[16]</sup>. To solve these problems, the MHLW started to investigate whether the case-mix classification system can be adopted to standardize medical profiling and payment<sup>[16-20]</sup>. In 2003, Japanese case-mix projects based on the DPC system were introduced to 80 university and 2 national hospitals.

DPC participating hospitals have adopted a unique reimbursement system, whereby the paid medical treatment fees become proportionally higher as the length of stay (LOS) becomes shorter. Therefore, a shorter hospitalization leads to an increase in income for the hospitals. Furthermore, payment per hospitalization is strictly determined by the DPC payment system. Currently, the number of DPC-participating hospitals has been increasing. Enormous amounts of data on hospitalization of patients have been collected annually, covering roughly 55% of the total hospitalizations, according to the report from the MHLW in 2014<sup>[21]</sup>.

### *Component of data in the DPC system*

This system collects important data during hospitalization in addition to the characteristics of the unique reimbursement system. Each patient's background information or discharge summary, which includes principal diagnosis, complications, comorbidities, and outcomes are recorded in the administrative database associated with the DPC system. These patient data are coded using the International Classification of Diseases and Injuries 10<sup>th</sup> Revision (ICD-10<sup>th</sup>) code. Also, this database includes the hospital information, number and date of clinical procedures, such as operations or drug therapies that are indexed in the original code determined by the MHLW<sup>[16-20]</sup>. Detailed contents of data in the database of the DPC system are shown in Table 1<sup>[22]</sup>.

### *Collection and use of DPC data*

Comprehensive surveys of DPC-participating hospitals are conducted by the DPC research group that has worked on the DPC data utilization project for research purposes, independently of the MHLW. DPC-participating hospitals sent the anonymized and provided detailed data to the DPC research group, which then sent to the server in the DPC research group. Using the sent data from DPC-participating hospitals, many studies have been reported in the various fields of medical research<sup>[16-20,23-26]</sup>.

**Table 1** Contents of data in the national administrative database<sup>[22]</sup>

Hospital information
Location of hospital
Number of beds
Patient background information
Age
Sex
Zip code
Diagnoses
Main diagnoses (coded with International Classification of Diseases and Injuries 10 <sup>th</sup> Revision (ICD-10 <sup>th</sup> ) code)
Main diagnoses (coded with the ICD-10 <sup>th</sup> codes)
Complications after admission (coded with the ICD-10 <sup>th</sup> codes)
Procedures for patients
Surgery, anesthesia and other procedures (coded with the Japanese original codes)
Drugs and devices (coded with the Japanese original codes)
Dates of each procedure
Dates of use for each drug and device
Admission and discharge data
Urgent or elective admission
Ambulance service use
Dates of admission and discharge; length of stay
Discharge status (discharge to home, rehabilitation hospital or other facility, or death)
Claim data
Total charge
Itemized charges for hospitalization, medication, examination, surgery and others
Other clinical data
Height/body weight
Smoking index
Pregnancy
Japan Coma Scale at admission
TNM classification of malignant tumors
Activity of Daily Living scale
Modified Rankin scale
Hugh-Jones classification of respiratory status
New York Heart Association classification of heart failure symptoms
Canadian Cardiovascular Society classification of angina pectoris
Killip classification of acute myocardial infarction
Severity classification of community-acquired pneumonia
Child-Pugh classification of liver cirrhosis
Severity classification of acute pancreatitis
Burn index
Global Assessment of Functioning scale

indicated that complications of ESD remained low. Therefore, the decrease in complication rates may suggest that the number of experienced endoscopists has been increasing between the early and late 2000s, and their technical skill level in ESD has been favorably stable from 2009 to 2011. In addition, the LOS and medical costs of patients had become significantly reduced in Japan (10.5 d in 2009 vs 9.8 d in 2010 vs 9.5 d in 2011 and 6768.4 US dollars in 2009 vs 6507.7 US dollars in 2010 vs 6427.6 US dollars in 2011;  $P < 0.001$ , respectively)<sup>[27]</sup>. The efficiency of ESD for gastric cancer as well as stable technical skills has been progressing in Japan.

**Outcomes of ESD in high-volume hospitals:** With respect to the report about hospital characteristics such as hospital volume, ESD-related complications were significantly lower in higher-volume hospitals (> 100 cases between 2009 and 2011) than lower (< 50 cases) or medium-volume hospitals (50-100 cases) in upper gastric cancer (6.5% in lower-volume hospitals vs 5.2% in medium-volume hospitals vs 3.4% in higher-volume hospitals;  $P = 0.017$ )<sup>[30]</sup>. Multivariate logistic regression analysis also revealed that high-volume hospitals were significantly associated with a decrease of relative risk of ESD-related complications in upper gastric cancer [odds ratio (OR) for higher-volume hospitals 0.51; 95% confidence interval (CI), 0.32-0.81,  $P = 0.005$ ]. Meanwhile, no significant differences for ESD-related complications were seen for middle and lower gastric cancers among the different hospital volume categories ( $P > 0.05$ )<sup>[30]</sup>. Some previous studies also pointed out that a higher skill level with ESD is required for upper gastric cancers than for middle or lower gastric cancers<sup>[31-33]</sup>. Higher volume hospitals were more likely to have experienced endoscopists can provide sufficient treatment, which significantly contributed to fewer complications or shorter LOS<sup>[34,35]</sup>. Thus, it is reasonable that the decreases in ESD-related complications and in LOS of patients with upper gastric cancer were observed at higher-volume hospitals.

## EPIDEMIOLOGICAL STUDIES ON ESD FOR GASTRIC CANCER USING DPC DATABASE

### ESD for gastric cancer (Table 2)

**Time trend of outcomes of ESD in Japan:** According to the report about the time trend of outcomes of ESD in Japan, the rate of ESD-related complications was stable (3.2% in 2009 vs 3.5% in 2010 vs 3.3% in 2011,  $P = 0.496$ ) between 2009 and 2011<sup>[27]</sup>. In the early 2000s, some clinical studies in single centers reported that the complication rate of ESD was from 5% to 8%<sup>[28,29]</sup>. However, the complication rate of ESD based on an administrative database was approximately 3% between 2009 and 2011, which

### Comparison between non-elderly and elderly patients treated by ESD:

A comparison between elderly (80 years or more) and non-elderly patients (less than 80 years) regarding outcome of ESD was also reported<sup>[36]</sup>. A recent study revealed that there was no statistically difference with regard to ESD-related complications (3.9% vs 4.3%,  $P = 0.152$ )<sup>[36]</sup>. The findings about complications of ESD has been consistent with those of some previous studies in Japan<sup>[37,38]</sup>. Kakushima *et al.*<sup>[37]</sup> showed that the complication rate of ESD in elderly patients was not significantly different from that in non-elderly patients, while Tokioka *et al.*<sup>[38]</sup> also reported that the occurrences of perforations during ESD were similar in non-elderly and elderly patients. However, length of hospitalization and direct costs during hospitalization

**Table 2** Reports of endoscopic and laparoscopic treatments for gastric cancer using national administrative database

	No. of patients	No. of hospitals	Study period	Investigated outcomes
Endoscopic submucosal dissection				
Murata <i>et al.</i> <sup>[27]</sup>	32943	907	2009-2011	Complications, length of stay, and medical costs
Murata <i>et al.</i> <sup>[30]</sup>	27385	867	2009-2011	Complications and length of stay
Murata <i>et al.</i> <sup>[36]</sup>	27385	867	2009-2011	Complications, length of stay, and medical costs
Laparoscopic gastrectomy				
Yasunaga <i>et al.</i> <sup>[40]</sup>	9388	805	2010	Complications, length of stay, medical costs, in-hospital mortality and 30-d readmission rates
Kuwabara <i>et al.</i> <sup>[41]</sup>	17761	258	2006-2008	Length of hospital stay, medical costs and operative time
Murata <i>et al.</i> <sup>[42]</sup>	14006	744	2009-2011	Complications, length of stay, medical costs and in-hospital mortality
Kuwabara <i>et al.</i> <sup>[46]</sup>	3054	420	2007	Complications and operative time
Kuwabara <i>et al.</i> <sup>[47]</sup>	3914	258	2006-2008	Complications, length of stay, medical costs, in-hospital mortality and blood transfusions
Ryu <i>et al.</i> <sup>[48]</sup>	209	5	2007-2008	Length of hospital stay (pre and post operative) and duration of antibiotic administration and post operative fasting

were significantly increased in elderly patients requiring ESD for gastric cancer, compared with non-elderly patients (12.2 d vs 9.3 d and 7346.3 US dollars vs 6295.6 US dollars;  $P < 0.001$ , respectively). The growing life expectancy and an aging population will unavoidably lead to an increasing number of elderly patients in Japan<sup>[39]</sup>. Therefore, providing appropriate care in endoscopic treatments for elderly patients is becoming significantly important in Japan. More efficient medical implementation for elderly patients with gastric cancer treated with ESD will be required in the future.

### LG for gastric cancer

**Comparison between LG and OG for gastric cancer:** Using the data in 2010, Yasunaga *et al.*<sup>[40]</sup> reported that patients treated by LG had shorter LOS compared with those with OG (13 d vs 15 d,  $P < 0.001$ ) while no significant difference was observed in mortality and occurrence of postoperative complications (LG vs OG, 0.36% vs 0.28%,  $P = 0.80$  and 12.9% vs 12.6%,  $P = 0.73$ , respectively). Kuwabara *et al.*<sup>[41]</sup> also reported that LG offered a significant economic advantage over OG (14405 US dollars vs 17260 US dollars,  $P < 0.001$ ). These results show that LG has been a beneficial treatment for patients who require surgical resection for gastric cancer.

**Influence of additional laparoscopic cho-lecystectomy on outcomes of LG for gastric cancer:** A recent report revealed that adding laparoscopic cholecystectomy did not influence to outcomes of patients undergoing LG for gastric cancer (OR for laparoscopy-related complications 1.02, 95%CI: 0.84-1.24,  $P = 0.788$  and OR for in-hospital mortality 1.16, 95%CI: 0.49-2.76,  $P = 0.727$ )<sup>[42]</sup>. These results have been consistent with previous studies in other developed countries<sup>[43,44]</sup>. The greater surgeon's experience and continuing technical progress for laparoscopic resection has resulted in expanded indications in Japan<sup>[42]</sup>. Besides, there has been an increase in the types of

surgical operations together with laparoscopic procedure, and the number of surgeons interested in simultaneous laparoscopic procedures has increased<sup>[45]</sup>. Thus these results indicate that the combined LG and cholecystectomy is safe procedure for patients with both gastric cancer and gallbladder stones.

### Impact of hospitals and regional differences for outcomes of LG for gastric cancer in Japan:

With regard to hospital characteristics in LG for gastric cancer, several studies reported that higher-volume hospitals had shorter operation times and postoperative LOS of patients compared with low case-volume hospitals<sup>[46,47]</sup>. In an analysis of regional differences in LG for gastric cancer, Ryu *et al.*<sup>[48]</sup> reported that there were significant differences with respect to rate of laparoscopic resection or duration of antibiotic administration between cancer centers of different regions. In addition, their report revealed that significant variation in pre- or postoperative LOS was observed between hospitals. Such reports could contribute to the quality of medical care for patients, which could have significant implications for decision making of health care policy in Japan.

### ADVANTAGE OF EPIDEMIOLOGICAL STUDIES USING DPC DATABASE

Unlike the single center study, these studies have been conducted based on a nationally representative sample of patients in a community setting. One of the advantages of the clinical epidemiological studies using DPC data is that they facilitated evaluation of a large sample of patients in unbiased manner<sup>[16-20]</sup>. Usually, ESD and LG are performed in hospitals that have more experienced endoscopists or surgeons as well as more resources or available facilities. The DPC participating hospitals play important roles in providing advanced care or medical studies, as well as educating students and medical residents<sup>[16-20]</sup>. Furthermore, medical data with regards to proce-

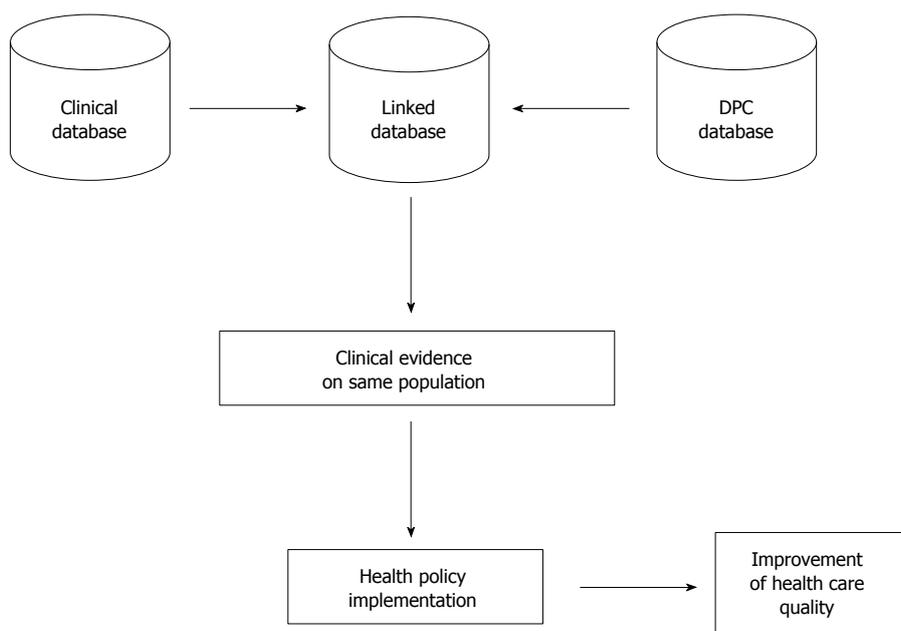


Figure 1 Framework for future clinical epidemiological studies. DPC: Diagnosis procedure combination.

dures or medications have been extensively indexed with original codes<sup>[16-20]</sup>. These data are recorded on a daily basis for each patient<sup>[16-20]</sup>. Therefore, this administrative database also enables to evaluate the clinical outcomes with detailed medical treatments, in particular for medical economic outcomes. The epidemiological studies using the DPC database directly reflect the present circumstances of endoscopic or surgical treatment for gastric cancer in Japan.

## LIMITATIONS OF EPIDEMIOLOGICAL STUDIES USING DPC DATABASE

Some potential limitations of clinical epidemiological studies using DPC data also should be acknowledged. This database does not contain patient data such as lesion size, histological type and staging of gastric cancer. It is reasonable that the lack of these data may influence the results of the studies using the DPC database. In addition, the types of devices for ESD or the kinds of stapling devices used for laparoscopic resection have not been included in the DPC database. Therefore, DPC data may be currently unsuitable to the detailed clinical investigation of ESD and LG for gastric cancer.

## FUTURE IMPLEMENTATION

To resolve the lack of detailed clinical data, a link between our database and the other database may be vital for future research about ESD and LG for gastric cancer in Japan. The Japanese Gastric Cancer Association (JGCA) began a project to register patients who were treated by ESD since 2011<sup>[49]</sup>. In addition, some

studies has been reported using the data of the National Clinical Database (NCD)<sup>[50,51]</sup>. The results from the database of this project will be useful information for the quality of ESD and LG for gastric cancer in the near future. However, we consider that more valuable information can be produced by a link between our administrative database and the database in this project. For example, the Surveillance, Epidemiology and End Results program of cancer registries, which is a cancer registry database in the United States, has been linked to the Medicare Claim Database, a payment system for medical services. As a result, many clinical studies have reported using these linked databases<sup>[52]</sup>. Therefore, we believe that a link between our database and the database of the JGCA or NCD may be vital for future research for ESD and LG for gastric cancer in Japan. If this is carried out, more valuable information showing the favorable quality of ESD for gastric cancer can be expected in patients who undergo ESD and LG for gastric cancer (Figure 1).

## CONCLUSION

From recent studies using the national administrative database, the various circumstances of endoscopic and laparoscopic treatments for gastric cancer are revealed. These findings are useful for future studies of the treatments of gastric cancer, which could in turn have important implications for care of patients with gastric cancer in Japan. However, this administrative database is still lacking detailed clinical data of gastric cancer. The link between the administrative database and the other detailed clinical database may be vital for future research into endoscopic and laparoscopic treatments for gastric cancer in Japan.

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