

Original Article

Efficacy of delayed primary closure with intrawound continuous negative pressure and irrigation treatment after surgery for colorectal perforation

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Aim: Surgical-site infections (SSIs) often occur after surgery for colorectal perforation. We introduced delayed primary closure (DPC) after intrawound continuous negative pressure and irrigation treatment (IW-CONPIT) to prevent SSIs. We aimed to evaluate the efficacy of DPC after IW-CONPIT compared with primary closure (PC) after surgery for colorectal perforation.

Methods: We undertook a retrospective study including 22 patients who underwent DPC (DPC group) and 18 patients who underwent PC (PC group) at our hospital between April 2015 and January 2017. The primary outcome was the SSI rate. The secondary outcomes were other complications (<30 days), length of hospital stay, and costs.

Results: The SSI rate was significantly lower in the DPC group than in the PC group (40% vs. 94%, $P = 0.0006$). Moreover, superficial and deep incisional SSIs, infectious complications, and Clavien–Dindo classification grade ≥ 2 complications were also significantly diminished in the DPC group. Conversely, the length of hospital stay and costs were not significantly different between the two groups. Multivariate analyses revealed that the significant independent protective factor against SSI after surgery for colorectal perforation was DPC after IW-CONPIT (odds ratio 0.04; 95% confidence interval, 0.002–0.25).

Conclusion: Delayed primary closure after IW-CONPIT reduced SSIs after surgery for colorectal perforation compared with PC.

Key words: Delayed primary closure, intrawound continuous negative pressure and irrigation treatment, surgical-site infection

INTRODUCTION

SURGICAL -site infections (SSIs) often occur after surgery for colorectal perforation. The occurrence of SSIs necessitates reopening and irrigating the wound, causing a decline in the quality of life and prolonging the length of hospital stay of patients. The efficacy of negative pressure wound therapy (NPWT)¹ and delayed primary closure (DPC)² for SSIs after colorectal perforation has been

reported. As NPWT could promote infection in dirty wounds, it must be carefully performed.³

Kiyokawa et al.⁴ reported the efficacy of intrawound continuous negative pressure and irrigation treatment (IW-CONPIT) for SSIs after orthopedic surgery and cardiovascular surgery. They reported that IW-CONPIT was effective for infected wounds.

We hypothesized that the IW-CONPIT would be effective for the prevention of SSIs even in the cases of colorectal perforation. We introduced IW-CONPIT and DPC after surgery for colorectal perforation in January 2016. In this study, we aimed to evaluate the efficacy of IW-CONPIT in patients who underwent surgery for colorectal perforation.

METHODS

Study setting and population

WE ENROLLED A total of 40 patients who underwent emergency surgery for diffuse peritonitis caused by

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colorectal perforation (Hinchey classification III or IV)⁵ at the Saiseikai Kumamoto Hospital (Kumamoto, Japan) between April 2015 and January 2017. We compared patients in whom primary closure (PC) was carried out (PC group, until December 2015) and patients in whom IW-CONPIT and DPC were applied (DPC group, after January 2016).

The Hinchey classification categorizes the stage of peritonitis due to diverticulum perforation in the large intestine; however, in this study, we adopted the classification for evaluating peritonitis due to colorectal perforation with various causes.

This study was carried out with approval from the Saiseikai Kumamoto Hospital Ethics Committee (ethical approval no. 736) and in accordance with the Declaration of Helsinki.

Surgical procedure

We resected the perforation site and created a stoma (Hartmann operation) in both groups. If the perforation site could not be resected, we created a loop stoma on the oral side. We used interrupted suturing at the fascia using monofilament sutures in both groups. The amount of incisional

wound irrigation was determined for each case. We closed the skin incision using buried sutures, staples, or nylon interrupted sutures in the PC group.

In the DPC group, wet gauzes and two tubes were placed inside the wound, which was subsequently covered with polyethylene film (Figure 1). The caudal-side tube was connected to a bottle of physiological saline solution, and the cranial-side tube was connected to a continuous aspirator. The volume of irrigation solution was set at 1,000 mL/day, and the aspiration pressure was 50 cm H₂O.

Wound management and diagnosis of SSIs

In the PC group, the attending physician checked the wound for the presence of SSIs every day. If SSIs were suspected, the wound was opened and the exudate was collected for culture. In the DPC group, we replaced the IW-CONPIT on postoperative day (POD) 2, 4, and 6. Each time, we washed the wound with 1,000 mL physiological saline. We carried out DPC with nylon interrupted sutures on POD 7 after confirming the absence of wound infection.

Surgical-site infections were categorized as superficial, deep, and organ/space. Surgical-site infections are recorded

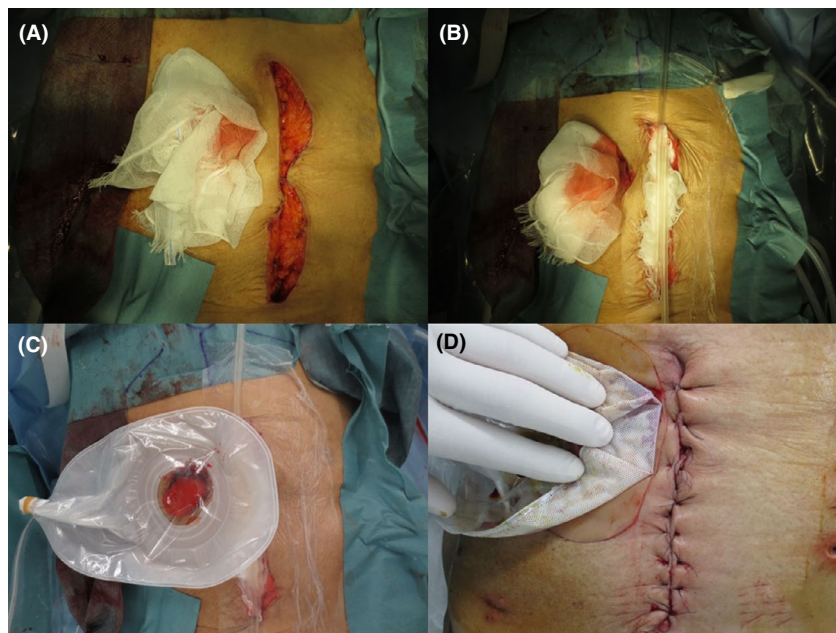


Fig. 1. Delayed primary closure after intrawound continuous negative pressure and irrigation treatment. A, Colostomy and fascia closure were carried out. B, Wet gauze and two tubes were placed inside the wound, which was subsequently covered with polyethylene film. C, The caudal-side tube was connected to a bottle of physiological saline solution, and the cranial-side tube was connected to a continuous aspirator. The volume of irrigation solution was set at 1,000 mL/day, and the aspiration pressure was 50 cm H₂O. D, The wound was closed after confirmation of no infection.

in the Japan Nosocomial Infections Surveillance system based on the guidelines stipulated by the National Nosocomial Infections Surveillance System of the Centers for Disease Control and Prevention.⁵

Data collection

We collected baseline data such as age, sex, vital signs, and laboratory results at the time of admission, for the calculation of various scores. We also collected the following information: Acute Physiology and Chronic Health Evaluation (APACHE) II score, Sequential Organ Failure Assessment (SOFA) score, disseminated intravascular coagulation (DIC) score, surgery-related factors (Hinchey classification, perforation site, cause of perforation, operative method, operation time, and blood loss), and additional treatment. As additional treatment, we used recombinant human soluble thrombomodulin for patients with a DIC score (Japanese Association for Acute Medicine) of ≥ 4 and steroids for patients with septic shock who were receiving vasopressor treatment.

Outcomes

The clinical data and outcomes were compared between the DPC and PC groups. The primary outcome was the total SSI rate. The secondary outcomes were superficial SSI and deep SSI rates, organ/space SSI rate, infectious complication rate, serious complication rate (Clavien–Dindo classification ≥ 2), 30-day survival rate, and length of hospital stay.

Statistical analyses

Variables are shown as median (25%–75% interquartile range), or number (percentage) of patients. Univariate analyses were carried out using the χ^2 -test for categorical variables and the Mann–Whitney *U*-test for continuous variables. In all tests, two-tailed *P*-values < 0.05 were considered statistically significant. We used JMP version 10.0.2 (SAS Institute, Cary, NC, USA) for statistical analyses.

RESULTS

A TOTAL OF 40 patients were analyzed during the study period (Table 1). The median patient age was 76 (68–85) years, 17 patients (43%) were men, and the median American Society of Anesthesiologists physical status (ASA-PS) score was 3 (3–3). According to the Hinchey classification, 19 patients had stage III peritonitis and 21 patients had stage IV peritonitis. The sigmoid colon (62%) was the most common perforation site. The causes of

Table 1. Characteristics of patients who underwent surgery for colorectal perforation

Age, years	76 (68–85)
Male	17 (43)
Body mass index	22 (19–26)
Performance status	0 (0–2)
ASA-PS	3 (3–3)
Hinchey classification III/IV	19/21
Location (cecum/ascending/transverse/ descending/sigmoid/rectum)	2/2/3/3/25/ 5
Disease (cancer/diverticulum/idiopathic/ iatrogenic/ischemia)	13/12/10/ 4/1
Scoring	
APACHE II score	12 (9–18)
SOFA score	3 (1–4.8)
SIRS score	2 (2–3)
DIC score (JAAM)	2 (1–3.8)
Operation procedure	
Surgery (Hartman procedure/stoma)	34/6
Operation time (min)	149 (120– 182)
Blood loss (cc)	100 (10– 400)
Additional treatment	
Recombinant human soluble thrombomodulin	18 (45)
Antithrombin III	8 (20)
γ -Globulin	6 (15)
Steroids	7 (18)
Polymyxin B-immobilized fiber column direct hemoperfusion	9 (25)
Continuous renal replacement therapy	3 (8)

Data are shown as number, *n* (%), or median (interquartile range).

APACHE, Acute Physiology and Chronic Health Evaluation; ASA-PS, American Society of Anesthesiologists physical status classification system; DIC, disseminated intravascular coagulation syndrome; JAAM, Japanese Association for Acute Medicine; SIRS, systemic inflammatory response syndrome; SOFA, Sequential Organ Failure Assessment.

perforation were carcinoma in 13 cases (32%), diverticulum in 12 cases (30%), and idiopathic in 10 cases (25%).

Table 2 compares the background characteristics of patients in the DPC group (22 patients) and those in the PC group (18 patients). No significant differences were observed in age, sex, or ASA-PS score between the two groups. In preoperative vital signs, the respiratory rate was significantly higher in the DPC group than in the PC group. With respect to surgery-related factors, although there were no significant differences in the Hinchey classification,

Table 2. Comparison of characteristics in patients who underwent surgery for colorectal perforation, treated with delayed primary closure (DPC) after intrawound continuous negative pressure and irrigation treatment or primary closure (PC)

	DPC group (n = 22)	PC group (n = 18)	P-value
Age, years	76 (69–85)	73 (65–83)	0.3300
Male	9 (41)	8 (44)	1.0000
Body mass index	23 (21–26)	21 (19–25)	0.4000
Performance status	1 (0–2)	0 (0–2)	0.7000
ASA-PS	3 (3–4)	3 (2–3)	0.6800
Hinchey classification III/IV	10/12	9/9	1.0000
Location (cecum/ascending/transverse/descending/sigmoid/rectum)	1/1/2/2/13/3	2/1/1/1/11/2	0.9600
Disease (cancer/diverticulum/idiopathic/iatrogenic/ischemia)	8/8/5/1/0	4/5/5/3/1	0.4500
Vital signs			
Glasgow Coma Scale	15 (14–15)	15 (14–15)	0.3868
Systolic blood pressure (mm Hg)	131 (112–150)	125 (99–140)	0.2828
Heart rate (b.p.m.)	100 (78–113)	92 (70–105)	0.3341
Respiratory rate (/min)	25 (23–31)	20 (17–24)	0.0116
Body temperature (°C)	37.7 (36.5–38.4)	37.3 (36.7–38.7)	0.8383
Lab data			
White blood cells (/μL)	5,900 (3,250–11,950)	5,950 (3,475–11,175)	0.9350
Hemoglobin (g/dL)	11 (9–14)	12 (10–13)	0.5679
Hematocrit (%)	35 (29–41)	36.6 (32.6–41.2)	0.3413
Platelets ($\times 10^4$ /L)	21 (14–24)	20 (13–26)	0.8278
Creatinine (mg/dL)	1.1 (0.6–1.8)	0.8 (0.6–1.4)	0.5680
Total bilirubin (mg/dL)	0.7 (0.6–1.1)	0.85 (0.58–1.22)	0.6722
Albumin (mg/dL)	3 (2.7–3.8)	3.3 (2.9–3.9)	0.4976
C-reactive protein (mg/dL)	8.6 (0.7–21)	12 (1.9–20)	0.8811
International normalized ratio of prothrombin time	1.1 (1–1.3)	1.1 (1–1.3)	0.7339
Lactate (mmol/L)	2.2 (1.6–3.9)	1.5 (1–3.2)	0.2310
Scoring			
APACHE II score	13 (10–18)	14 (11–24)	0.2095
SOFA score	2.5 (1–4.3)	2.5 (1–5)	0.6198
SIRS score	3 (2–3)	2 (1–3)	0.0830
DIC score (JAAM)	3 (1–4)	2 (0.8–2.3)	0.1980
Operation procedure			
Surgery (Hartman procedure/stoma)	21/1	13/5	0.0700
Operation time (min)	149 (125–181)	143 (118–196)	0.9100
Blood loss (cc)	150 (40–385)	95 (5–400)	0.8400
Wound protector	19 (86)	14 (78)	0.6700
Peritoneal lavage (cc)	10,000 (9,750–13,000)	10,000 (9,500–11,000)	0.6000
Incisional wound irrigation (cc)	1,000 (500–1,000)	500 (500–500)	0.0160
Subcutaneous drain	0 (0)	3 (17)	0.0800
Antimicrobial-coated suture	17 (77)	10 (55)	0.1800
Changing of surgical instruments	6 (27)	1 (5)	0.1000
Additional treatment			
Recombinant human soluble thrombomodulin	12 (54)	6 (33)	0.2100
Antithrombin III	5 (23)	3 (17)	0.7080
Steroids	6 (27)	1 (6)	0.1048
Polymyxin B-immobilized fiber column direct hemoperfusion	7 (32)	2 (11)	0.1489
Continuous renal replacement therapy	3 (14)	0 (0)	0.2385

Data are shown as number, n (%), or median (interquartile range).

APACHE, Acute Physiology and Chronic Health Evaluation; ASA-PS, American Society of Anesthesiologists physical status classification system; DIC, disseminated intravascular coagulation syndrome; JAAM, Japanese Association for Acute Medicine; SIRS, systemic inflammatory response syndrome; SOFA, Sequential Organ Failure Assessment.

Table 3. Comparison of outcomes in patients who underwent surgery for colorectal perforation, treated with delayed primary closure (DPC) after intrawound continuous negative pressure and irrigation treatment or primary closure (PC)

	DPC group (n = 22)	PC group (n = 18)	P-value
Primary outcome			
Total SSIs	9 (40)	17 (94)	0.0006
Secondary outcomes			
Superficial/deep SSI	2 (9)	15 (83)	0.0010
Organ/space SSI	8 (36)	10 (56)	0.3300
Infectious complications	11 (50)	17 (94)	0.0043
Severe complications (CD \geq 2)	14 (64)	17 (94)	0.0260
30 days survival	18 (81)	17 (94)	0.3500
Length of hospital stay	24 (21–29)	25 (20–36)	0.4300
Length of ICU stay, median	8 (4–12)	4 (3–7)	0.0200
Duration of mechanical ventilation	3 (0–4)	0 (0–1)	0.0100
Reoperation	1 (5)	3 (17)	0.3100
Readmission	1 (5)	3 (17)	0.3100
Costs (¥1,000)			
Total	3,098 (2,000–4,467)	2,364 (1,784–3,011)	0.2650
Surgical	947 (647–1,160)	638 (548–1,058)	0.1279
Non-surgical	1,979 (1,388–3,557)	15,97 (1,265–2,048)	0.4305

Data are shown as n (%) or median (interquartile range).
CD, xxx; ICU, intensive care unit; SSI, surgical-site infection.

perforation site, cause of perforation, or operative method, the volume of incisional wound irrigation was significantly higher in the DPC group. No significant differences in the use of recombinant human soluble thrombomodulin or continuous renal replacement therapy were found between the two groups.

Table 3 compares the outcomes in the two groups. The total SSI rate (primary outcome) was significantly lower in the DPC group than in the PC group (40% vs. 94%, $P = 0.0006$). Among the secondary outcomes, the superficial and deep SSI rates were significantly lower in the DPC group than in the PC group (9% vs. 83%, $P = 0.001$). The infectious complication rate was significantly lower in the DPC group (50% vs. 94%, $P = 0.004$). No significant differences were observed in the organ/space SSI rate, 30-day survival rate, or the length of hospital stay between the two groups.

We undertook logistic regression analysis to determine the predictors of SSIs (Table 4). The cut-off values of various factors were determined using receiver operating characteristic curve analysis. In the univariate analysis, volume of incisional wound irrigation \geq 1,000 mL (odds ratio 0.14; 95% confidence interval, 0.03–0.58) and DPC (odds ratio 0.04; 95% CI, 0.002–0.25) were significant protective factors.

We carried out a subgroup analysis by dividing the patients according to the Hinchey classification. The total SSI rate was significantly lower in the DPC group than in the PC group regardless of the Hinchey classification (Hinchey classification III, 20% vs. 88%; Hinchey classification IV, 58% vs. 100%), and the superficial and deep SSI rates were also significantly decreased. The two groups showed no difference in the length of hospital stay.

DISCUSSION

THIS IS THE first study to evaluate the efficacy of IW-CONPIT and DPC after surgery for colorectal perforation. The combination of IW-CONPIT and DPC reduced the SSI rate compared with PC.

The incidence of SSIs is high after surgery for diffuse peritonitis. In a previous report, the SSI rate of dirty wounds was 40%.⁶ Surgical-site infections frequently require wound irrigation, decrease the patient's quality of life, and prolong hospital stay.

Cohn et al. reported a randomized controlled trial on DPC for dirty abdominal wounds associated with appendicitis or gastrointestinal perforation.² Delayed primary closure for dirty abdominal wounds reduced the SSI rate from 48% to 12%. Many studies on DPC for perforated appendicitis have

Table 4. Logistic regression analysis for surgical-site infections following surgery for colorectal perforation

	Univariate analysis		P-value
	OR	95% CI	
Male	1.50	0.40–6.20	0.5200
Age ≥ 69 years	3.10	0.75–14.00	0.1100
Hinchey classification IV	2.80	0.76–11.00	0.1100
Body mass index ≥ 24	0.44	0.11–1.69	0.2300
ASA-PS ≥ 4	0.59	0.12–2.80	0.5000
Perforation site (sigmoid)	0.50	0.12–2.11	0.3800
Hartman procedure	0.32	0.01–2.30	0.2800
Operation time ≥ 136 min	1.80	0.50–7.20	0.3400
Wound protector	0.25	0.01–1.70	0.1700
Peritoneal lavage ≥ 10,000 mL	3.00	0.66–15.00	0.1400
Incisional wound irrigation ≥ 1,000 mL	0.14	0.03–0.58	0.0061
Antimicrobial-coated suture	1.25	0.30–4.90	0.7500
Subcutaneous drain	1.08	0.09–24.00	0.9400
DPC with IW-CONPIT	0.04	0.002–0.250	0.0002
SOFA score ≥ 5	2.60	0.50–19.00	0.2300
Albumin ≥ 3.8 mg/dL	1.90	0.40–10.00	0.3700
C-reactive protein ≥ 26 mg/dL	0.20	0.02–1.20	0.0800
Lactate ≥ 4.0 mmol	5.70	0.80–113.00	0.0600

ASA-PS, American Society of Anesthesiologists physical status classification; CI, confidence interval; DPC, delayed primary closure; IW-CONPIT, intrawound continuous negative pressure and irrigation treatment; OR, odds ratio; SOFA, Sequential Organ Failure Assessment.

been published; however, they generally reported negative effects of DPC.^{7–11} A recent meta-analysis by Tsang et al. revealed that DPC was a better option for preventing infection in patients with comorbidities, and that poor surgical conditions, such as the presence of immunodeficiency diseases, diabetes mellitus, malnutrition, poor operating room environment, and prolonged operation duration, could increase the possibility of wound infection.⁹ However, there have been no reports on the efficacy of DPC specifically limited to colorectal perforation.

The efficacy of NPWT as a method for preventing SSIs after surgery for diffuse peritonitis has been evaluated in several studies. Danno et al.¹ reported that NPWT reduced SSIs after surgery for peritonitis caused by lower gastrointestinal perforation. However, no significant difference was observed between the groups in terms of the length of hospital stay. The greatest drawback of NPWT is that it is difficult to use for infected wounds. Weed et al. reported that NPWT

usually promotes a higher level of bacterial bioburden in wounds.³

Therefore, we introduced IW-CONPIT, which can also be used for infected wounds, from the day of surgery and carried out DPC at 7 days after surgery. In 2007, Kiyokawa et al.⁴ reported IW-CONPIT as a method for continuously irrigating and applying negative pressure on infected head wounds and mediastinitis after cardiovascular surgery. It is a useful technique for infected wounds because the wound area is continuously irrigated with saline solution for 24 h, thus eliminating the opportunity for bacterial regrowth. We continued IW-CONPIT for 7 days after surgery and carried out DPC after confirming the absence of signs of infection at the wound site. In this study, IW-CONPIT + DPC significantly reduced the total SSI (DPC group 40% vs. PC group 94%, $P = 0.0006$) and superficial and deep SSI rates (DPC group 9% vs. PC group 83%, $P = 0.001$). In addition, infectious complications and serious complications (Clavien–Dindo classification ≥ 2) were also significantly reduced.

However, the length of hospital stay and costs did not differ between the two groups. The differences in the background characteristics of patients might have contributed to the lack of difference in the length of hospital stay. The preoperative respiratory rate was significantly higher in the DPC group. The duration of mechanical ventilation was significantly longer in the DPC group (3 days in the DPC group vs. 0 days in the PC group, $P = 0.02$), and the length of intensive care unit stay was also significantly prolonged in the DPC group (8 days in the DPC group vs. 4 days in the PC group, $P = 0.01$). Although there was no significant difference in the preoperative SOFA score or APACHE II score between the two groups, the SOFA score on POD 1 tended to be higher in the DPC group (DPC group 7 vs. PC group 3, $P = 0.057$). This could be attributed to the possibility that more seriously ill patients were included in the DPC group than in the PC group. In the DPC group, the extubation time was not prolonged because the wound was open.

In the univariate analysis, DPC with IW-CONPIT and incisional wound irrigation volume ≥ 1,000 mL were extracted as factors that reduced SSI after colon perforation. Few studies have been published on the use of IW-CONPIT in abdominal surgery, although, notably, IW-CONPIT has been reported under the name “NPWT with instillation” using the V.A.C. ULTA system. Conversely, there are many reports in the orthopedic field; however, the reported effect was controversial.^{12–14} In the field of abdominal surgery, only one case report of Fournier’s gangrene¹⁵ and a report on the efficacy of IW-CONPIT in open wounds with exposed meshes¹⁶ have been published. This is the first report on the use of IW-CONPIT for the prevention of SSI after surgery for colorectal perforation. Intrawound

continuous negative pressure and irrigation treatment can be used to treat infected wounds. Because saline solution is injected, water leakage could occur unless negative pressure is applied. In this study, unexpected replacement was needed in a small number of cases because of water leakage. However, no complications due to IW-CONPIT, such as skin irritation or bleeding, were observed.

This study had several limitations. First, this was a retrospective cohort study. In our department, we had used PC after surgery for colorectal perforation until December 2015. We introduced DPC with IW-CONPIT from January 2016. Thus, there may be differences in historical background. With respect to additional treatments, no significant difference was observed between the two groups; however, a higher sample size could result in a significant difference in additional treatments, such as the use of steroids. Moreover, the results of the univariate analysis showed that the volume of incisional wound irrigation was also a factor that reduced SSIs. The fact that the volume of incisional wound irrigation was higher in the DPC group than in the PC group might have influenced this result. Even after the introduction of DPC, there were cases in which PC was selected according to the doctor's judgment, and this could have introduced a selection bias. Therefore, we have initiated a single-center randomized controlled trial evaluating the efficacy of DPC after surgery for colorectal perforation (UMIN000032357), which is currently ongoing.

CONCLUSION

DELAYED PRIMARY CLOSURE after IW-CONPIT reduces superficial and deep SSIs after surgery for colorectal perforation, compared with PC.

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DISCLOSURES

Approval of the research protocol: The present study was approved by the institutional review board of Saiseikai Kumamoto Hospital.

Informed consent: Because this was a retrospective review of medical records, consent to participate was not required from the patients.

Registry and registration no. of the study/trial: N/A.

Animal studies: N/A.

Conflict of interest: None.

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