Epidural analgesia is infrequently used in patients with acute pancreatitis : a retrospective cohort study

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Abstract

***Background and aims* : Epidural analgesia is an option for pain control in patients with acute pancreatitis. The aim of this study is to describe characteristics, morbidity and mortality of patients with acute pancreatitis treated with epidural analgesia.**

Patients and Methods : Data was extracted from a national inpatient database in Japan on patients hospitalized with acute pancreatitis between July 2010 and March 2013. A total of 44,146 patients discharged from acute care hospitals were included in this retrospective cohort study. The patient background, timing and duration of epidural analgesia, complications (epidural hematoma or abscess), surgery (for cholelithiasis / cholecystitis or complications) and mortality were verified.

***Results* : Epidural analgesia was used in 307 patients (0.70 %). The mean age was 64.0 years (standard deviation, 15.4 years) and 116 (37.8%) of the patients were female. The median duration of epidural analgesia was four days (interquartile range, 3-5 days). No patient underwent surgery for epidural hematoma or abscess. Six (2.0%) patients died during hospitalization. Most likely causes of death were pulmonary embolism, multiple organ failure, sepsis, and methicillin-resistant staphylococcus aureus enterocolitis. The responsible physician for 250 of the patients (81.4%) was a gastroenterological surgeon. Epidural analgesia was started on the day of surgery in 278 (90.6%) patients.**

***Conclusions* : Epidural analgesia is rarely used in patients with acute pancreatitis. None of the patients included in the study required surgery for epidural hematoma or abscess. Further research to evaluate the efficacy and safety of epidural analgesia in patients with acute pancreatitis is warranted.** (Acta gastroenterol. belg., **2017**, 80, **381-384**).

Key words: Acute pancreatitis, epidural analgesia, administrative data.

Introduction

Acute pancreatitis cause severe pain, which sometimes cannot be adequately controlled by drugs such as opioids. Since first reported by Orr and Warren (1), the continuous epidural analgesia has been an option for pain control in patients with acute pancreatitis. More recently, epidural analgesia for acute pancreatitis has been shown to be associated with increased pancreatic microcirculation (2,3) and attenuated systemic response (3), pancreatic necrosis (2,4), and mortality (3,4) in experimental animal models. However, data have been lacking whether epidural analgesia for pain control in patients with acute pancreatitis has become widespread in clinical practice. Accordingly, the aim of the present study is to describe the characteristics, morbidity and mortality of patients with acute pancreatitis treated with epidural analgesia using a nationwide administrative database in Japan.

Materials and Methods

The Institutional Review Board of the University of Tokyo approved this study. Informed consent was waived because there were no patient health information identifiers in this data.

Data source

Inpatient data was extracted from the Diagnosis Procedure Combination database, a nationwide, voluntary, administrative claims and discharge abstract database. It represents approximately 50% of all admissions to acute care hospitals in Japan (5). The Diagnosis Procedure Combination database provides (i) patient demographic data, (ii) admission-precipitating diagnosis, pre-existing comorbidities on admission, complications during hospitalization coded with the International Classification of Diseases, Tenth Revision (ICD-10) codes, (iii) hospital identification number, (iv) procedures coded with Japanese original codes (including continuous regional arterial infusion, open or laparoscopic cholecystectomy, endoscopic sphincterotomy, surgery for pseudocyst), dates when the procedures were performed, (v) discharge status (dead or alive), (vi) Japanese severity score for acute pancreatitis, (vii) contrast-enhanced computed tomography (CT) grade (6,7), (viii) specialty of the responsible physician for each patient, (ix) medications used (including opioids, vasopressor, antibiotics, and protease inhibitors), (x) nutrition (parenteral or enteral) and (xi) the transfusion of blood products. The Charlson comorbidity index was calculated based on Quan's protocol (8). Most likely causes of death were estimated by scrutinizing ICD-10 codes within the complications during hospitalization.

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Japanese severity score for acute pancreatitis

The Japanese severity score for acute pancreatitis was revised by the Research Committee of Intractable Diseases of the Pancreas, supported by the Japanese Ministry of Health, Labour and Welfare. The scoring system consists of prognostic factors and contrast-enhanced CT grade (Table 1) (6,7). The Japanese severity score was reported as a good predictor for persistent organ failure and in-hospital mortality (6,9).

Prognostic factors for in-hospital morality include nine separate factors related to the severity of acute pancreatitis (Table 1), which the total number of factors present within 48 hours of admission is presented as the overall severity score. The contrast-enhanced CT grade is a classification scheme for severity assessment using the combination of two factors and each factor is allocated score of 0 to 2 (Table 1), which sum of the scores of the two factors is presented as CT grade. A severity score more than or equal to 3 and a CT grade more than or equal to 2 are used as the definition of severe acute pancreatitis.

Table 1. — **Measure in systemic inflammatory response syndrome criteria include (i) fever of more than 38°C or less than 36°C, (ii) heart rate of more than 90 beats per minute, (iii) respiratory rate of more than 20 breaths per minute or arterial carbon dioxide tension ($PaCO_2$) of less than 32 mm Hg, and (iv) white blood cell count > 12,000/m^3, or < 4,000/m^3, or 10% immature (band) forms**

Scoring system	Description of the factor
Prognostic factor (Number of the factors presented)	
1	Base Excess ≦ -3 mEq/L, or systolic blood pressure ≦ 80 mmHg
2	PaO_2 ≦ 60 (room air) or the need for mechanical ventilation
3	Blood urea nitrogen ≧ 60 mg/dL, serum creatinine ≦ 2 mg/dL, or oliguria (urine output ≦ 400 ml/day, even after intravenous fluid resuscitation)
4	Lactate 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	Number of positive measures in systemic inflammatory response syndrome criteria ≧ 3
9	Age ≧ 70 years
CT grade (Sum of scores for each factor)	
1	Degree of extra-pancreatic progression of inflammation
	Score
	0 Anterior pararenal space
	1 Root of mesocolon
	2 Beyond lower pole of kidney
2	Extent of the poorly enhanced area. Pancreas is divided into three segments (head, body, and tail)
	Score
	0 Localized in each segment or only surrounding the pancreas
	1 Extended to two segment
	2 Occupy two entire segment of more

Patient selection

Data was extracted for all patients admitted from July 2010 to March 2013 who were admitted with an admission-precipitating diagnosis of acute pancreatitis (ICD10, K85). The present study included patients who underwent epidural analgesia during their hospitalization.

Table 2. — **Patient Demographic Data (n = 307)**

Factor	
Age, years, mean (SD)	64.0 (15.4)
Gender (female), n (%)	116 (37.8)
Charlson Comorbidity Index	
0, n (%)	128 (41.7)
1-2, n (%)	134 (43.6)
≧ 3, n (%)	45 (14.7)
Specialty of the physician in charge	
Gastroenterologist, n (%)	47 (15.3)
Gastroenterological surgeon, n (%)	250 (81.4)
Anesthesiologist, n (%)	0 (0)
Other, n (%)	10 (3.3)
Opioids, n (%)	307 (100)
Vasopressor, n (%)	91 (29.6)
Parenteral nutrition, n (%)	238 (77.5)
Enteral nutrition, n (%)	26 (8.5)
Continuous regional arterial infusion, n (%)	10 (3.3)
Antibiotics, n (%)	305 (99.3)
Protease inhibitor, n (%)	285 (92.8)
Transfusion of platelet concentration of fresh frozen plasma, n (%)	22 (7.2)
Epidural analgesia on the day of surgery	
Cholecystectomy, n (%)	196 (63.8)
Operation for pseudocyst, n (%)	9 (2.9)
Other surgery, n (%)	73 (23.8)
Non-surgical intervention	
Endoscopic sphincterotomy, n (%)	64 (20.8)
Percutaneous drainage, n (%)	2 (0.7)
Duration of epidural analgesia, day, median (IQR)	4 (3-5)

Table 3. — **Prognostic factors and CT grade (n = 307)**

Prognostic factor	n (%)
0	157 (51.1)
1	82 (26.7)
2	31 (10.1)
3	24 (7.8)
4	8 (2.6)
5	2 (0.7)
≧ 6	3 (1.0)
CT grade	
0	161 (52.4)
1	63 (20.5)
2	55 (17.9)
3	20 (6.5)
4	8 (2.6)

Table 4. — **Outcomes of patients with acute pancreatitis treated with epidural analgesia. (n = 307)**

Outcomes	
In-hospital mortality, n (%)	6 (2.0)
Hospital Length of Stay, days, median (IQR)	39 (24-61)
Complication of epidural analgesia	
Surgery for epidural hematoma or epidural abscess, n (%)	0 (0)

Statistical analysis

Continuous variables are presented as the mean with the standard deviation or the median with the interquartile range (IQR). Categorical variables are presented as a percentage. All analyses were conducted using SPSS version 22 (SPSS Inc, Chicago, IL).

Results

Of 44,146 patients admitted with acute pancreatitis during the study period, we identified 307 patients (0.70 %) who underwent epidural analgesia during their hospitalization. Table 2 shows the demographics of these 307 patients. The mean age was 64.0 years (standard deviation; SD, 15.4 years) and 116 patients (37.8%) were female. The median duration of epidural analgesia was four days (interquartile range; IQR, 3-5 days). Ninety-one patients (29.6%) were also treated with vasopressor medications. The responsible physician for 250 of the patients (81.4%) was a gastroenterological surgeon. Overall, 278 patients (90.6%) underwent surgery on the same day that epidural analgesia was started.

Table 3 shows the distribution of prognostic factors and CT grades in the study group. The number of patients with severe acute pancreatitis based on prognostic factors and CT grade was 37 (12.1%) and 83 (27.0%), respectively.

The outcomes are shown in Table 4. No patient underwent surgery for epidural hematoma or epidural abscess. Six patients (2.0%) died during hospitalization.

Two patients died with pulmonary embolism, two with multiple organ failure, one with sepsis, and one with methicillin-resistant staphylococcus aureus enterocolitis.

Discussion

This study describes patients with acute pancreatitis treated with epidural analgesia. Overall, epidural analgesia was performed for pain management in only 0.7% of patients with acute pancreatitis. Severe complications associated with epidural analgesia such as epidural hematoma or abscess was not seen in this population. However, the number of patients in the study group may be too small to detect these rare complications (10). The distribution of the patients with each of the prognostic factors and CT grades is similar to that in a previous study including approximately 18,000 patients with acute pancreatitis (6).

Since Orr and Warren (1) first reported continuous epidural analgesia for patients with acute pancreatitis, several reports suggested that epidural analgesia was effective for pain relief for these patients (11-15). However, the present study shows that patients with acute pancreatitis are rarely managed with epidural analgesia. Several possible explanations may be responsible for this result. First, the physicians who manage patients with acute pancreatitis may not be familiar with epidural analgesia. In the present study, no anesthesiologist was the physician in charge of treating patients with acute pancreatitis. Anesthesiologists may participate in the management only when the patients need an invasive procedure. This would explain why more than 90% of patients underwent epidural analgesia on the day of surgery. The second reason patients with acute pancreatitis are rarely managed with epidural analgesia is the concern that the patients may develop a concomitant coagulopathy (16) leading to an epidural hematoma. In this study, twenty-two patients (7.2%) underwent transfusions of platelet concentrate or fresh frozen plasma. If patients have coagulopathy, the risk of developing epidural hematoma increases not only when the catheter is inserted but also when the catheter is removed (17). Even if patients do not have coagulopathy at the time of epidural catheter insertion, it is hard to predict whether a patient may develop coagulopathy sometime later with an indwelling epidural catheter. The third reason physicians may have concerns for the use of epidural analgesia to treat the pain caused by acute pancreatitis is the possible risk of catheter infection. Since the duration of pain related to acute pancreatitis may be long, using the same epidural catheter to provide analgesia for the longer durations of pain increases the risk of catheter infection (18).

The pain with severe acute pancreatitis may last for several weeks. The signs and symptoms of infection may be difficult to detect because the clinical presentation of infection is masked by acute pancreatitis (19). Lastly, physicians may hesitate to use epidural analgesia for acute pancreatitis due to its potentials for hypotension. In our cohort, 29.6% of the patients received a vasopressor.

This study may be confounded by the fact that patients may have undergone epidural analgesia for control of surgical pain rather than the pain of acute pancreatitis, because they underwent epidural analgesia on the day of surgery. The reason for placement of the epidural catheter is not evident in the database. Cholecystectomy is recommended after improvement of symptoms in the Japanese guidelines for acute pancreatitis treatment (20). For such patients, it is possible that the pain due to acute pancreatitis had already resolved when epidural analgesia was initiated.

The present study shows no subsequent surgical interventions for epidural hematoma or abscess. These results may underestimate because patients with a

subclinical infection or hematoma may have been undetected. Other complications, which have been associated with epidural analgesia, such as urinary retention, and motor blockade were not able to detect in the database.

In this cohort, a total of 238 (77.5%) patients received parenteral nutrition. A number of studies suggested that enteral nutrition was preferable to parenteral nutrition for patients with acute pancreatitis, and current guidelines suggests that parenteral nutrition should be considered only when enteral nutrition is not tolerated (21, 22). However, Japanese guidelines does not make any recommendation with regard to nutritional support (23). Physicians in Japan may have not changed their practice since the past when total parenteral nutrition was considered as standard supportive care for acute pancreatitis (24).

The strength of this study is that it represents the largest case series using a nationwide administrative database. We acknowledge that the present study has some limitations. First, data on the effectiveness of epidural analgesia for pain relief was not included in the database. Second, the etiology of acute pancreatitis was thought to be gallstone pancreatitis in patients who underwent cholecystectomy or sphincterotomy. However, information about other etiologies was not available in the database. Third, the database does not include the date of onset of acute pancreatitis. Therefore, it is not known whether patients had pain due to acute pancreatitis at the time of surgery.

In conclusion, although the efficacy of epidural analgesia in the management of pain in patients with acute pancreatitis has been reported, this study demonstrates that epidural analgesia is not widely used for pain management in these patients in Japan. No patient required surgery for complications such as epidural hematoma or abscess. Further research to evaluate the efficacy and safety of epidural analgesia in patients with acute pancreatitis is warranted.

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