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ORIGINAL ARTICLE—LIVER, PANCREAS, AND BILIARY TRACT

Impact of hospital volume on outcomes in acute pancreatitis: a study using a nationwide administrative database

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Abstract

Background Although several population-based studies have shown higher hospital volume (HV) to be associated with better outcomes in acute pancreatitis, they failed to adjust for disease severity and did not take into account the potentially non-linear relationship between HV and outcomes. Using a Japanese nationwide administrative database, this study aimed to evaluate the volume–outcome relationship in acute pancreatitis by means of statistical methods that permitted such considerations.

Methods In-hospital mortality, length of stay, and total costs for patients with acute pancreatitis were analyzed using multivariate regression models fitted with generalized estimating equations. Adjustment for severity was based on the Japanese Severity Scoring System and other patient characteristics. We used restricted cubic spline functions to examine the potential non-linear relationships between HV and outcomes.

Results In all, 17,415 eligible patients with acute pancreatitis were identified from 1,032 hospitals between 1 July 2010 and 30 September 2011. The in-hospital mortality rate was 2.6 %, and the median total costs were US $7,740 (interquartile range, 5,150–11,920). The overall and non-linear volume–outcome relationships were not significant either for in-hospital mortality or total costs. The median length of stay was 14 days (interquartile range, 10–22), and high HV was positively associated with shorter hospitalization (overall, $P < 0.001$; non-linear, $P = 0.194$).

Conclusions Despite the shorter hospitalization with higher HV, no inverse volume–outcome relationship was evident for acute pancreatitis. Further evidence is required to justify the volume-based selective referral of acute pancreatitis patients.

Keywords Acute pancreatitis · Database · Hospital volume · Mortality

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Introduction

Acute pancreatitis is an acute-onset inflammatory process of the pancreas. It usually requires inpatient medical care and is a major financial burden on health-care systems in many countries [1, 2]. This condition covers a wide range of severity and mortality, and despite recent advances in critical care, severe acute pancreatitis is associated with a high mortality rate and prolonged hospitalization [3, 4].

Population-based studies have accumulated evidence on the relationship between hospital volume (HV) and improvement in clinical outcomes with surgical procedures and medical conditions [5–8]. A greater HV is associated with better clinical outcomes. Identification of the inverse relationship between volume and outcome is important in terms of policy making since patient outcomes can be improved through selective referral based on HV.

In acute pancreatitis, the inverse volume–outcome relationship has been reported in several studies [9–11]. However, owing to lack of information in the databases, those studies failed to adjust for disease severity using an established severity scoring system. Given the wide variety of severity with acute pancreatitis, adjustment for disease severity needs to be made when analyzing outcomes of acute pancreatitis [12]. Furthermore, the above studies categorized HV into tertiles [9, 10] or quartiles [11] and did not take into account the potential non-linear relationship between HV and outcomes. Using arbitrarily defined thresholds may result in an apparently significant volume–outcome relationship [13].

In this study, we aimed to evaluate the volume–outcome relationship in acute pancreatitis using several methodological improvements, including (1) adjustment for severity of pancreatitis based on the Japanese Severity Scoring system [14] and (2) assessment of the potential non-linear relationship between HV and outcomes by means of restricted cubic spline (RCS) functions [13]. We conducted this study using a large sample of patients derived from the Diagnosis Procedure Combination (DPC) database.

Methods

Data source

The DPC database is a nationwide inpatient database in Japan, and it includes discharge abstract data and administrative claims data, covering approximately 50 % of all acute-care hospitalizations in Japan in 2011 [8, 15]. Data on diagnoses, comorbidities present at admission, and complications occurring during hospitalization, are coded using the International Classification of Diseases and Related Health Problems 10th Revision (ICD-10) codes accompanied by text data in Japanese. The database also contains the following details: patients' age and sex; length of hospital stay; discharge status, including in-hospital death; status of consciousness based on the Japan Coma Scale (JCS) on admission and discharge [16, 17]; intensive care unit (ICU) admission; and interventional or surgical procedures, medications, and devices indexed by means of original codes in Japanese. The database also includes estimated total costs based on reference prices in the Japanese national fee schedule that determine item-by-item prices for surgical, pharmaceutical, laboratory, and other inpatient services. With regard to acute pancreatitis, each patient with a primary diagnosis of the condition was given a prognostic factor and computed tomography (CT) scores according to the Japanese Severity Scoring system by the attending physicians [14].

This study was approved by the institutional review board of The University of Tokyo, which waived the requirement for patient informed consent because of the anonymous nature of the data.

Patient selection

We identified adult patients (≥20-year-old) who were admitted to the participating hospitals with a principle diagnosis of acute pancreatitis (ICD-10 code, K85) and were discharged between 1 July 2010 and 30 September 2011. We excluded patients who were transferred to other hospitals within 7 days of hospitalization since early transfer of severe cases to tertiary-care hospitals could underestimate adverse outcomes in low-volume hospitals.

Outcomes

The primary outcome of this study was all-cause in-hospital mortality. Secondary outcomes included length of stay and total costs calculated in 2013 US dollars.

Hospital volume

HV was defined as the annual number of cases of acute pancreatitis admitted to each individual hospital, and it was calculated using unique hospital identifiers.

The severity scoring system of acute pancreatitis of the Japanese Ministry of Health, Labour and Welfare (2008) [14]

The Japanese Severity Scoring system is determined as the sum of nine prognostic factors together with CT severity grade. It has been reported to have good predictive ability for persistent organ failure [18] and mortality [19, 20]. Severe acute pancreatitis was diagnosed with a prognostic factor score of ≥3 or a CT Grade of ≥2.

The prognostic factors consist of the following nine factors, with each taking a score of 1 if positive: (1) base excess ≤−3 mEq/L or shock (systolic blood pressure <80 mmHg); (2) PaO_2 ≤60 mmHg (room air) or respiratory failure requiring respirator assistance; (3) blood urea nitrogen ≥40 mg/dL (or creatinine ≥2.0 mg/dL) or oliguria (daily urine output <400 mL even after intravenous fluid resuscitation); (4) lactic dehydrogenase ≥ twice the upper limit of normal; (5) platelet count ≤100,000/mm^3; (6) serum calcium ≤7.5 mg/dL; (7) C-reactive protein ≥15 mg/dL; (8) the number of positive measures in systemic inflammatory response syndrome diagnostic criteria

≥3; and (9) age ≥70 years. Measures in systemic inflammatory response syndrome criteria include body temperature >38 °C or <36 °C, heart rate >90 beats/min, respiratory rate >20 breaths/min or $PaCO_2$ <32 torr, and white blood cell counts >12,000 cells/mm^3, <4,000 cells/mm^3, or >10 % immature (band) forms.

The contrast-enhanced CT Grade is determined using a combination of the following two factors: (1) the degree of extrapancreatic progression of inflammation (anterior pararenal space, 0; root of the mesocolon, 1; and beyond the lower pole of the kidney, 2); and (2) the extent of the hypoenhanced lesion of the pancreas (localized in each segment (head, body, or tail) or only surrounding the pancreas, 0; extension to two segments, 1; and occupation of two or more entire segments, 2). A total score of 0 or 1 is defined as CT Grade 1, a total score of 2 as Grade 2, and a total score of 3 or more as Grade 3.

Other variables

The following patient baseline characteristics were also collected. Disturbance of consciousness (DOC) was diagnosed based on the recorded JCS, and it was categorized as follows: JCS 0 represents alert consciousness; one-digit codes (1–3) signify patients who are awake without stimulation; two-digit codes (10–30) indicate patients who can be aroused by some stimuli; and three-digit codes (100–300) represent coma. The JCS and Glasgow Coma Scale assessments correlate well [16, 17]. Each ICD-10 code of comorbidity was converted to a score, and the sum was used to calculate a Charlson Comorbidity Index (CCI) based on Quan's algorithm [21]. CCI was categorized into the three groups: low, 0; medium, 1–2; and high, ≥3. Hospital type was categorized into university and non-university.

We also collected data on several potentially effective treatments for acute pancreatitis, including protease inhibitors [22, 23], enteral nutrition [24, 25], selective decontamination of the digestive tract [26], continuous hemodiafiltration, continuous regional arterial infusion [27, 28], endoscopic treatment (nasopancreatic drainage, pancreatic pseudocyst drainage, and necrosectomy) [29, 30], and surgery (surgical drainage and necrosectomy) [31, 32].

Statistical analyses

Multivariate logistic regression for in-hospital mortality and multivariate linear regressions for length of stay and total costs were performed to analyze the relationship between HV and outcomes with adjustment for patients' sex, CCI, DOC, ICU admission, hospital type, prognostic factor score, and CT Grade. Since data derived from multiple hospitals were structured by two strata (hospitals and patients), we accounted for clustering within hospitals using generalized estimating equations (GEE) with an independent working correlation matrix and a robust estimator variance–covariance matrix [33, 34]. Here, we utilized GEE, instead of basic regression approaches, to account for clustering within hospitals, because the outcomes of patients with acute pancreatitis in the same hospital should be correlated, thus violating independence assumptions made by basic regression approaches. Using GEE with a unique hospital identifier as a subject variable, the correlation between the patients in the same hospital can be taken into account.

The relationship between HV and outcomes may not be linear, and, thus, we used RCS functions to fit the potential non-linear relationships of HV with three knots (5th, 50th, and 95th percentiles) and the reference value of median HV. RCS functions have the advantage of allowing smooth, plausible dose–response curves to demonstrate the non-linear relationship between a continuous independent variable and a dependent variable. The splines were restricted to be linear below the first knot and above the last. The GEEs with RCS regression models were constructed using the % RCS_Reg SAS macro developed by Desquilbet and Mariotti [13]. Tests for overall and non-linear relationships between HV and the outcomes were performed using χ^2 tests.

Older age has been reported to be a risk factor for in-hospital mortality associated with acute pancreatitis [35]. However, it was not included in this model, which considered the multicollinearity between age and prognostic factor score and included the factor "age ≥70 years."

All statistical analyses were performed using SAS version 9.2 (SAS Institute, Cary, NC, USA). A P value <0.05 was considered significant.

Results

Patient characteristics

In total, we identified 21,468 patients aged ≥20 years with acute pancreatitis from 1,032 participating hospitals (116 university and 916 community hospitals) during the 15-months study period; the prognostic factor score and CT severity score on admission were recorded for 17,702 patients. After excluding 287 patients who were transferred within 7 days of hospitalization, 17,415 patients were included in our analysis (Table 1). The median HV was 22.4: range, 1–82; 5th percentile, 6.4; 25th percentile, 14.0; 75th percentile, 32.0 and 95th percentile, 59.2.

The treatments administered were as follows: protease inhibitors in 91.1 % of patients; enteral nutrition in 10.0 %; selective decontamination of the digestive tract in 0.7 %; continuous hemodiafiltration in 1.2 %; continuous regional arterial infusion in 1.6 %; endoscopic procedures (naso-pancreatic drainage, pancreatic pseudocyst drainage, or necrosectomy) in 0.4 %; percutaneous abscess drainage in 0.4 %; and surgical drainage or necrosectomy in 0.2 %.

Relationship between HV and outcomes in patients with acute pancreatitis

Figures 1, 2 and 3 present the adjusted dose–response relationship between HV and outcomes. Table 2 shows the results of overall and non-linear relationships between HV and outcomes in acute pancreatitis.

Table 1 Characteristics of patients with acute pancreatitis ($n = 17{,}415$)

Age (years)	61.1 ± 17.8
Sex	
Males/Females (%)	65.3/34.7
Charlson comorbidity index	
0/1–2/≥3 (%)	42.9/44.0/13.1
Japan coma scale	
0/1–3/10–30/100–300 (%)	94.3/4.5/0.8/0.4
Prognostic factor score	
0/1/2/3/4/5/≥6 (%)	54.9/25.1/10.4/4.9/2.2/1.3/1.2
Computed tomography grade	
1/2/3 (%)	79.0/14.2/6.8
Use of intensive care unit (%)	2.8
Hospital type	
Academic/non-academic (%)	14.9/85.1
Hospital volume (per 12 months)	22.4 (1–82)

Age shown as mean and standard deviation. Hospital volume shown as medians and ranges. A Charlson comorbidity index was calculated based on Quan's algorithm [21]. Prognostic factor score and computed tomography grade were based on the Japanese severity for acute pancreatitis (2008 revision) [14]

The in-hospital mortality rate of patients with acute pancreatitis was 2.6 % and that of patients with severe acute pancreatitis was 7.1 %. Figure 1 displays the results of the RCS logistic regressions for in-hospital mortality. The odds ratios of in-hospital mortality at 5th-, 25th-, 75th- and 95th-percentile HV did not significantly differ from that at the median HV. The tests for overall and non-linear relationships between HV and in-hospital mortality did not produce significant results (Table 2).

The mean length of stay was 14 days (interquartile range, 10–22) for all acute pancreatitis patients. Figure 2 shows the results of the RCS linear regression for the length of stay. The length of stay was significantly lower at 75th-percentile and 95th-percentile HV and was significantly higher at 5th-percentile and 25th-percentile HV compared with the median HV. The test for the overall relationship between HV and length of stay was significant, whereas that for the non-linear relationship was not significant; this indicates that high HV was positively associated with shorter hospitalization (Table 2).

The mean total costs were US $7,740 (interquartile range, 5,150–11,920). Figure 3 presents the results of the RCS linear regression for total costs. The coefficient of total costs at 5th-percentile, 25th-percentile, 75th-percentile and 95th-percentile HV did not significantly differ from that at the median HV. The tests for overall and non-linear relationships between HV and total costs did not produce significant results (Table 2).

Discussion

In this nationwide study based on a Japanese administrative database, the median HV was 22.4 (range, 1–82), and we confirmed that higher HV was associated with shorter

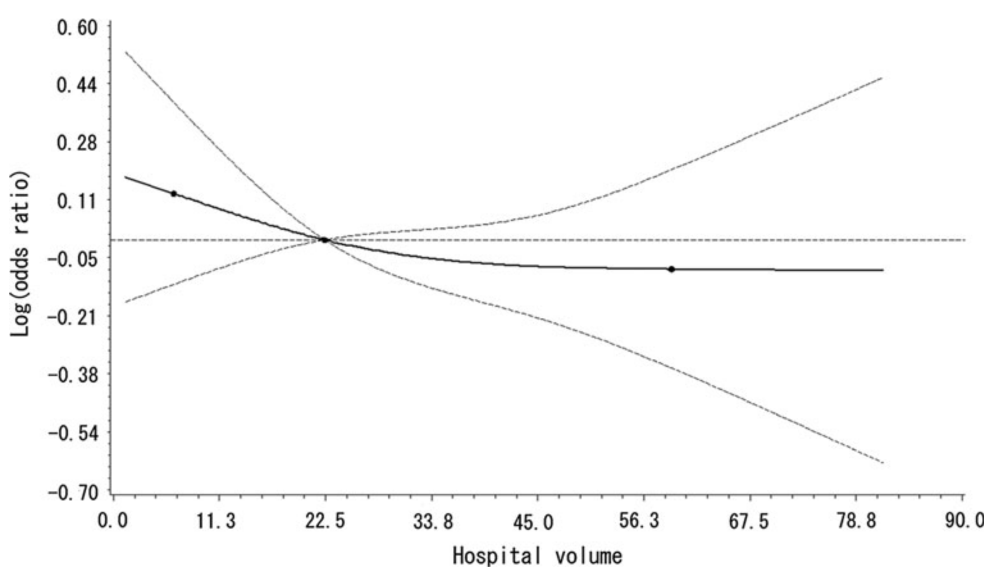

Fig. 1 Adjusted dose–response relationship between hospital volume and in-hospital mortality in acute pancreatitis using restricted cubic splines with three knots. The *y-axis* represents the odds ratio for in-hospital mortality according to hospital volume compared with the reference value of 22.4. The *dashed lines* indicate the 95 % confidence interval

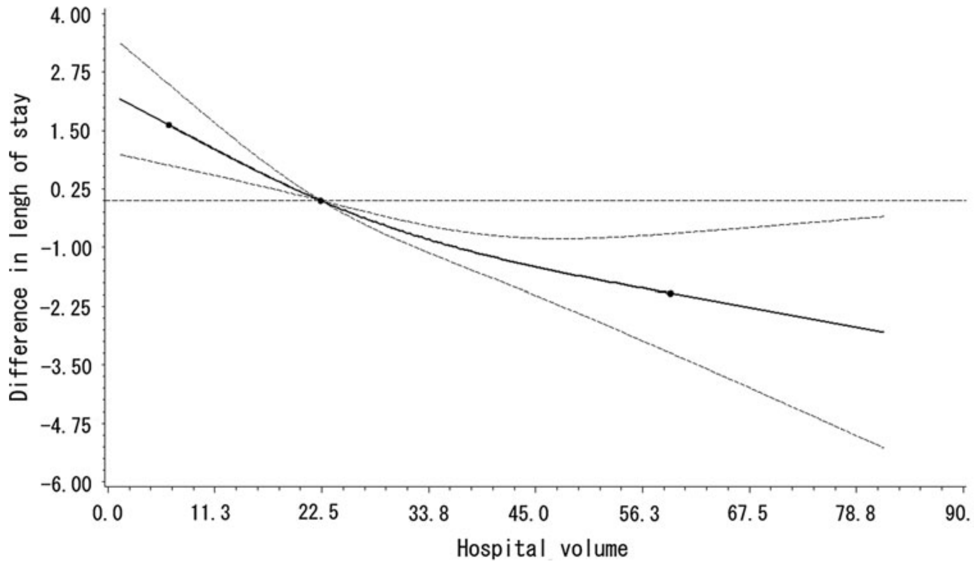

Fig. 2 Adjusted dose–response relationship between hospital volume and the length of stay in acute pancreatitis using restricted cubic splines with three knots. The *y-axis* represents the difference between length of stay according to hospital volume compared with the reference value of 22.4. The *dashed lines* indicate the 95 % confidence interval

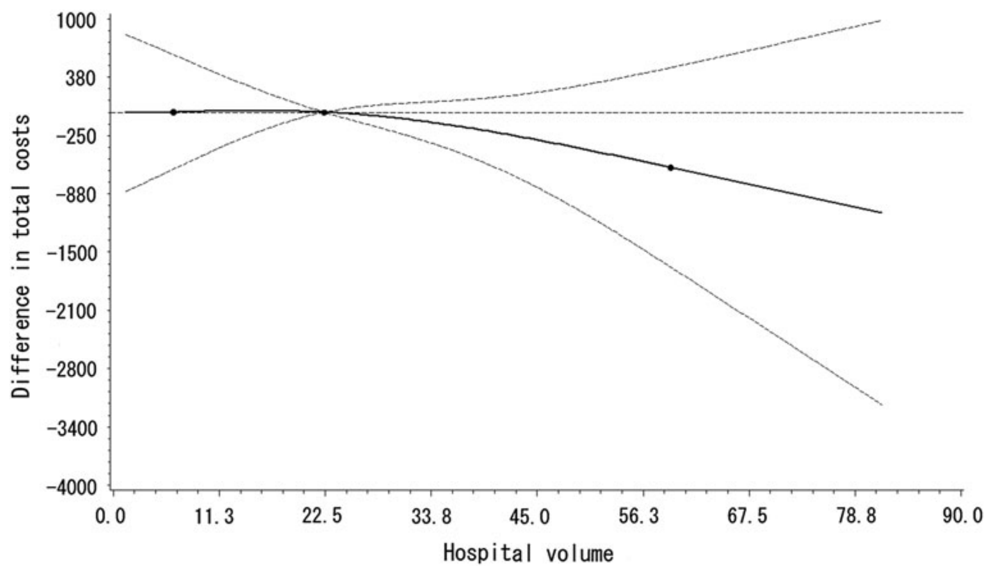

Fig. 3 Adjusted dose–response relationship between hospital volume and total costs in acute pancreatitis using restricted cubic splines with three knots. The *y-axis* represents the difference in total costs according to hospital volume compared with the reference value of 22.4. The *dashed lines* indicate the 95 % confidence interval

Table 2 Relationship between hospital volume and outcomes by means of restricted cubic spline functions with adjustment for patients' sex, Charlson comorbidity index, disturbance of consciousness, intensive care unit admission, hospital type, prognostic factor score, and computed tomography grade

	In-hospital mortality		Length of stay		Total costs	
	Log (OR)	*P* value	Estimate	*P* value	Estimate	*P* value
Linear spline of HV	–0.0090 (–0.0276, 0.0095)	0.341	–0.1087 (–0.1727, –0.0446)	0.001	2.231 (–43.39, 47.85)	0.924
First spline of HV	0.0000 (–0.0000, 0.0000)	0.535	0.0000 (–0.0000, 0.0001)	0.194	–0.0094 (–0.0418, 0.0230)	0.569
Overall relationship		0.459		<0.001		0.522
Non-linear relationship		0.535		0.194		0.569

Values in parentheses are 95 % confidence intervals

HV hospital volume, *OR* odds ratio

length of stay in acute pancreatitis. However, the inverse volume–outcome relationship was not evident in in-hospital mortality and total costs.

Given the increasing incidence [9] and high costs required for inpatient care of acute pancreatitis, a proper understanding of the volume–outcome relationship can help in optimizing medical care and resource utilization in clinical practice. It may also assist in deciding on appropriate referral patterns and future policy planning. Centralization of patients based on the concept of HV may thus facilitate the effective utilization of medical resources. To date, several population-based studies have shown high HV in acute pancreatitis to be associated with a lower mortality rate [9–11], shorter length of hospital stay [9–11], and lower total costs [9, 11]. There are several possible explanations for the impact of HV on outcomes in acute pancreatitis. First, various treatment options have recently been developed in managing acute pancreatitis, including aggressive fluid resuscitation, enteral nutrition [24, 25], and endoscopic, radiological, and operative interventions for specific complications [29–32]. The availability of these specific treatments in high-volume hospitals can offer better outcomes, especially in patients with severe acute pancreatitis. Second, the outcomes may be improved by the broader experience of physicians in high-volume hospitals, such physicians are able to administer specific treatments appropriately and coordinate multidisciplinary care.

This is the first study to have successfully adjusted for baseline disease severity using an established scoring system to evaluate the volume–outcome relationship in acute pancreatitis. The major drawback of studies examining the inverse volume–outcome relationship in acute pancreatitis has been the failure to adjust for the severity of pancreatitis based on an established scoring system [11]. Although several severity scoring systems have been developed and investigated for their effectiveness in predicting clinical outcomes [18, 35–38], a number of studies [9–11] failed to carry out risk adjustment through a lack of severity score in the databases employed. A review article about the volume–outcome relationship [39] reported that methodologically sophisticated risk adjustment using clinical data was less likely to report a positive effect of HV on outcomes. Thus, it could be that the inverse volume–outcome relationship in in-hospital mortality reported in studies of acute pancreatitis is less pronounced when appropriate adjustments are made for disease severity. We have previously found the Japanese Severity Scoring system to be useful for predicting in-hospital mortality [20]; the increase in prognostic factor score and CT Grade were both significantly correlated with in-hospital mortality. Using both the prognostic factor score and CT Grade, we successfully evaluated the volume–outcome relationship after adjusting for baseline disease severity.

The present study features another area of methodological strength. To date, no investigation has accounted for the potential non-linear relationship between HV and the outcomes associated with acute pancreatitis. Since the drawbacks of categorizing quantitative variables include loss of information and reduction in power [13], HV as a continuous variable was modeled using the RCS functions in the present study, thereby permitting a non-linear relationship between a variable and an outcome.

In the present study, we examined the inverse and linear volume–outcome relationship in terms of length of stay. After adjusting for specific treatment factors for acute pancreatitis, the inverse volume–outcome relationship was evident with length of stay (data not shown). Unlike previous studies [9–11], however, the present investigation failed to demonstrate a significant inverse volume–outcome relationship in in-hospital mortality in that HV had no effect on in-hospital mortality. Furthermore, the effect of HV on total costs was found to be insignificant. Improved analyses with successful risk adjustment could attenuate the apparently positive effects of high HV on mortality and total costs, as described above. The clinical practice guideline for acute pancreatitis is widely recognized in Japan, and the transfer of severe cases with $\geq$3 prognostic factor score to a specialized medical institution is recommended [14]. The Japanese prognostic factor score [19, 20] can be determined on the patient's presentation at a DPC participating hospital, and adherence to the guideline allows patients with severe acute pancreatitis to be treated in specialized high-volume hospitals. Since the relationships of HV and in-hospital mortality/total costs were found to be insignificant in the present study, a redundant transfer of patients with mild acute pancreatitis who could be appropriately managed in low-volume hospitals should not be justified in terms of cost-effectiveness. From a viewpoint of appropriate reallocation of medical resources, the selection criteria for transfer to high-volume hospitals should be evaluated to balance clinical outcomes and cost-effectiveness.

There are some limitations with the present study. First, some important clinical data were unavailable in the DPC database, such as the etiology of acute pancreatitis, past history of acute or chronic pancreatitis [40–42], and severity based on the revised Atlanta classification [43]. Second, although the analyzed national administrative database covers a large number of patients admitted to acute-care hospitals in Japan, most participating hospitals are secondary-care and tertiary-care centers.In these centers physicians have relatively wide experience in managing acute pancreatitis, which may attenuate the impact of HV on the outcomes.

In conclusion, the present population-based study failed to demonstrate an inverse volume–outcome relationship with in-hospital mortality and costs associated with acute pancreatitis. This was despite the shorter length of stay in higher HV. Further evidence is required to justify the volume-based selective referral of acute pancreatitis.

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Conflict of interest The authors declare that they have no conflict of interest.

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