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*Original Article*

# Impact of Body Mass Index of Japanese Gallbladder Cancer Patients on their Postoperative Outcomes

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**We investigated the relationship between body mass index (BMI) and postoperative outcomes in 450 gallbladder cancer patients in Japan. We collected patient information, including sex, age, underlying disease, BMI, stage, surgery method, postoperative time to discharge, and postoperative Medicare fees, from the Japanese administrative database associated with the Diagnosis Procedure Combination system. We classified patient BMIs as underweight (BMI < 18.5 kg/m$^2$), normal (BMI ≥ 18.5 kg/m$^2$ and < 25 kg/m$^2$) or overweight/obese (BMI ≥ 25 kg/m$^2$), then investigated the relationship between these categories and two postoperative outcomes: time to discharge and postoperative Medicare fees. The median postoperative time to discharge was 12 days in all patients, and 12 days in each of the three weight groups ($p = 0.62$, n.s.). The median postoperative Medicare fees from surgery until discharge were (USD): all patients, $5,002; underweight, $5,875; normal weight, $4,797; and overweight/obese, $5,179 ($p = 0.146$, n.s.). A multivariate analysis with adjustment for competing risk factors revealed that BMI was not associated with increased risk of longer postoperative time to discharge (normal weight: HR 1.17, $p = 0.29$; overweight/obese: HR 1.17, $p = 0.37$) or higher postoperative Medicare fees (OR 0.99, $p = 0.86$, n.s.). Thus, high BMI was not found to be a factor for poor postoperative outcomes in Japanese patients with gallbladder cancer.**

**Key words:** body mass index, gallbladder cancer, surgery, obesity

Gallbladder cancer (GBC) is the most common malignancy of the biliary tract, accounting for 80–95% of biliary tract cancers worldwide [1-3]. GBC ranks fifth among gastrointestinal cancers, and is traditionally regarded as a highly lethal disease, with an overall 5-year survival rate of less than 5%. The overall mean survival time for patients with GBC is 6 months. GBC is highly fatal and usually diagnosed at advanced stages due to the absence of specific clinical findings in the early stages [4-8]. It has been reported that the age-adjusted incidence rate of GBC is 1.4 per 100,000 in the U.S., and steadily increases with age [9]. Despite recent advances in diagnostic techniques and therapeutic management, the prognosis for patients with GBC remains dismal.

Many studies have reported multiple factors closely related to GBC, such as gallstones, alcohol consumption, smoking, blood glucose and diabetes mellitus (DM), genetic susceptibility, and obesity [10-12]. In recent years, it has become apparent that overweight and obesity, as defined by body mass index (BMI), is a

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risk factor for GBC. This is particularly true in middle-aged women [13]. The number of overweight individuals has increased dramatically worldwide; it is estimated that today there are approximately 1.6 billion individuals who are overweight and 400 million who are obese [14, 15]. High BMI—both overweight and obesity—is a well-recognized risk factor for several chronic degenerative diseases, such as cardiovascular disease and diabetes, and for numerous types of cancer, including GBC. According to the most recent 2014 Cancer Progress Report from the American Association for Cancer Research, a high BMI is responsible for nearly 25% of the relative contribution to cancer incidence, ranking second only to tobacco use [16, 17].

There are few reports regarding the effects of high BMI on the outcomes of surgery for GBC, and a consensus has not been reached. The number of overweight patients who undergo surgery for GBC has increased, but data concerning short-term and long-term outcomes for this procedure in overweight patients are lacking. There is also little information about the relationship between BMI and the postoperative outcomes of Japanese GBC patients in particular. The survival time of GBC is short, so the level of disease progression upon admission for surgery has a great effect on the overall progression.

In the present study, we used the Japanese administrative database associated with the Diagnosis Procedure Combination (DPC) system to examine the relationship between preoperative BMI and postoperative time to discharge and postoperative Medicare fees in Japanese GBC patients who underwent surgery. The DPC is the original Japanese case-mix classification system, in which each case has a code consisting of diagnosis and treatment procedures. Per diem payments vary according to the length of hospitalization, which is determined for each code. The system was developed to standardize and evaluate the cost and quality of medical services in Japan. One of the advantages of the DPC is that the data can be collected in a common electronic format [18-21].

## Patients and Methods

***Patients.*** We selected the cases of 450 patients with GBC who were >30 years old from the National Saiseikai Hospital DPC survey between April 2011 and March 2017. The principal diagnosis of GBC was recorded using the International Classification of Diseases and Injuries (ICD)-10th code edition. In the present analysis, GBC was defined as code C23 in the ICD-10th code edition. We excluded 84 cases for which the stage of disease was unclear.

***Methods.*** From the DPC data we extracted data on age, sex, underlying disease, BMI, disease stage, operative method, postoperative duration of antibiotic therapy, postoperative time to discharge, and postoperative Medicare fee for the 450 patients with GBC. Each patient's BMI was calculated as weight in kilograms (kg) divided by height in meters squared ($m^2$), both of which were measured upon admittance to the hospital for GBC surgery. For the analyses, we divided the patients into three groups based on their BMI values as described by the World Health Organization classification: underweight (BMI < 18.5 kg/$m^2$), normal weight (BMI ≥ 18.5 kg/$m^2$ and < 25 kg/$m^2$), and overweight/obese (BMI ≥ 25 kg/$m^2$). The GBC stage was defined by the Union for International Cancer Control (UICC) classification system. Regarding the operative method, a laparoscopic or open cholecystectomy, minor liver resection, major liver resection, or hepatopancreatoduodenectomy was performed. Laparoscopic or open cholecystectomy and minor liver resection were treated as less aggressive surgery while major liver resection and hepatopancreatoduodenectomy were treated as highly aggressive surgery. Postoperative outcomes were evaluated based on the median time of antibiotic therapy after the operation, the postoperative median time to discharge and the postoperative Medicare fee. The antibiotic therapy after the operation was performed for about 1-3 days in all cases except one for the prevention of surgical site infection. For the single case with symptoms of infection, antibiotics were administered for a longer period.

***Statistical methods.*** Statistical analyses were performed with STATA 13 software (StataCorp, College Station, TX, USA). Student's *t*-test was used to compare the means of the continuous variables, and Fisher's exact test was used to compare the frequencies of the categorical variables between groups. The Kaplan-Meier method and log–rank test were used to analyze the time of antibiotic therapy after the operation and the postoperative time to discharge (time from surgery until discharge, regardless of cause). After we performed a univariate analysis, we subjected the significant variables to a multivariate analysis using a Cox propor-

tional hazards model. An analysis of variance (ANOVA) was used to compare the postoperative Medicare fees in the different BMI groups. A logistic analysis was used to determine independent factors associated with the postoperative Medicare fee. We accepted $p$-values $<0.05$ as significant. The research protocol of the study was approved by the Institutional Review Board at Okayama Saiseikai General Hospital (no. 170509).

## Results

The patients' background characteristics are presented in Table 1. Within the group of 450 patients, 12.2% (n = 55) were underweight, 68.7% (n = 309) were normal weight, and 19.1% (n = 86) were overweight/obese. The sex ratio (numbers of males/females) was 25/30 in the underweight group, 146/163 in the normal weight group, and 49/37 in the overweight/obese group ($p = 0.24$). The median (range) age of the patients was 74 (43-89) years in the underweight group, 73 (33-94) years in the normal weight group, and 70 (30-91) years in the overweight/obese group ($p = 0.62$). No significant differences in underlying disease, such as hypertension, hyperlipidemia, or DM, were observed among the three groups.

The disease stage of the GBC cases (I/II/IIIA vs. IIIB/IV) was 50/5 patients in the underweight group, 281/28 patients in the normal weight group, and 75/11 patients in the overweight/obese group ($p = 0.58$). The surgery (open/laparoscopic surgery) was 52/3 patients in the underweight group, 282/27 patients in the normal weight group, and 75/11 patients in the overweight/obese group ($p = 0.31$). In terms of operative method, the ratios of less aggressive surgery to highly aggressive surgery were 51/4 patients in the underweight group, 290/19 patients in the normal weight group, and 80/6 patients in the overweight/obese group ($p = 0.93$). Postoperative blood transfusion was performed in 5 of the 450 patients (1.1%). Six of the 450 patients died during hospitalization after surgery (1.3%). There were no significant differences in postoperative blood transfusion or mortality during hospitalization after surgery among the three BMI groups.

The duration of postoperative antibiotic therapy was 3 days in all patients, and 5, 3 and 5 days in the underweight, normal weight and overweight/obese groups, respectively. Log-rank tests showed significance for each group ($p = 0.028$). The postoperative time to discharge was 12 days in all patients, and 12 days in all three BMI groups (Fig. 1). Log-rank tests showed no significant differences among any of the groups ($p = 0.62$).

Table 1 Baseline characteristics of the study population

| | No. (%) | | | | $p$-value |
|---|---|---|---|---|---|
| | All patients | Underweight | Normal weight | Overweight/obese | |
| No. of patients | 450 | 55 (12.2) | 309 (68.7) | 86 (19.1) | |
| Population Characteristics | | | | | |
| Sex (male) | 220 (48.9) | 25 (11.3) | 146 (66.4) | 49 (22.3) | 0.24 |
| Age (median, y) | 73 | 74 | 73 | 70 | 0.62 |
| Underlying disease | | | | | |
| Hypertension | 141 (31.3) | 10 (18.2) | 106 (34.3) | 25 (29.1) | 0.05 |
| Hyperlipidemia | 72 (16) | 7 (12.7) | 55 (17.8) | 10 (11.6) | 0.3 |
| Diabetes mellitus | 88 (19.6) | 9 (16.4) | 57 (18.4) | 22 (25.6) | 0.27 |
| Stage (UICC) | | | | | 0.58 |
| Stage I, II, IIIA | 406 (90.2) | 50 (12.3) | 281 (69.2) | 75 (18.5) | |
| Stage IIIB, IV | 44 (9.8) | 5 (11.4) | 28 (63.6) | 11 (25.0) | |
| Surgery | | | | | 0.31 |
| Laparoscopic | 41 (9.1) | 3 (7.3) | 27 (65.9) | 11 (26.8) | |
| Open | 409 (90.9) | 52 (12.7) | 282 (69.0) | 75 (18.3) | |
| Operative method | | | | | 0.93 |
| Less aggressive (laparoscopic or opened Cholecystectomy, minor liver resection) | 421 (93.6) | 51 (12.1) | 290 (68.9) | 80 (19.0) | |
| Highly aggressive (major liver resection, hepatopancreatoduodenectomy) | 29 (6.4) | 4 (13.8) | 19 (65.5) | 6 (20.7) | |
| Mortality | 6 (1.3) | 1 (16.7) | 4 (66.7) | 1 (16.7) | 0.95 |

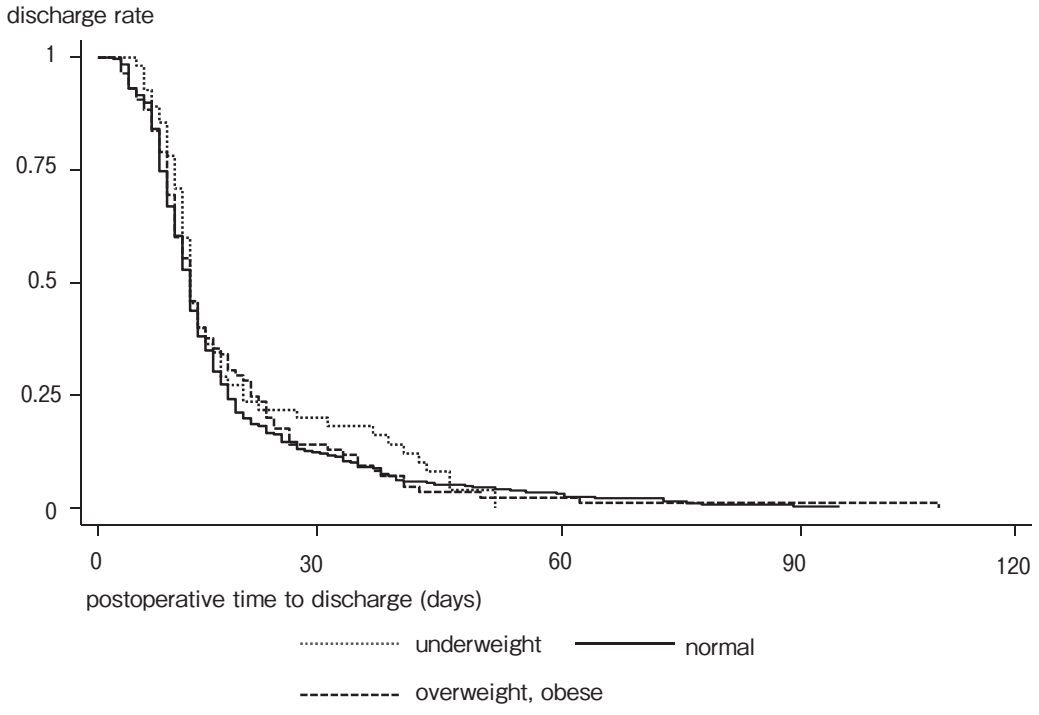


**Fig. 1** Postoperative time to discharge according to BMI
According to BMI, the postoperative time to discharge was 12 days in all patients, 12 days in the underweight group, 12 days in the normal weight group, and 12 days in the overweight/obese group. Log-rank testing did not show significant differences among any of the groups ($p = 0.62$).

The median postoperative Medicare fees from surgery until discharge were as follows (USD) ($1 = 110 yen): all patients, $5,002; underweight, $5,875; normal weight, $4,797; and overweight/obese, $5,179 ($p = 0.146$) (Table 2).

With respect to stage, the duration of postoperative antibiotic therapy was 3 days in all patients, 3 days in the stage I/II/IIIA group, and 9 days in the stage IIIB/IV group. Log-rank tests showed a significant difference between the 2 groups ($p < 0.0001$). The postoperative time to discharge was 12 days in all patients, 12 days in the stage I/II/IIIA group, and 20 days in the stage IIIB/IV group. Log-rank tests showed a significant difference between the 2 groups ($p < 0.0001$). The median postoperative Medicare fee from surgery until discharge was as follows (USD): all patients, $5,002; stage I/II/IIIA, $4,563; and stage IIIB/IV, $9,054 ($p < 0.001$) (Table 3).

In the comparison of operative methods, the duration of postoperative antibiotic therapy was 3 days in all patients, 3 days in the less aggressive surgery group, and 10 days in the highly aggressive surgery group. Log-rank tests showed a significant difference between groups ($p = 0.0006$). The postoperative time to discharge was 12 days in all patients, 12 days in the less aggressive surgery group, and 19 days in the highly

**Table 2** Outcome according to BMI

| | No. of patients | Time of antibiotic therapy after the operation (days) (95%CI) | Postoperative time to discharge (days) (95%CI) | The median postoperative Medicare fees ($) |
|---|---|---|---|---|
| All patients | 450 | 3 (3–4) | 12 (11–12) | 5,002 |
| Underweight | 55 | 5 (3–6) | 12 (11–14) | 5,875 |
| Normal weight | 309 | 3 (3–3) | 12 (11–12) | 4,797 |
| Overweight/Obese | 86 | 5 (3–6) | 12 (10–14) | 5,179 |
| *p*-value | | 0.028 | 0.62 | 0.146 |

aggressive surgery group. Log-rank tests showed a significant difference between groups ($p<0.0001$). The median postoperative Medicare fees from surgery until discharge were as follows (USD): all patients, $5,002; less aggressive surgery, $4,580; and highly aggressive surgery, $11,130 ($p<0.001$) (Table 4).

The univariate analysis for duration of postoperative antibiotic therapy identified the disease stage (I/II/IIIA vs. IIIB/IV) (hazard ratio [HR] 0.52, 95% confidence interval [CI] 0.37-0.72, $p<0.001$) and operative method (less aggressive surgery vs. highly aggressive surgery) (HR 0.54, 95%CI 0.36-0.80, $p=0.002$) as significant predictors. The multivariate analysis indicated that the same two factors were significantly associated with the postoperative outcomes: disease stage (I/II/IIIA vs. IIIB/IV) (HR 0.56, 95%CI 0.40-0.78, $p=0.001$) and operative method (less aggressive surgery vs. highly aggressive surgery) (HR 0.62, 95%CI 0.41-0.93, $p=0.019$) (Table 5).

The univariate analysis identified as significant predictors of postoperative time to discharge both disease stage (I/II/IIIA vs. IIIB/IV) (HR 0.51, 95%CI 0.37-0.71, $p<0.001$) and operative method (less aggressive surgery vs. highly aggressive surgery) (HR 0.41, 95%CI 0.27-0.61, $p<0.001$). The multivariate analysis indicated that the same two factors were significantly associated with

**Table 3** Outcome according to stage

| | No. of patients | Time of antibiotic therapy after the operation (days) (95%CI) | Postoperative time to discharge (days) (95%CI) | The median postoperative Medicare fees ($) |
|---|---|---|---|---|
| All patients | 450 | 3 (3–4) | 12 (11–12) | 5,002 |
| Stage I, II, IIIA | 406 | 3 (3–4) | 12 (11–12) | 4,563 |
| Stage IIIB, IV | 44 | 9 (4–12) | 20 (15–25) | 9,054 |
| *p*-value | | < 0.0001 | < 0.0001 | < 0.001 |

**Table 4** Outcome according to operative method

| | No. of patients | Time of antibiotic therapy after the operation (days) (95%CI) | Postoperative time to discharge (days) (95%CI) | The median postoperative Medicare fees ($) |
|---|---|---|---|---|
| All patients | 450 | 3 (3–4) | 12 (11–12) | 5,002 |
| Less aggressive surgery | 421 | 3 (3–4) | 12 (11–12) | 4,580 |
| Highly aggressive surgery | 29 | 10 (4–11) | 19 (15–37) | 11,130 |
| *p*-value | | 0.0006 | < 0.0001 | < 0.001 |

**Table 5** Factors related to the duration of postoperative antibiotic therapy for Japanese patients with gallbladder cancer

| Variable | Univariate analysis | | | Multivariate analysis | | |
|---|---|---|---|---|---|---|
| | Hazard ratio | 95%CI | *p*-value | Hazard ratio | 95%CI | *p*-value |
| Sex | | | | | | |
| Male | 1 | | | 1 | | |
| Female | 1.08 | 0.89–1.30 | 0.428 | 1.05 | 0.87–1.27 | 0.580 |
| Age (year) | | | | | | |
| < 80 | 1 | | | | | |
| ≧ 80 | 1.12 | 0.90–1.39 | 0.321 | 1.13 | 0.91–1.41 | 0.266 |
| Stage (UICC) | | | | | | |
| Stage I, II, IIIA | 1 | | | 1 | | |
| Stage IIIB, IV | 0.52 | 0.37–0.72 | < 0.001 | 0.56 | 0.40–0.78 | 0.001 |
| Operative method | | | | | | |
| Less aggressive | 1 | | | 1 | | |
| Highly aggressive | 0.54 | 0.36–0.80 | 0.002 | 0.62 | 0.41–0.93 | 0.019 |
| BMI | | | | | | |
| Underweight | 1 | | | 1 | | |
| Normal weight | 1.31 | 0.98–1.77 | 0.064 | 1.33 | 0.99–1.79 | 0.059 |
| Overweight/Obese | 1.05 | 0.74–1.48 | 0.793 | 1.10 | 0.78–1.56 | 0.581 |

postoperative outcomes: disease stage (I/II/IIIA vs. IIIB/IV) (HR 0.58, 95%CI 0.41-0.80, $p=0.001$) and operative method (less aggressive surgery vs. highly aggressive surgery) (HR 0.45, 95%CI 0.30-0.68, $p<0.001$) (Table 6).

The univariate analysis for postoperative Medicare fees from surgery until discharge identified disease stage (I/II/IIIA vs. IIIB/IV) (OR 1.84, 95%CI 1.56-2.17, $p<0.001$) and operative method (less aggressive surgery vs. highly aggressive surgery) (OR 2.50, 95%CI 1.89-3.31, $p<0.001$) as significant predictors. The multivariate analysis indicated that the same 2 factors were significantly associated with postoperative outcomes: disease stage (I/II/IIIA vs. IIIB/IV) (OR 1.68, 95%CI 1.41-2.00, $p<0.001$) and operative method (less aggressive surgery vs. highly aggressive surgery) (OR 2.16, 95%CI 1.61-2.91, $p<0.001$) (Table 7). Thus, advanced disease stage and operative method were associated with poor postoperative outcomes. An overweight/obese BMI was not a factor for poor postoperative outcomes. In addition, age and sex were not postoperative outcome factors.

## Discussion

GBC, a common malignant tumor in the digestive system, has a high mortality rate and lacks diagnostic specificity, posing a great challenge for preoperative and early-stage diagnosis. The overall mean survival duration for patients with GBC is 6 months [22,23]. Previous studies highlighted extensive disease and the number of positive lymph nodes as important predictors of worse outcomes [23-25].

The incidence of GBC increases with age. Europe has a low overall incidence of 0-4/100,000, while Japan has a higher incidence at 7/100,000 [3,8,26]. The present findings regarding GBC in Japan are thus especially useful.

**Table 6** Factors related to the postoperative time to discharge among Japanese patients with gallbladder cancer

| Variable | Univariate analysis | | | Multivariate analysis | | |
|---|---|---|---|---|---|---|
| | Hazard ratio | 95%CI | *p*-value | Hazard ratio | 95%CI | *p*-value |
| Sex | | | | | | |
| Male | 1 | | | 1 | | |
| Female | 1.13 | 0.94–1.36 | 0.198 | 1.13 | 0.94–1.37 | 0.193 |
| Age (year) | | | | | | |
| ＜80 | 1 | | | | | |
| ≧80 | 0.98 | 0.79–1.22 | 0.887 | 0.97 | 0.78–1.21 | 0.812 |
| Stage (UICC) | | | | | | |
| Stage I, II, IIIA | 1 | | | 1 | | |
| Stage IIIB, IV | 0.51 | 0.37–0.71 | ＜0.001 | 0.58 | 0.41–0.80 | 0.001 |
| Operative method | | | | | | |
| Less aggressive | 1 | | | 1 | | |
| Highly aggressive | 0.41 | 0.27–0.61 | ＜0.001 | 0.45 | 0.30–0.68 | ＜0.001 |
| BMI | | | | | | |
| Underweight | 1 | | | 1 | | |
| Normal weight | 1.14 | 0.85–1.53 | 0.368 | 1.17 | 0.87–1.57 | 0.290 |
| Overweight/Obese | 1.09 | 0.77–1.53 | 0.637 | 1.17 | 0.83–1.65 | 0.366 |

**Table 7** Factors related to postoperative Medicare fees from surgery until discharge among Japanese patients with gallbladder cancer

| Variable | Univariate analysis | | | Multivariate analysis | | |
|---|---|---|---|---|---|---|
| | Odds ratio | 95%CI | *p*-value | Odds ratio | 95%CI | *p*-value |
| Sex | 0.90 | 0.59–1.38 | 0.625 | 0.80 | 0.49–1.31 | 0.378 |
| Age (year) | 1.00 | 0.98–1.02 | 0.952 | 1.01 | 0.98–1.04 | 0.470 |
| Stage (UICC) | 1.84 | 1.56–2.17 | ＜0.001 | 1.68 | 1.41–2.00 | ＜0.001 |
| Operative method | 2.50 | 1.89–3.31 | ＜0.001 | 2.16 | 1.61–2.91 | ＜0.001 |
| BMI | 0.99 | 0.93–1.05 | 0.655 | 0.99 | 0.93–1.06 | 0.862 |

The most significant risk factor for GBC is gallstones (relative risk [RR] = 3.0-23.8), which are present in the majority (69-85%) of GBC patients. Recently, it was reported that obesity is a risk factor for GBC in middle–aged women [13].

The following theories have been proposed regarding the mechanism of GBC in obese patients. Obesity could increase the prevalence of GBC by promoting the formation of gallstones and elevating blood glucose levels. Some studies have shown that retinol-binding protein 4 (RBP4) is closely associated with insulin resistance and obesity. Elevated RBP4 has been associated with an increased incidence of gallstone disease. Wang *et al.* reported that the level of bile RBP4 was correlated positively with BMI. Therefore, increased BMI may play a role in the course of gallstone formation and thereby influence the morbidity of GBC by elevating RBP4. These interconnected pathways may suggest the pathophysiological mechanism of the obesity–cancer link [27-32]. Despite these suggested theories, there have been few reports regarding the influence of excess body weight on the outcomes of GBC, and the findings from these studies have been controversial.

There are few reports from Japan about the relationship between BMI and the postoperative outcomes of GBC. We investigated postoperative outcomes according to BMI in a large sample of patients with GBC (n = 450) using a Japanese national DPC database. Our analyses revealed that excess body weight was not a factor for poor outcomes in Japanese patients with GBC who underwent surgery. On the other hand, an advanced disease stage and highly aggressive surgery were poor outcome factors in terms of the postoperative duration of antibiotic therapy, postoperative time to discharge and postoperative Medicare fees. We did not examine perioperative stress parameters, such as the operation time or the amount of blood loss; however, the mortality rate during hospitalization after surgery was 1.3%, which was low.

We were not able to examine the details of the postoperative complications of this series of patients with GBC. There were very few postoperative deaths or blood transfusions during hospitalization, and there were no significant differences among the BMI groups in terms of postoperative time to discharge, postoperative Medicare fees, postoperative deaths or blood transfusion during hospitalization.

However, log-rank testing did show significant differences among the BMI groups in terms of antibiotic therapy after the operation. Obesity is a high-risk factor for postoperative complications [33]. We suspect that in the present overweight/obesity group, antibiotics were used for a longer time than in the normal BMI group, either for the prevention of postoperative infectious complications or because of their existence. In addition, the underweight group might have included cases in particularly bad condition such as sarcopenia cases; hence, antibiotics were used for a longer time than in the normal group for similar reasons. However, BMI was not an independent factor for the duration of postoperative antibiotic therapy by multivariate analysis, and the differences among groups were only a few days. Accordingly, the postoperative antibiotic therapy did not affect the postoperative time to discharge or postoperative Medicare fees.

Highly aggressive surgery was an independent factor of both postoperative time to discharge and postoperative Medicare fees. We considered that highly aggressive surgery caused the postoperative complications in those cases in which such complications arose. However, the study had a preponderance of less aggressive surgeries (93.6%). Thus, BMI was not shown to affect postoperative time to discharge or postoperative Medicare fees. There were particularly few cases of pancreatoduodenectomy (1.1%) and thus we speculate that BMI did not contribute to postoperative complications that would affect postoperative time to discharge and postoperative Medicare fees. Further studies enrolling more cases by each operative method will be needed in the future.

High BMI is a risk factor for GBC, and appropriate weight control is important for GBC prevention. For good postoperative outcomes, it is also important to (1) educate obese patients regarding the risk of GBC, (2) identify GBC in the early stages during a routine medical check, and (3) perform surgery as early as possible. Consequently, we suggest that it is better for overweight or obese patients with GBC to undergo surgery as soon as possible, rather than wait until after body weight loss.

The greatest strength of the present study is its use of individual data. One of the advantages of using the administrative database associated with the DPC system was that it allowed for the participation of a large number of acute-care hospitals; as a result, our investigation enrolled a nationally representative sample of

patients in a community setting. In addition, medical data such as procedures, drugs, and devices were coded with the original Japanese payment codes for the DPC reimbursement system. These data were recorded for each patient on a daily basis [18-21]. Therefore, this administrative database enabled a detailed evaluation of patients with GBC based on individual medical treatments.

This study has some possible limitations. The database did not contain detailed patient information such as previous illness, laboratory data, image data after admission and peri-postoperative complications. In addition, because we could not examine the patients' nutritional conditions in detail, this issue must be addressed in the future. The rate of obesity may vary by race; it was 19.1% in the current study, and 57% in a Mexican study. Similarly, the rate of underweight in Westerners is much lower than that in the Japanese population. The obese population in Japan is small compared to those in Europe and the U.S. In Japan, the obesity rate is reported to be 28.7% in males and 21.3% in females, and the underweight rate is 4.5% in males and 10.4% in females [34]. Therefore, a global analysis, especially concerning the relationship between BMI and postoperative outcomes of surgery for GBC, would be useful. In addition, in this study, stage IIIB or IV disease was present in 9.8% of the patients, and highly aggressive surgery was carried out in 6.4%. Few patients had advanced-stage disease; hence, it was difficult to find statistical evidence of the effect of BMI in such patients. Also, we did not examine the use of adjuvant or neo-adjuvant chemotherapy. Studies of GBC outcomes incorporating these points are expected in the future. Furthermore, in this study, we examined short-term outcomes until discharge from surgery for GBC. Examination of the long-term course, including survival rates, is also expected in the future.

In conclusion, our study revealed that excess body weight does not significantly influence immediate postoperative outcomes in Japanese patients with GBC who undergo surgery. Specifically, time to discharge and Medicare fees after surgery for GBC were not associated with BMI. Additional studies are needed to investigate the influence of other factors on postoperative outcomes in GBC patients, especially those with advanced stage or facing aggressive surgery.

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