Correlation of Operative Mortality and Morbidity With Preoperative C-Reactive Protein/Albumin Ratio, Neutrophil/Lymphocyte Ratio, and Prognostic Nutritional Index in Patients Undergoing Emergent Operations Due to Strangulation Ileus

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Emergent surgery is necessary in patients with strangulation ileus. However, such procedures are associated with high morbidity and mortality. A retrospective analysis was performed to determine whether the preoperative C-reactive protein/albumin ratio (CAR); neutrophil/lymphocyte ratio (NLR); and prognostic nutritional index (PNI) are good indicators of mortality or morbidity in patients undergoing emergent operations for treatment of strangulation ileus. Emergent surgery was performed for 1698 patients at Tottori Prefectural Central Hospital from 2012 and 2015. Among them, 45 patients (2.7%) were preoperatively diagnosed with strangulation ileus. We evaluated the clinical importance of the preoperative CAR, NLR, and PNI in these patients. We excluded pediatric patients from this study. Postoperative complications developed in 14 of 45 (31.1%) patients. The mean postoperative hospital stay among the 14 patients with postoperative complications was significantly longer than that of the 31 patients without postoperative complications (44.0 versus 11.3 days, respectively; \( P = 0.006 \)). Three patients died of postoperative complications. The overall operative mortality and morbidity rates were 6.7% and 31.1%, respectively. We found strong correlations of postoperative complications with older age, a longer operation time, and an abnormal preoperative
CAR, NLR, and PNI. Not only inflammation, but also a patients’ nutritional and immune status appear to be strongly correlated with mortality or morbidity after emergent operations for strangulation ileus. Patients with a high CAR and NLR and low PNI preoperatively must be closely monitored for the occurrence of postoperative complications such as surgical site infections or pulmonary complications.

Key words: C-reactive protein-albumin ratio – Neutrophil-lymphocyte ratio – Postoperative complication – Prognostic nutritional index – Strangulation ileus

Strangulation ileus is an intestinal obstruction associated with ischemia of the intestinal tract. If the ischemic intestine is left untreated, the resulting intestinal necrosis could become fatal because of intestinal perforation. Therefore, rapid diagnosis and emergent surgical treatment are required to save the lives of patients with strangulation ileus. However, many patients develop postoperative complications, and a considerable number of patients die of these postoperative complications. Fevang et al.1 reported that the morbidity and mortality rates after surgical treatment of small bowel obstruction were 22.3% and 5.2%, respectively. Knowledge of the preoperative factors that affect the occurrence of postoperative complications is necessary to reduce the incidence of these complications.

In the present study, we focused on patients’ preoperative C-reactive protein/albumin ratio (CAR); neutrophil/lymphocyte ratio (NLR); and prognostic nutritional index (PNI). The CAR has been used in combination with other parameters to not only diagnose chronic inflammation, but also assess the nutritional status of patients with cancer. Additionally, the pretreatment CAR has been shown to be a significant prognostic indicator in various carcinomas.2-4 The NLR and PNI are markers of chronic systemic inflammation and the patients’ immune status and nutritional condition.5-7 We analyzed whether the CAR, NLR, and PNI are effective indicators of postoperative complications in patients undergoing emergent operations for strangulation ileus independent of age or treatment delay, which are thought to be significant risk factors for the occurrence of postoperative complications.

Patients and Methods

Patients

From 2012 to 2015, emergent surgery was performed for 1698 patients at Tottori Prefectural Central Hospital. Obstruction ileus was detected in 102 patients; among them, strangulation ileus was preoperatively diagnosed in 45 patients (44.1%). We excluded pediatric patients from this study. The average age of patients was 72 years (range: 17–93 years). A total of 25 patients were male and 20 were female. Informed consent regarding medical treatment and use of the patients’ clinical data was obtained from all patients. This study was approved by the ethical review board of Tottori Prefectural Central Hospital (approval number: 2016-19).

Diagnosis of strangulation ileus

Each patient underwent a physical examination, simple X-ray examination, laboratory tests, and contrast computed tomography (CT) before surgery. Strangulation ileus was diagnosed when patients showed any signs of peritonitis on physical examination or intestinal ischemia on contrast CT.8

Laboratory tests

The preoperative laboratory tests comprised measurement of the white blood cell count, absolute neutrophil count, C-reactive protein concentration, albumin concentration, lactate dehydrogenase concentration, creatine kinase concentration, and pH and base excess in the blood gas analysis. The serum albumin concentration, C-reactive protein concentration, and total lymphocyte count were recorded.

Parameters

The following parameters thought to affect the occurrence of postoperative complications and a long hospital stay were assessed: 1) age; 2) time from symptom onset to surgery (symptom onset was considered the time at which the patient began to feel acute abdominal pain); 3) operation time; 4) laparoscopic or open surgery; 5) resection of the small intestine; and 6) preoperative CAR, NLR, and PNI. The PNI was calculated using the following
Statistical analysis

Differences between two normally distributed parameters were compared using the $\chi^2$ test and Fisher’s exact probability test. The Mann-Whitney U test was used to compare differences between two parameters with non-normal distributions. The 45 patients were divided into 2 subgroups for each of the following parameters: median age (76 years; high and low subgroups), median time from symptom onset to surgery (12.5 hours; long and short subgroups), and median operation time (86 minutes; long and short subgroups). The cutoff levels of the CAR, NLR, and PNI were determined using mean $+2 \times SD$ for the CAR and NLR, and mean $-2 \times SD$ for the PNI according to previous studies.9,10 Correlations were determined using Spearman’s rank correlation coefficient. The presence of a strong correlation between the various parameters and the occurrence of postoperative complications was determined using logistic-regression analysis. All data were analyzed using a commercial software package (StatView; Abacus Concepts, Inc., Berkeley, CA, USA). A $P < 0.05$ was considered statistically significant.

Results

The clinical characteristics of the 45 patients with strangulation ileus are shown in Table 1. Postoperative complications developed in 14 (31.1%) patients: surgical site infection in 6, pulmonary disease in 4, adhesion in 2, sepsis in 1, and cardiac disease in 1. The mean postoperative hospital stay among the 14 patients with postoperative complications was significantly longer than that of the 31 patients without postoperative complications (44.0 versus 11.3 days, respectively, $P = 0.006$). Three patients died of postoperative complications. One patient died of sepsis 2 days after surgery, 1 died of pulmonary dysfunction 10 days after surgery, and 1 died of a surgical site infection 35 days after surgery. Thus, the operative mortality and morbidity rates in our series were 6.7% and 31.1%, respectively.

| Parameters | Age, y, mean ± SD | Sex, male/female | Time to surgery from onset time, h, mean ± SD | Operation time, min, mean ± SD | Operative approach, open/laparoscopic | Resection of intestine, yes/no | Postoperative hospital stay, d, mean ± SD |
|------------|------------------|-----------------|---------------------------------------------|-------------------------------|------------------------------------|-------------------------------|------------------------------------|
|            | 72 ± 16.6        | 25/20           | 27.7 ± 41.5                                 | 94.4 ± 51                     | 32/13                              | 20/25                         | 21.5 ± 27.6                      |

The mean CAR, NLR, and PNI among of the 147 control patients with inguinal hernia were 0.037 (range: 0.002–0.464); 2.5 (range: 0.9–19.4); and 49.9 (range: 35.2–61.7), respectively. The SDs of the CAR, NLR, and PNI among the control patients were 0.061, 1.9, and 4.8, respectively. Thus, the cutoff levels of the CAR, NLR, and PNI were 0.159, 6.3, and 40.3, respectively. The mean CAR, NLR, and PNI among the 45 patients with strangulation ileus were 0.726 (range: 0.002–6.3); 12.7 (range: 0.6–57.9); and 44.4 (range: 30.1–61.3), respectively. According to the cutoff levels of CAR, NLR, and PNI, an abnormal CAR (>0.159) was detected in 20 patients (44.4%); an abnormal NLR (>6.3) was detected in 33 patients (73.3%); and an abnormal PNI (<40.3) was detected in 15 patients (33.3%). All 3 factors (CAR, NLR, and PNI) were abnormal in 12 patients (26.7%). The mean preoperative CAR and NLR of the 14 patients with postoperative complications (CAR: 2.0, NLR: 18.3) were higher than those of the 31 patients without postoperative complications (CAR: 0.151, $P < 0.001$ and NLR: 1.0, $P = 0.045$). Additionally, the mean preoperative PNI of the 14 patients with postoperative complications was significantly lower than that of the 31 patients without postoperative complications (39.2 versus 46.9, respectively: $P = 0.003$). We found a strong positive correlation between the CAR and NLR ($\rho = 0.413, P = 0.008$) and a strong negative correlation between the CAR and PNI, and between the NLR and PNI ($\rho = -0.631, P < 0.001$ and $\rho = -0.419, P = 0.007$, respectively).

We analyzed factors thought to influence the occurrence of postoperative complications after surgery for strangulation ileus. The 6 candidate factors were 1) age, 2) time from onset of symptoms to surgery (onset of symptoms was the time at which the patient began to feel acute abdominal...
pain); 3) operation time; 4) laparoscopic or open surgery; 5) resection of the small intestine; and 6) preoperative CAR, NLR, and PNI. Table 2 shows the results derived from the logistic-regression analysis. Older age, a longer operation time, and an abnormal preoperative CAR, NLR, and PNI were proven to be extremely strong risk factors for postoperative complications (Table 2).

We also found that abnormal preoperative CAR, NLR, and PNI were strongly correlated with the time from onset of symptoms to surgery (Table 3). Resection of the small intestine was not a significant risk factor for postoperative complications according to the multivariate analysis. The 20 patients who underwent resection of the small intestine had a higher incidence of postoperative complications than the 25 patients who did not undergo resection (60% versus 8%, respectively, \( P < 0.001 \)). Additionally, resection of the small intestine was associated with a longer mean operation time than were operations performed without resection (129.5 versus 66.4 minutes, respectively, \( P < 0.001 \)). However, the time from onset of symptoms to surgery was not correlated with resection of the small intestine (\( P = 0.213 \)), and abnormal preoperative CAR, NLR, and PNI were not correlated with resection of the small intestine (\( P = 0.258 \)).

### Discussion

High morbidity and mortality rates after surgery for treatment of strangulation ileus have been serious problems for many surgeons. Rapid establishment of a precise diagnosis performance of emergent surgery may be the keys to favorable postoperative outcomes. However, rapid diagnosis of strangulation ileus is sometimes difficult even when using enhanced CT.\(^{11}\) This delay in the diagnosis may result in progression of the anoxic mucosal injury of the intestine and an ultimate requirement for resection of the ischemic intestine. In such cases, the operation time is prolonged and postoperative complications frequently occur. As a result, patients are forced to undergo a long hospital stay. However, Takahashi et al.\(^{8}\) reported that bowel resection due to bowel gangrene was not correlated with postoperative complications. In the present study, resection of the small intestine was associated with a high incidence of postoperative complications, but resection of the small intestine was not a significant risk factor for postoperative complications in the multivariate analysis. These findings may indicate that not only the operative complexity, but also the patient’s immune and nutritional status affects the occurrence of postoperative complications. Tempel et al.\(^{12}\) and Bohl et al.\(^{13}\)

### Table 2 Factors affecting the occurrence of postoperative complications

|                           | N  | Postoperative complication, n (%) | Odds ratio | \( P \)   |
|---------------------------|----|----------------------------------|------------|-------|
| Patients’ age             |    |                                  |            |       |
| High > 76 years old       | 22 | 10 (45.5)                        | 4.918      | 0.027 |
| Low < 76 years old        | 23 | 4 (17.4)                         |            |       |
| Time to surgery from onset time |    |                                  |            |       |
| Long > 12 h               | 21 | 9 (42.9)                         | 0.075      | 0.784 |
| Short < 12 h              | 24 | 5 (20.8)                         |            |       |
| Operation time            |    |                                  |            |       |
| Long > 86 min             | 22 | 12 (54.5)                        | 6.775      | 0.009 |
| Short < 86 min            | 23 | 2 (8.7)                          |            |       |
| Operative approach        |    |                                  |            |       |
| Laparoscopic              | 13 | 2 (15.4)                         | 0.061      | 0.805 |
| Open                      | 32 | 12 (37.5)                        |            |       |
| Resection of small intestine |    |                                  |            |       |
| Yes                       | 20 | 12 (60)                          | 2.259      | 0.133 |
| No                        | 25 | 2 (8)                            |            |       |
| Abnormality of CAR, NLR, and PNI |    |                                  |            |       |
| All                       | 12 | 8 (66.7)                         | 9.721      | 0.002 |
| No or, 1 or 2 factors    | 33 | 6 (18.2)                         |            |       |

### Table 3 Correlations of abnormal preoperative CAR, NLR, and PNI with other factors

|                           | N  | Age, y, mean ± SD | Time to surgery from onset time, h, mean ± SD | Operation time, min, mean ± SD | Postoperative hospital stay, d, mean ± SD |
|---------------------------|----|------------------|-----------------------------------------------|--------------------------------|----------------------------------------|
| Abnormality of preoperative CAR, NLR, and PNI levels |    |                  |                                              |                                |                                        |
| All                       | 12 | 76.8 ± 8.5       | 49.1 ± 58.2                                   | 97.2 ± 43.4                    | 37.8 ± 44.8                            |
| No or, 1 or 2 factors    | 33 | 70.2 ± 18.5      | 19.9 ± 31.1                                   | 93.4 ± 54.1                    | 15.6 ± 14.8                            |
| \( P \)                   |    | 0.426            | 0.021                                         | 0.488                          | 0.194                                  |
reported that among patients undergoing spinal surgery or joint arthroplasty, those with preoperative hypoalbuminemia had a higher risk of surgical site infection, pneumonia, extended length of stay, and readmission than patients with a normal preoperative albumin concentration. Thus, preoperative immunological or nutritional markers should be useful to predict the occurrence of postoperative complications after surgery for strangulation ileus.

In the present study, the preoperative CAR, NLR, and PNI were good predictors of the occurrence of postoperative complications. The CAR, NLR, and PNI represent chronic inflammation, the nutritional status, and immunity. Recent studies have revealed a strong correlation between abnormalities of these parameters and poor survival or poor chemosensitivity of patients with various cancers.14–17 Blomberg et al.18 reported that low albumin and high C-reactive protein concentrations indicated a substantial increased risk of short-term mortality after percutaneous endoscopic gastrostomy. Additionally, Markar et al.19 found that the NLR appeared to have greater diagnostic accuracy for appendicitis. Thus, operations for strangulation ileus should be performed while the preoperative CAR, NLR, and PNI are normal to prevent the occurrence of postoperative complications.

Conclusion

Surgical treatment of strangulation ileus should be performed while the preoperative CAR, NLR, and PNI are normal to prevent the occurrence of postoperative complications.

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