ORIGINAL ARTICLE

Multivariate Analysis of Factors Influencing Length of Hospitalization and Medical Costs of Cholecystectomy for Acute Cholecystitis in Japan: A National Database Analysis

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Little information is available on the factors influencing length of stay (LOS) in hospital and medical costs during hospitalization associated with cholecystectomy for acute cholecystitis. We determined the independent factors affecting LOS and medical costs of patients who underwent cholecystectomy for acute cholecystitis based on data from the Diagnosis Procedure Combination (DPC) database. In 2008, a total of 2176 patients with acute cholecystitis were referred for cholecystectomy to 624 hospitals in Japan. We collected patient characteristics and data on treatments for acute cholecystitis using the DPC database and identified independent factors affecting LOS and medical costs during hospitalization using multiple linear regression models. Analysis revealed that early cholecystectomy was significantly associated with a decrease in LOS, whereas longer preoperative antimicrobial therapy was significantly associated with an increase of LOS: the standardized coefficient for early cholecystectomy was −0.372 and that for preoperative antimicrobial therapy was 0.353 ($P < 0.001$). These procedures were also significant independent factors with regard to medical costs during hospitalization: the standardized coefficient for early cholecystectomy was −0.391 and that for preoperative antimicrobial therapy was 0.335 ($P < 0.001$). Early cholecystectomy significantly reduces the LOS and medical costs of cholecystectomy for acute cholecystitis, while preoperative antimicrobial therapy increases LOS and medical costs during hospitalization. These results highlight the need for health care implementations such as promotion of early cholecystectomy, appropriate use of antimicrobial drugs, and centralization of patients with cholecystectomy for acute cholecystitis in Japan.
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***Keywords*: acute cholecystitis, health care costs, cholecystectomy, antimicrobial therapy, database**

Introduction

Acute cholecystitis is an acute inflammatory disease of the gallbladder usually caused by bacterial infection and biliary tract obstruction.[1,2] In the United States, acute cholecystitis afflicts more than 20 million people annually and results in direct costs of more than US$6.3 billion.[2,3] According to a comprehensive survey of health

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and welfare in Japan, the number of those with acute cholecystitis increased by approximately three times between the 1970s and 1990s.[4] Acute cholecystitis is one of the most frequently encountered conditions in daily medical practice in developed countries.

Cholecystectomy is widely performed in many countries as a surgical treatment for acute cholecystitis.[5–8] In particular, laparoscopic cholecystectomy has been increasingly adopted as the standard method of surgery over the past 15 years, and the safety and efficacy of this surgical approach have been confirmed by many studies.[6–8] Furthermore, laparoscopic cholecystectomy is recognized as a cost-effective treatment for patients with acute cholecystitis.[8–10] Zacks et al.[9] reported that laparoscopic cholecystectomy significantly reduced hospital costs as well as length of stay (LOS) and mortality compared with open procedures. Therefore, laparoscopic cholecystectomy is a significant advance in health care quality for patients with acute cholecystitis.[9,10]

Little information is available on the factors influencing LOS in hospital and medical costs during hospitalization associated with cholecystectomy for acute cholecystitis. In addition, there have been no reports of analyses of LOS and medical costs based on hospital discharge data taking into account patient characteristics, other treatments for the management of acute cholecystitis, and the type of cholecystectomy. Determination of independent factors that affect LOS and medical costs during hospitalization of patients who undergo cholecystectomy for acute cholecystitis could benefit the quality management of patient medical care and could have significant implications for health care policy decision making in Japan.

In this study, we determined the factors affecting LOS and medical costs during hospitalization of patients undergoing cholecystectomy for acute cholecystitis. This was achieved using the national administrative database developed in a Japanese case-mix system project named Diagnosis Procedure Combination (DPC).

Materials and Methods

Administrative database associated with the DPC system

In Japan, the health care system has severe financial issues due to expensive advances in medical technology, a rapidly aging society, and extended patient hospitalizations.[11] To address these issues, the Ministry of Health, Labour and Welfare and its affiliated research institute have begun investigating whether the Japanese case-mix classification system can be used to standardize medical profiling and payment.[11] In 2003, this resulted in Japanese case-mix projects based on the DPC system being introduced to 82 academic hospitals (the National Cancer Center, the National Cardiovascular Center, and 80 university hospitals).[12–14] Reimbursement of insurance based on the DPC system is common practice in Japan. The number of acute care hospitals has increased in the administrative database of the DPC system. Data from approximately 450,000 inpatients have been collected as of 2007, and these make up approximately 90% of the total acute care inpatient hospitalizations during this time.[12–14]

Each patient's financial data, claim information, and discharge summary, including principal diagnosis, complications, and comorbidities during hospitalization, are recorded in the administrative database of the DPC system. These data are coded according to the International Classification of Diseases and Injuries 10th Revision (ICD-10). This administrative database also contains comprehensive medical information, including all interventional and surgical procedures, medications, and devices that have been indexed in the original Japanese code. The Ministry of Health, Labour and Welfare of Japan assigns these codes (e.g., laparoscopic cholecystectomy is defined as K672-2 in the original code).[11–14] The administrative database of the DPC system contains total medical costs, including all costs for each completed procedure. These costs are obtained using a standardized fee-for-service payment system and are recorded in the nationally uniform fee table.[15] The date and the amount of care delivered that day are also recorded in the DPC administrative database.[11–15]

Study setting

We selected 2176 patients diagnosed with acute cholecystitis who underwent cholecystectomy during hospitalization in 624 DPC participating hospitals (56 academic and 568 community hospitals) between April and December 2008. These hospitals are dispersed throughout Japan and play a leading role in providing acute care medicine, advancing medical research, and educating students and medical residents.[11–15] The principal diagnosis of acute cholecystitis was recorded using the ICD-10 code; in the present analysis, acute cholecystitis was coded as K810.

The use of DPC data was permitted by all institutions and hospitals that provided detailed data. The research protocol of the study was approved by the ethics committee of medical care and research of the University of Occupational and Environmental Health, Kitakyushu, Japan.

Study variables

Study variables included the type of cholecystectomy (laparoscopic or open procedures), the timing of cholecystectomy (early or delayed procedures), cholecystectomy-related complications, age, sex, chronic comorbid conditions, use of ambulance transportation and the intensive care unit (ICU), hospital type and size, in-hospital mortality, LOS, and medical costs during hospitalization.

Early cholecystectomy was defined as cholecystectomy performed within 4 days of admission, as described in previous studies.[16,17] Cholecystectomy-related complications were defined as any of the following ICD-10 codes: cholecystectomy-related complications (T80-T87); bowel obstruction (K650, K658-9, K660, and K913); and peritonitis (K560, K562, and K565-7).[18] Age categories were stratified as follows: less than 50 years, 50–59 years, 60–69 years, 70–79 years, and 80 years or more. The Charlson Comorbidity Index (CCI) was used to determine the severity of chronic comorbid conditions. The CCI is widely used for measuring comorbidity and has been previously validated.[11,13–15] The CCI score was calculated for each patient; previous studies have demonstrated an association between the CCI and the ICD-10 code.[19] The CCI score represented the score of all types of comorbidity, and we initially analyzed it as a continuous variable. However, to simplify the results, we established three categories of severity of comorbidity for categorical variables as follows: 0=mild; 1=moderate; and ≥2=severe.[11,13–15] We classified the type of hospital as academic or community. We also categorized the size of hospitals into three groups based on the number of hospital beds as follows: small (<200 beds), medium (200–600 beds), and large (>600 beds).[15] Regarding the analysis of medical costs, we assumed a yen-to-dollar exchange rate of approximately 80 yen to the US dollar (October 2012).

In addition, we collected data in the DPC database with regard treatments for acute cholecystitis other than cholecystectomy, i.e., intravenous antimicrobial therapy and gallbladder drainage (endoscopic or percutaneous procedures). In this study, we classified the preoperative and postoperative administration of intravenous antimicrobial drugs and calculated the duration of antimicrobial therapy for each patient. Regarding the selection of these treatments, we referred to the Tokyo Guidelines for acute cholecystitis.[7,20,21]

Statistical analysis

For tests of statistical significance, we used the chi-square test for categorical data and the Mann–Whitney *U* test for continuous variables. For the main analyses of LOS and medical costs during hospitalization, multiple linear regression models were used to identify the independent factors for patients that affected LOS and medical costs. These models addressed potential confounding variables in the case mix data by controlling for the severities of chronic comorbid conditions and additional factors related to LOS and medical costs during hospitalization, such as types and timing of cholecystectomy, cholecystectomy-related complications, age, sex, use of ambulance transportation and the ICU, duration of preoperative and postoperative intravenous antimicrobial therapy, gallbladder drainage, and hospital type and size. We also performed a stratified analysis to take into account the severity of acute cholecystitis using data for hospital type and size. Because the distributions of LOS and medical costs during hospitalization were skewed to the right, LOS and medical costs were log-transformed in this model. In addition, the variance inflation factor (VIF) was used as a measure for the degree of multicollinearity of each independent variable with the other independent variables in a regression model.

A value of $P < 0.05$ was considered significant. All statistical analyses were performed using the STATA statistical software package version 11.0 (Stata Corporation, College Station, TX, USA).

Results

A total of 2126 patients who had undergone cholecystectomy for acute cholecystitis were identified for this study: 1271 patients underwent laparoscopic cholecystectomy and 855 patients underwent open cholecystectomy across 624 hospitals. The in-hospital mortality after admission was 0.7%, while the in-hospital mortality within 30 days after admission was 0.4%. The mean LOS of all patients was 21.1 ± 17.3 days and the mean medical cost was US$12,341.5 ± US$14,083. The breakdown of LOS and medical costs during hospitalization is shown in **Figure 1A and B**.

The clinical characteristics and presentations of the patients are shown in **Table 1**. Patients who underwent laparoscopic cholecystectomy were significantly more likely to have had early cholecystectomy ($P < 0.001$). There was no significant difference with regard to the proportion of cholecystectomy-related complications and male patients between procedures. Use of the ICU was significantly higher in patients who had open cholecystectomy than in those who had laparoscopic procedures (19.3% vs. 7.4%, $P < 0.001$). Regarding other treatments for acute cholecystitis, patients who had open cholecystectomy underwent longer postoperative antimicrobial therapy and more gallbladder drainage before cholecystectomy compared with those who had laparoscopic cholecystectomy ($P < 0.001$). The in-hospital mortality of patients was significantly higher in patients who underwent open cholecystectomy compared with those who underwent laparoscopic cholecystectomy (1.5% vs. 0.1%, $P < 0.001$). A significant variation of mean LOS and medical costs during hospitalization was observed between groups ($P < 0.001$). The mean LOS and costs during hospitalization were significantly higher for delayed procedures than for early procedures for both laparoscopic and open procedures ($P < 0.001$; **Fig. 2A and B**).

Multiple linear regression analyses of factors associated with hospital LOS are presented in **Table 2**. The largest VIF among all the variables was 2.80 (patients aged 80 years or more), indicating little need for concern regarding problems caused by multicollinearity. After

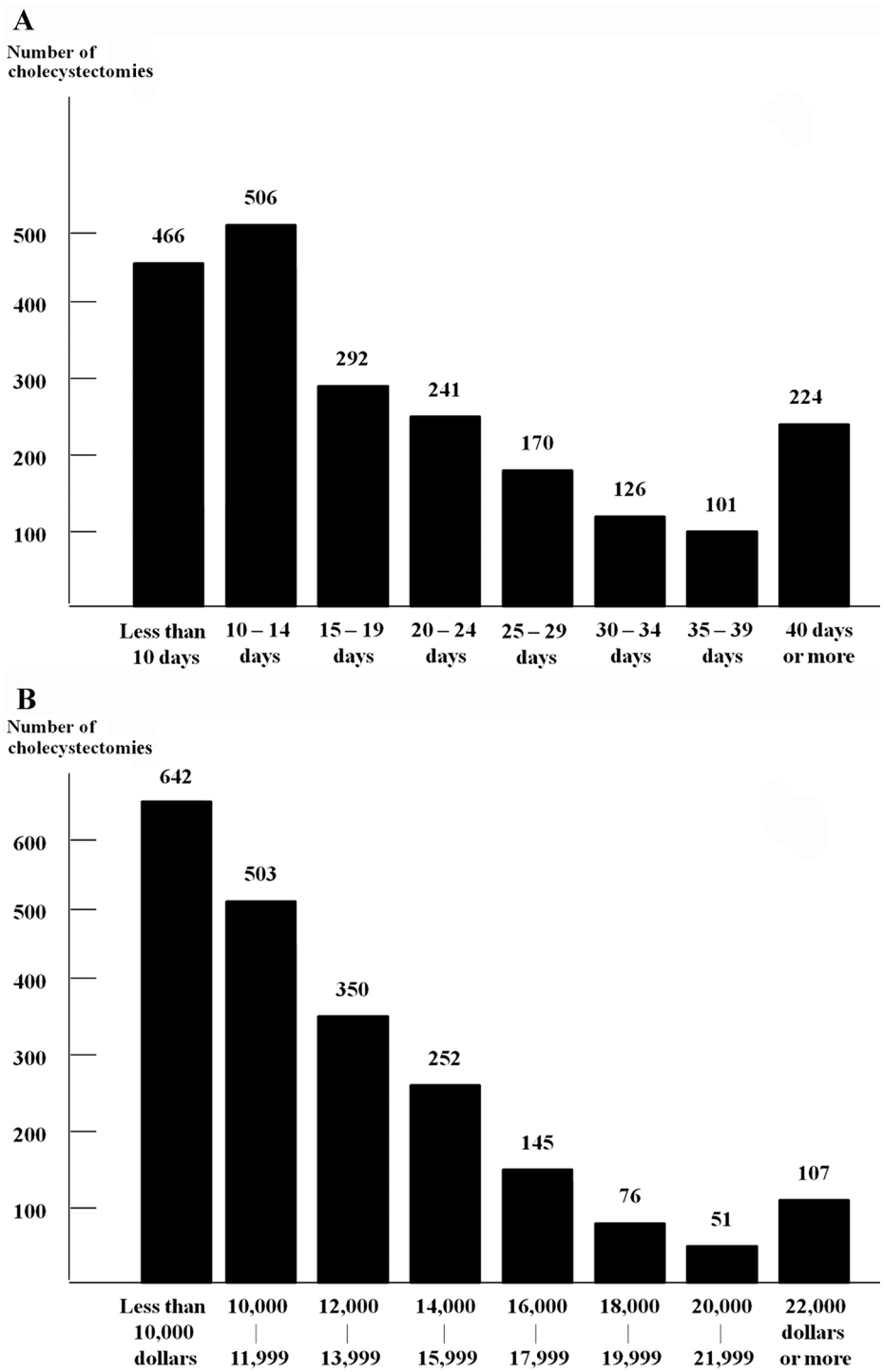

Fig. 1 The length of stay (LOS) and medical costs during hospitalization.
Breakdown of the data for hospital LOS (A) and medical costs during hospitalization (B).

adjustment for potentially confounding demographic and clinical variables, early cholecystectomy was most significantly associated with a decrease in LOS. The standardized coefficient for early cholecystectomy was −0.372 ($P < 0.001$). In addition, laparoscopic cholecystectomy was also associated with a decrease in LOS with a standardized coefficient of −0.184 ($P < 0.001$). These results indicate that LOS was significantly shorter in patients

Table 1 Clinical characteristics and presentations of patients based on Japanese national administrative database

	Laparoscopic cholecystectomy (n = 1271)	Open cholecystectomy (n = 855)	*P* value
Cholecystectomy			
Timing of cholecystectomy (%)			
Early (within 4 days)	50.3	42.3	<0.001
Delayed (5 days or more)	49.7	57.7	
Cholecystectomy-related complications (%)	1.6	1.8	0.766
Patient characteristics			
Age categories (%)			
Less than 50 years	10.2	10.1	0.479
50–59 years	11.1	12.5	
60–69 years	21.6	18.8	
70–79 years	29.3	28.9	
80 years or more	27.8	29.7	
Sex (%)			
Male patients	56.1	57.6	0.498
Severity of comorbid conditions (%)			
Mild (CCI, 0)	64.4	49.8	<0.001
Moderate (1)	18.5	25.2	
Severe (2 or more)	17.1	25.0	
Ambulance transportation (%)	17.9	16.7	0.465
Use of intensive care unit (%)	7.4	19.3	<0.001
Other treatments for acute cholecystitis			
Antimicrobial therapy			
Preoperative administration (days, SD)	5.3 (5.9)	5.6 (7.0)	0.248
Postoperative administration (days, SD)	3.9 (4.4)	6.3 (6.7)	<0.001
Gallbladder drainage before cholecystectomy (%)	21.4	33.5	<0.001
Hospital characteristics			
Hospital type (%)			
Academic hospitals	10.3	11.4	0.448
Community hospitals	89.7	88.6	
Hospital size (%)			
Small (< 200 beds)	23.1	22.2	0.008
Medium (200–600 beds)	54.0	60.0	
Large (> 600 beds)	22.9	17.8	
Clinical outcomes			
In-hospital mortality (%)	0.1	1.5	<0.001
Mean length of stay (days, SD)	18.3 (15.0)	25.2 (19.4)	<0.001
Mean medical costs (dollars, SD)	10765.1 (11824.4)	14684.9 (16626.1)	<0.001

CCI, Charlson comorbidity index; SD, standard deviation.

who underwent early cholecystectomy or laparoscopic cholecystectomy. Conversely, longer preoperative antimicrobial therapy was significantly associated with an increase in LOS with a standardized coefficient of 0.353 ($P < 0.001$). Furthermore, longer postoperative antimicrobial therapy was also associated with an increase in LOS with a standardized coefficient of 0.312 ($P < 0.001$). Patients aged 70–79 years and those aged 80 years or more, moderate and severe comorbid conditions, use of an ICU, and gallbladder drainage were slightly associated with an increase in LOS.

Early cholecystectomy and laparoscopic cholecystectomy were also considerably associated with a decrease in medical costs during hospitalization (**Table 3**). The standardized coefficient for early cholecystectomy was −0.391, while that for laparoscopic cholecystectomy was −0.187 ($P < 0.001$). Medium-sized and large hospitals were slightly associated with a decrease in medical costs

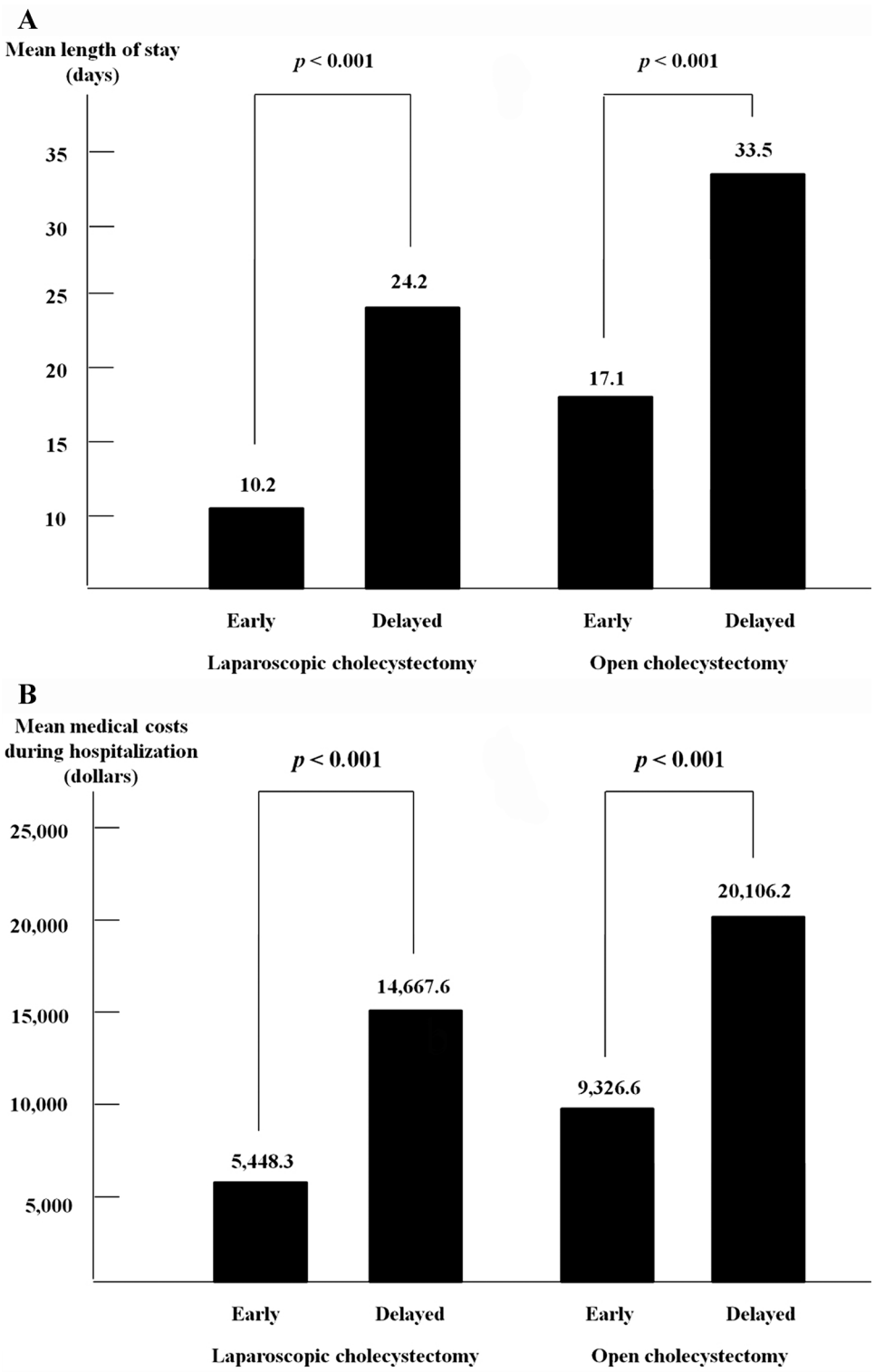

Fig. 2 Effect of early and delayed procedures on mean LOS and medical costs during hospitalization.
Effect of early and delayed procedures for both laparoscopic and open cholecystectomies: Mean hospital LOS (A) and mean medical costs during hospitalization (B).

Table 2 Linear regression analysis of factors associated with log-transformed length of hospitalization

Independent variables	Unstandardized coefficient	95% confidence interval	Standardized coefficient	*P* value
Kinds of cholecystectomy				
Laparoscopic cholecystectomy	– 0.256	[– 0.296, – 0.216]	– 0.184	<0.001
(Reference: open cholecystectomy)				
Timing of cholecystectomy				
Early cholecystectomy	– 0.523	[– 0.567, – 0.480]	– 0.372	<0.001
(Reference: delayed cholecystectomy)				
Cholecystectomy-related complications				
Occurred	0.057	[– 0.084, 0.199]	0.010	0.428
(Reference: did not occur)				
Age				
50–59 years	0.004	[– 0.027, 0.109]	0.026	0.245
60–69 years	0.038	[– 0.029, 0.106]	0.025	0.267
70–79 years	0.075	[0.003, 0.146]	0.044	0.039
80 years or more	0.099	[0.019, 0.179]	0.046	0.014
(Reference: less than 50 years)				
Sex				
Male patients	– 0.001	[– 0.039, 0.036]	– 0.001	0.928
(Reference: female patients)				
Severity of comorbid conditions				
Moderate conditions	0.067	[0.019, 0.114]	0.040	0.005
Severe conditions	0.130	[0.082, 0.179]	0.077	<0.001
(Reference: mild conditions)				
Ambulance transportation				
Used	0.024	[– 0.024, 0.074]	0.013	0.328
(Reference: not used)				
Intensive care unit				
Used	0.086	[0.027, 0.145]	0.041	0.004
(Reference: not used)				
Antimicrobial therapy				
Preoperative administration (per day)	0.037	[0.034, 0.041]	0.353	<0.001
Postoperative administration (per day)	0.038	[0.035, 0.042]	0.312	<0.001
Gallbladder drainage				
Performed	0.112	[0.066, 0.157]	0.072	<0.001
(Reference: not performed)				
Hospital type				
Academic hospitals	– 0.065	[– 0.125, – 0.004]	– 0.029	0.035
(Reference: community hospitals)				
Hospital size				
Medium-sized hospitals	– 0.057	[– 0.103, – 0.011]	– 0.041	0.015
Large hospitals	– 0.066	[– 0.123, – 0.010]	– 0.039	0.021
(Reference: small hospitals)				

F-test for the model: $P < 0.001$, $R^2 = 0.594$.

during hospitalization (standardized coefficients: −0.047 and −0.041, respectively). The largest VIFs among all the variables were 2.78 (patients aged 80 years or more), indicating little need for concern regarding problems caused by multicollinearity. Increased duration of preoperative and postoperative antimicrobial therapies significantly raised medical costs during hospitalization. The standardized coefficient for preoperative antimicrobial therapy was 0.335, while that for postoperative antimicrobial therapy was 0.294 ($P < 0.001$).

Table 3 Linear regression analysis of factors associated with log-transformed medical costs during hospitalization

Independent variables	Unstandardized coefficient	95% confidence interval	Standardized coefficient	*P* value
Kinds of Cholecystectomy				
Laparoscopic cholecystectomy	– 0.286	[– 0.331, – 0.242]	– 0.187	<0.001
(Reference: open cholecystectomy)				
Timing of cholecystectomy				
Early cholecystectomy	– 0.605	[– 0.654, – 0.556]	– 0.391	<0.001
(Reference: delayed cholecystectomy)				
Cholecystectomy-related complications				
Occurred	0.072	[– 0.086, 0.230]	0.012	0.371
(Reference: did not occur)				
Age				
50–59 years	0.043	[– 0.033, 0.120]	0.026	0.266
60–69 years	0.039	[– 0.036, 0.115]	0.023	0.312
70–79 years	0.073	[– 0.006, 0.153]	0.039	0.071
80 years or more	0.091	[0.001, 0.180]	0.038	0.045
(Reference: less than 50 years)				
Sex				
Male patients	– 0.003	[– 0.046, 0.039]	– 0.002	0.877
(Reference: female patients)				
Severity of comorbid conditions				
Moderate conditions	0.084	[0.030, 0.137]	0.045	0.002
Severe conditions	0.152	[0.097, 0.206]	0.081	<0.001
(Reference: mild conditions)				
Ambulance transportation				
Used	0.026	[– 0.028, 0.081]	0.013	0.347
(Reference: not used)				
Intensive care unit				
Used	0.077	[0.011, 0.144]	0.033	0.021
(Reference: not used)				
Antimicrobial therapy				
Preoperative administration (per day)	0.039	[0.036, 0.043]	0.335	<0.001
Postoperative administration (per day)	0.039	[0.035, 0.044]	0.294	<0.001
Gallbladder drainage				
Performed	0.126	[0.075, 0.178]	0.074	<0.001
(Reference: not performed)				
Hospital type				
Academic hospitals	– 0.063	[– 0.131, 0.004]	– 0.026	0.067
(Reference: community hospitals)				
Hospital size				
Medium-sized hospitals	– 0.071	[– 0.123, – 0.020]	– 0.047	0.007
Large hospitals	– 0.075	[– 0.139, – 0.012]	– 0.041	0.019
(Reference: small hospitals)				

F-test for the model: $P < 0.001$, $R^2 = 0.581$.

Finally, stratified analyses for log-transformed LOS and medical costs during hospitalization were performed using a multiple linear regression model. Early cholecystectomy, laparoscopic cholecystectomy, and preoperative and postoperative antimicrobial therapies were independent factors that influenced LOS and costs during hospitalization (**Tables 4 and 5**).

Table 4 Stratified analysis associated with log-transformed length of hospitalization

Independent variables	Unstandardized coefficient	95% confidence interval	Standardized coefficient	*P* value
Academic hospitals				
Large hospitals				
Laparoscopic cholecystectomy	– 0.263	[– 0.380, – 0.147]	– 0.185	<0.001
Early cholecystectomy	– 0.453	[– 0.582, – 0.324]	– 0.320	<0.001
Preoperative administration	0.055	[0.044, 0.066]	0.450	<0.001
Postoperative administration	0.039	[0.029, 0.050]	0.330	<0.001
Community hospitals				
Small hospitals				
Laparoscopic cholecystectomy	– 0.210	[– 0.299, – 0.103]	– 0.137	<0.001
Early cholecystectomy	– 0.410	[– 0.517, – 0.303]	– 0.286	<0.001
Preoperative administration	0.052	[0.041, 0.062]	0.400	<0.001
Postoperative administration	0.025	[0.018, 0.033]	0.245	<0.001
Medium-sized hospitals				
Laparoscopic cholecystectomy	– 0.266	[–.322, –.210]	– 0.192	<0.001
Early cholecystectomy	– 0.584	[–.645, –.523]	– 0.410	<0.001
Preoperative administration	0.031	[0.027, 0.035]	0.331	<0.001
Postoperative administration	0.046	[0.040, 0.051]	0.349	<0.001
Large hospitals				
Laparoscopic cholecystectomy	– 0.276	[– 0.362, – 0.191]	– 0.207	<0.001
Early cholecystectomy	– 0.468	[– 0.567, – 0.369]	– 0.348	<0.001
Preoperative administration	0.047	[0.037, 0.056]	0.386	<0.001
Postoperative administration	0.033	[0.025, 0.041]	0.274	<0.001

There were no academic hospitals with less than 600 beds.

Discussion

Numerous studies regarding analysis of LOS and medical costs for patients undergoing cholecystectomy for acute cholecystitis have been reported worldwide. However, few studies have analyzed LOS and medical costs of patients undergoing cholecystectomy for acute cholecystitis taking into account patient characteristics and other treatments using a national administrative database. Therefore, an analysis focusing on patient characteristics and other treatments, rather than solely on the type of cholecystectomy, was required to develop more effective strategies for the management of acute cholecystitis. We conducted the present study using the Japanese administrative database to determine the factors that affect LOS and medical costs during hospitalization of patients who had undergone cholecystectomy for acute cholecystitis . The current study demonstrated that early cholecystectomy reduced LOS and medical costs, whereas preoperative antimicrobial therapy for cholecystectomy significantly increased LOS and medical costs during hospitalization.

Regarding the effect of early cholecystectomy on LOS and medical costs of patients who underwent cholecystectomy for acute cholecystitis, our current results are consistent with those of several previous studies.[22–25] From the 1980s (when laparoscopic cholecystectomy was not common) onward, early cholecystectomy has been recognized as a relatively cost-effective procedure for patients with acute cholecystitis.[22,23] In the past 10 years, the efficacy of early cholecystectomy, especially in laparoscopic procedures, has been emphasized.[24,25] Chandler et al.[24] reported that early laparoscopic cholecystectomy significantly reduces LOS and hospital costs, as well as operative blood loss. In a meta-analysis of early laparoscopic cholecystectomy, Gurusamy et al.[25] reported that LOS is shorter by 4 days for early laparoscopic cholecystectomy compared with delayed laparoscopic cholecystectomy. Therefore, it is plausible that early cholecystectomy is beneficial for the management of acute cholecystitis in terms of reducing LOS and medical costs during hospitalization.

Conversely, we found that longer preoperative antimicrobial therapy was significantly associated with an increase in LOS and medical costs during hospitalization. Recent studies also suggest that pharmacological expense is associated with LOS and medical costs during hospitalization for acute cholecystitis.[26,27] However, we consider that our results may reflect special circumstances unique to Japan, and the association between preoperative antimicrobial therapy and LOS and medical costs could be explained by several factors. First, many physicians in Japan routinely prescribe a long course of anti-

Table 5 Stratified analysis with log-transformed medical costs during hospitalization

Independent variables	Unstandardized coefficient	95% confidence interval	Standardized coefficient	*P* value
Academic hospitals				
Large hospitals				
Laparoscopic cholecystectomy	– 0.299	[– 0.424, – 0.175]	– 0.198	<0.001
Early cholecystectomy	– 0.495	[– 0.633, – 0.356]	– 0.328	<0.001
Preoperative administration	0.063	[0.051, 0.075]	0.484	<0.001
Postoperative administration	0.030	[0.019, 0.041]	0.236	<0.001
Community hospitals				
Small hospitals				
Laparoscopic cholecystectomy	– 0.314	[– 0.409, – 0.218]	– 0.209	<0.001
Early cholecystectomy	– 0.535	[– 0.646, – 0.424]	– 0.353	<0.001
Preoperative administration	0.054	[0.044, 0.065]	0.399	<0.001
Postoperative administration	0.035	[0.026, 0.043]	0.253	<0.001
Medium-sized hospitals				
Laparoscopic cholecystectomy	– 0.299	[– 0.362, – 0.236]	– 0.195	<0.001
Early cholecystectomy	– 0.677	[– 0.745, – 0.608]	– 0.431	<0.001
Preoperative administration	0.031	[0.026, 0.036]	0.300	<0.001
Postoperative administration	0.050	[0.044, 0.056]	0.347	<0.001
Large hospitals				
Laparoscopic cholecystectomy	– 0.217	[– 0.326, – 0.109]	– 0.136	<0.001
Early cholecystectomy	– 0.478	[– 0.596, – 0.359]	– 0.305	<0.001
Preoperative administration	0.053	[0.041, 0.064]	0.374	<0.001
Postoperative administration	0.026	[0.018, 0.034]	0.231	<0.001

There were no academic hospitals with less than 600 beds.

microbial prophylaxis to prevent possible postoperative infections.[28,29] In addition, physicians may be motivated by the concern that their patients may accuse them of negligence if short-course prophylaxis were to result in postoperative infection.[30] Therefore, some patients may receive unnecessary antimicrobial therapy before undergoing cholecystectomy for acute cholecystitis. Second, some reports have suggested that preoperative LOS in Japan is significantly longer than that in other developed countries.[30–32] Sekimoto et al.[30] reported that the timing of cholecystectomy for acute cholecystitis was mainly determined by the institutional policy or facilities' ability in Japan, rather than by the clinical course of the patients. A shortage of surgeons has been recognized as a serious problem and may have resulted from unfavorable working environments for surgeons or increased risks of malpractice suits, so early surgery may impose a heavy burden on many hospitals in Japan that suffer a shortage of human resources.[33] Therefore, we consider that a dependence on antimicrobial therapy, which is the mainstay of conservative treatments for acute cholecystitis, rather than early cholecystectomy, possibly explains why preoperative antimicrobial therapy was significantly associated with an increase in LOS and medical costs during hospitalization in the current study.

A major strength of the current study is the clinical data used. Cholecystectomy for acute cholecystitis is usually performed in acute care hospitals. One of the benefits of this national database is that it enables evaluation of a large number of acute care hospitals in an unbiased manner. Our investigation involved a nationally representative sample of patients who underwent cholecystectomy for acute cholecystitis in a community setting.[11–13] Therefore, the DPC data accurately represent the actual procedures and treatments performed for acute cholecystitis. Additionally, Japanese original payment codes were applied for details of medical data, including all procedures, devices, and medications used.[11–15] These data were documented daily for each patient.[11–15] Therefore, this administrative database also enables interested parties to evaluate outcomes with respect to individual detailed medical treatments.

Several potential limitations of this study warrant mention. First, the Tokyo Guidelines determine the severity of acute cholecystitis based on laboratory data and imaging findings of patients.[34] Regrettably, these patients' laboratory and imaging data are not recorded in the Japanese administrative database.[11,13,14] The severity of acute cholecystitis may determine the use of some procedures such as ventilation and hemodiafiltration or treatments

such as vasopressors and so may affect LOS or medical costs.[35] In particular, severe cholecystitis may be related to longer antimicrobial therapy or delayed cholecystectomy because the condition may result in serious sequelae, such as organ dysfunction or septic shock.[36] Therefore, further clinical studies evaluating the factors affecting LOS and medical costs for patients with cholecystectomy are required that use stricter criteria to define the severity of acute cholecystitis.

Despite these limitations, the current study demonstrated that early cholecystectomy reduced LOS and medical costs, whereas preoperative antimicrobial therapy significantly increased LOS and medical costs during hospitalization. The current study has implications for health care policy decision making and quality of patient care. Yamashita et al.[7] reported that 72% of surgeons from abroad favored early cholecystectomy, whereas only 33% of Japanese doctors favored early cholecystectomy in a consensus meeting for acute cholecystitis. Although one explanation for this discrepancy could be the difference in circumstances relating to surgery between Japan and other developed countries, there is no doubt that early cholecystectomy is a relatively cost-effective procedure for patients with acute cholecystitis. Therefore, further promotion of early cholecystectomy may result in decreasing LOS and savings in medical costs during hospitalization in Japan. In addition, a previous report suggested that antimicrobial prophylaxis may not be necessary for low-risk patients with acute cholecystitis undergoing laparoscopic cholecystectomy.[37] Therefore, if unnecessary administration of antimicrobial therapy can be lessened, a reduction in LOS and medical costs can be achieved while maintaining the quality of patient care. Further clinical studies are required to determine the appropriate use of antimicrobial drugs for patients with cholecystectomy, especially in the preoperative stage.

However, it is impractical to promote early cholecystectomy in all hospitals when considering the current circumstances relating to surgery in Japan. Therefore, we consider that it is also essential to promote the centralization of patients who require cholecystectomy for acute cholecystitis and promote early cholecystectomy in Japan. Regarding medical care in Japan, the specialist healthcare service provider system has been criticized for being poorly organized with nonsystematic delivery of services, because health policy has been based on free access to hospitals, unlike in many European countries or in the United States.[14,38,39] Therefore, centralization of patient care associated with a policy of concentrating medical services, and consequent reduction of local hospital care, is unlikely to occur in Japan.[14,39] However, the current findings provide good evidence to support the centralization of patients who require cholecystectomy for acute cholecystitis. Further clinical studies regarding such centralization also might contribute to the patient referral policy in Japan.

In conclusion, we have demonstrated that early cholecystectomy significantly reduces the LOS and medical costs of cholecystectomy for acute cholecystitis, whereas preoperative antimicrobial therapy increases LOS and medical costs during hospitalization. These results highlight the need for health care implementations such as promotion of early cholecystectomy and appropriate use of antimicrobial drugs or centralization of patients undergoing cholecystectomy for acute cholecystitis in Japan. Further clinical studies are required in the near future to realize these health care implementations for reducing medical costs while maintaining the quality of patient care.

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