Observational Study

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Usefulness of delta neutrophil index as a biomarker to predict postoperative complication in patients who underwent esophagectomy

A case-control study

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Abstract

Esophagectomy demonstrates a high incidence of complications owing to its complexity and invasiveness; hence, early detection of complications is important. We aimed to evaluate the predictive value of the delta neutrophil index (DNI) for complications after esophagectomy.

We retrospectively analyzed patients who underwent esophagectomy in the department of general surgery at a single institution between January 2011 and October 2020. Patient characteristics, laboratory findings, and clinical outcomes were assessed.

Fifty-seven patients were enrolled in this study, of whom 31 (54.4%) had complications. The complication group had significantly longer mean mechanical ventilation, hospital stay and intensive care unit stay periods, and higher acute physiology, age, chronic health evaluation score and mortality rate than the noncomplication group. DNI on postoperative day (POD) 2 was also significantly higher in the complication group. Logistic regression analysis showed that DNI on POD 2 was an independent risk factor associated with the complications. Receiver operating characteristic curve analysis showed that the area under curve of DNI on POD 2 was 0.712 (cutoff value: 2.15%, sensitivity 61.5%, and specificity 70.8%).

Our study indicated that postoperative DNI can be useful as an early predictive biomarker of the complications after esophagectomy.

Abbreviations: AKI = acute kidney injury, APACHEII = acute physiology, age, chronic health evaluation, CBC = complete blood count, CI = confidence interval, CRP = C-reactive protein, DNI = delta neutrophil index, ICU = intensive care unit, OR = odds ratio, POD = postoperative day, ROC = receiver operating characteristics, WBC = white blood cell.

Keywords: biomarkers, delta neutrophil index, esophagectomy, postoperative complications

1. Introduction

Esophagectomy is an established surgical procedure for the treatment of various benign and malignant lesions of the esophagus[1] Since the esophagus is located deep in the posterior midline of the mediastinum, and esophagectomy often involves extensive ranges of surgical regions such as the thorax, abdomen, and neck, this procedure is highly complex and invasive, and thus associated with a high incidence of complications.[2,3] The complications after esophagectomy vary, from common respiratory complications like pneumonia to less common complications such as pericarditis.[1,2] In particular, anastomotic leakage, with incidences ranging from 0 to 40%, is the most life-threatening complication associated with prolonged hospital stay and increased health care costs.[1,2,4] Therefore, early detection of the complications that may occur after esophagectomy is very important.

The common biomarkers that predict the occurrence of surgical complications include C-reactive protein (CRP), lactate, leukocytes, percentage of neutrophils, and procalcitonin.[4–9] However, there are only a few studies on the use of biomarkers to predict the complications after esophagectomy, even most of these studies are merely about anastomotic leakage.[6–10]

The delta neutrophil index (DNI) is the proportion of circulating immature granulocytes which can be obtained from the differences between the leukocyte subfraction measured in the myeloperoxidase channel and the nuclear lobularity channel.[11–13] Recently, several studies have reported that DNI is associated with the severity and prognosis of surgical conditions such as acute appendicitis, acute cholecystitis, intestinal obstruction, and secondary peritonitis.[14–17]

Therefore, we hypothesized that DNI could predict the complications in patients who underwent esophagectomy, and the objective of this study was to evaluate the usefulness of DNI for predicting the complications after esophagectomy. To our

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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knowledge, this study is the first on the usefulness of DNI as a predictor of complications after esophagectomy.

2. Materials and methods

2.1. Patient selection and data collection

This study was approved by the institutional review board of Wonju Severance Christian Hospital (IRB no. CR320038). This single-center cohort study included 135 patients who had undergone esophageal surgery at the Wonju Severance Christian Hospital between January 2011 and October 2020. The exclusion criteria were: treatment at a department other than general surgery, age below 19 years, an insufficient DNI score, and surgery other than esophagectomy. Finally, 57 patients were evaluated (Fig. 1). The demographics and clinical characteristics of the patients such as age, sex, past medical history, presence of cancer, used type of conduit, American Society of Anesthesiologists physical status classification system, acute physiology, age, chronic health evaluation (APACHEII) score, hospital stay days, intensive care unit (ICU) stay days, period of mechanical ventilation, and complications were reviewed retrospectively. Postoperative complications were defined as those that occurred within 30 days after surgery or during the postoperative hospital stay. The severity of postoperative complications was evaluated based on the Clavien–Dindo classification, and complications of grade II or higher were considered in this study.[18] Surgical site infection was defined in this study as deep incisional infection or organ space infection according to the diagnostic criteria of the National Nosocomial Infections Surveillance system by the Centers for Disease Control and Prevention.[19] Anastomotic stricture and anastomotic leakage were defined as those confirmed by endoscopic or radiologic findings such as contrast swallow or computed tomography. Acute kidney injury (AKI) was included according to the risk of renal dysfunction, injury to the kidney, failure of kidney function, loss of kidney function and end-stage kidney disease criteria.[20] Pneumonia was defined as new or progressive lung infiltrations in chest radiography with clinical signs such as purulent sputum, cough or dyspnea, and increased oxygen-requirement or need for respiratory assistance.[21]

2.2. DNI and laboratory tests

Before surgery and immediately after surgery, the values of laboratory tests such as albumin, hemoglobin, white blood cell (WBC) count, neutrophil count, and base excess were measured. Also, the values of WBC, neutrophil, DNI, and CRP were measured serially from postoperative day (POD) 1 to POD 3. DNI is included in the complete blood count (CBC) tests at no additional cost in our institution. DNI was determined by the following formula: DNI = (the leukocyte subfraction assayed in the myeloperoxidase channel on cytochemical reaction) – (the leukocyte subfraction assayed in the nuclear lobularity channel using the reflected light beam).[13] A specific type of automatic cell

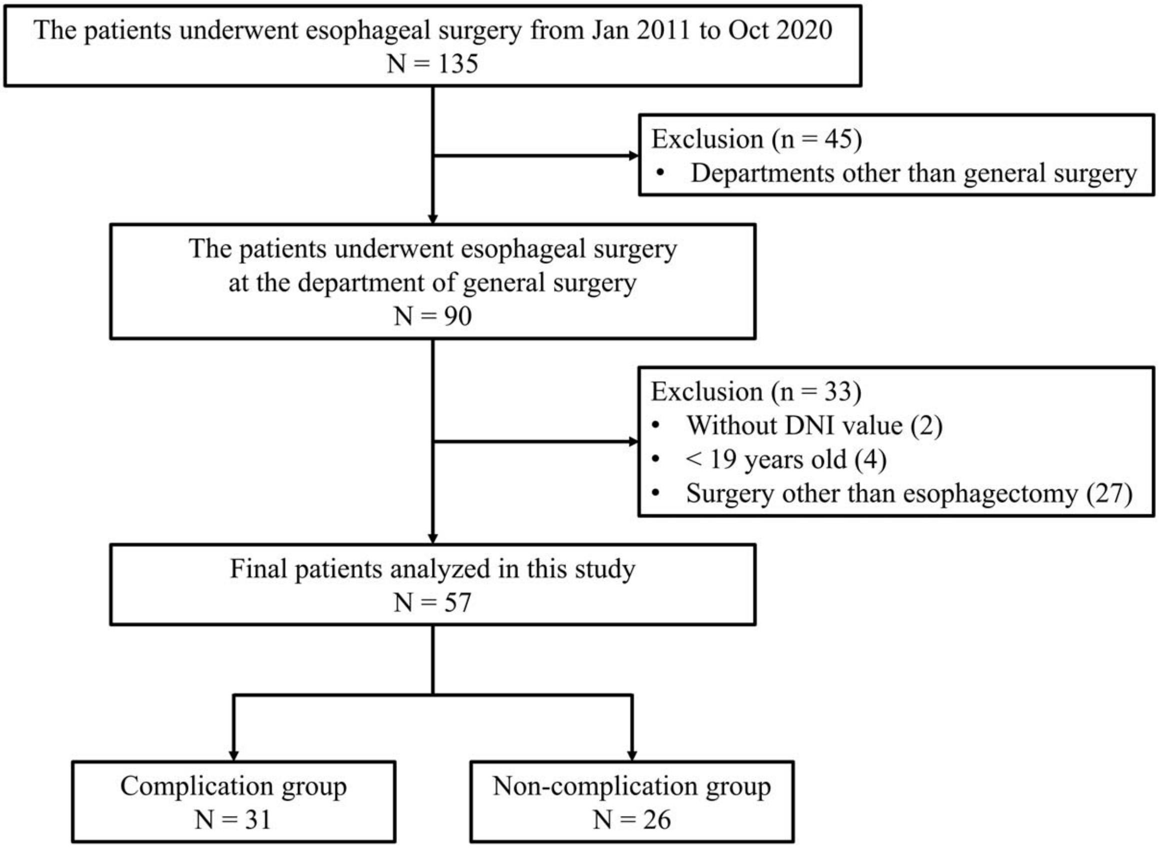

Figure 1. Order of investigations.

analyzer (ADVIA 120/212; Siemens, Tarrytown, NY) was used for DNI calculation.

2.3. Statistical analysis

Continuous variables are presented in the mean ± standard deviation or the median values (minimum-maximum), and the comparison between the 2 groups was analyzed by either the Student *t* test or the Mann–Whitney *U* test. Categorical variables were analyzed using the Chi-square test and the Fisher exact test. Moreover, logistic regression analysis was used to identify the independent risk factors of postoperative complications. Receiver operating characteristic (ROC) curve analysis was performed and the Youden Index method was used to find the optimal cutoff values for DNI to predict the postoperative complications. All statistical analyses were performed using SPSS version 25 (IBM, Armonk, NY) and the values of $P < .05$ were considered statistically significant.

2.3.1. Patient and public involvement. Written informed consent by the patients was waived due to the retrospective nature of our study. Patients or the public were not involved in the design, conduct, reporting or dissemination plans of this study.

3. Results

3.1. Baseline clinical characteristics

Fifty-seven patients who underwent esophagectomy were enrolled in this study. The mean age was 61.0 ± 10.0 years, and 50 (87.7%) patients were men. The most common past medical history was cardiovascular disease (36.8%), and 46 (80.7%) patients were diagnosed with cancer. Total and partial esophagectomies were performed for 36 (63.2%) and 21 (36.8%) patients, respectively. The most common type of conduit was the stomach (82.5%) followed by the small bowel (12.3%). The mean mechanical ventilation period after the surgery was 4.7 ± 5.4 days. Most patients had an American Society of Anesthesiologists class of 2 and the mean APACHEII was 12.0 ± 3.4. Thirty-one (54.4%) patients had complications, and the most common complication was pneumonia (24.6%) followed by anastomotic leakage (15.8%). The mean hospital stay days and ICU stay days were 33.4 ± 19.4 and 9.4 ± 11.4 days, respectively, and 9 (15.8%) patients died (Tables 1 and 2).

3.2. Comparison between complication and noncomplication groups

The mean mechanical ventilation period (6.2 ± 6.6 vs 2.9 ± 2.5 days, $P = .012$), hospital stay days (38.7 ± 20.9 vs 27.2 ± 15.6 days, $P = .024$) and ICU stay days (13.3 ± 14.2 vs 4.9 ± 3.1 days, $P = .003$) were significantly longer in the complication group than in the noncomplication group. Additionally, APACHEII score was significantly higher in the complication group than in the noncomplication group (12.9 ± 3.9 vs 11.0 ± 2.4, $P = .029$). In addition, the mortality rate was significantly higher in the complication group (29.0 vs 0.0%, $P = .003$) (Table 1).

Immediate postoperative hemoglobin was significantly lower in the complication group than in the noncomplication group (12.0 ± 1.5 vs 12.9 ± 1.1 g/dL, $P = .017$). DNI was significantly higher in the complication group than in the noncomplication group (4.3 vs 1.7%, $P = .027$) on POD 2, but WBC counts, neutrophil counts, and CRP were not statistically significant in postoperative serial labs (Table 3).

3.3. Independent risk factors associated with complications in patients who underwent esophagectomy

The multivariate analysis using variables that were significant in the univariate analysis showed that age [odds ratio (OR) 1.096 [95% confidence interval (CI) 1.019–1.178], $P = .013$] and DNI on POD 2 [OR 1.451 (95% CI 1.046–2.014), $P = .026$] were independent risk factors associated with the complications (Table 4).

3.4. ROC curve analysis of DNI to predict complications in patients who underwent esophagectomy

When analyzing the ROC curve of DNI on POD 2 to predict the occurrence of the complications, area under curve was 0.712 (95% CI 0.567–0.856, $P = .01$). The optimal cutoff value was 2.15% (sensitivity 61.5%, specificity 70.8%) (Fig. 2).

We also combined DNI on POD 2 with other laboratory values to improve its discriminatory power. When analyzing the ROC curve for DNI on POD 2 combined with WBC on POD 3, the area under curve was 0.763 (95% CI: 0.634–0.892, $P < .01$), and the optimal cutoff DNI score and WBC count were 2.15% and 8515 cells/μL, respectively (sensitivity 75.9%, specificity 73.1%) (Fig. 3).

4. Discussion

Esophageal cancer is the eighth most common cancer worldwide, and the sixth leading cause of cancer deaths.[22] Despite advances in multimodal approaches to treat esophageal cancer, surgical resection remains the mainstay of treatment. Several complications of esophagectomy can be fatal to patients, the most life-threatening of which is anastomotic leakage. Therefore, early detection is crucial.[4] As this study has a relatively small sample size, the statistical significance may be weak, and drawing definite conclusions may be difficult. However, considering that the number of patients included in previous studies on the association between complications of esophagectomy and biomarkers was not as large as 45 to 102,[8,23,24] this study may have novelty.

In this study, the DNI on POD 2 was identified as an independent risk factor that could predict the occurrence of the postoperative complications in patients undergoing esophagectomy. Moreover, the optimal cutoff value in the ROC curve for DNI on POD 2 was 2.15%, and the sensitivity and specificity were 61.5% and 70.8%, respectively. In addition, when analyzing the combination of DNI on POD 2 and WBC on POD 3, the sensitivity and specificity were 75.9% and 73.1%, respectively, which further improved discrimination. Because DNI can be measured along with CBC without additional cost in this institution, checking the serial change of DNI greatly helps to identify the patients' condition. As shown in Figure 4, DNI showed a marked difference in the patterns of postoperative change between the complication and noncomplication groups, unlike other biomarkers such as WBC, neutrophil, and CRP (Fig. 4).

Several studies to date have reported that DNI can be used as a useful biomarker to predict disease severity or prognosis in patients with various infectious conditions or sepsis. In 2008, Nahm et al[13] reported for the first that DNI was implicated in identifying disease severity in patients with sepsis, Subsequently, several studies have reported on the usefulness of DNI for various infectious diseases such as pneumonia, urinary tract infection,

Table 1

Clinical characteristics and comparison between complication and noncomplication groups.

Variables	N=57 (%)	Complication (n=31)	Noncomplication (n=26)	*P* value
Age (yr)	61.0±10.0	63.2±9.7	58.3±9.8	.061
Sex (male, %)	50 (87.7)	28 (90.3)	22 (84.6)	.691*
Past history	34 (59.6)	19 (61.3)	15 (57.7)	.783
Chronic renal failure	1 (1.8)	0 (0.0)	1 (3.8)	.456*
Diabetes mellitus	11 (19.3)	5 (16.1)	6 (23.1)	.508
Cardiovascular	21 (36.8)	13 (41.9)	8 (30.8)	.384
Pulmonary	4 (7.0)	3 (9.7)	1 (3.8)	.617*
Liver	7 (12.3)	3 (9.7)	4 (15.4)	.691*
Cancer	46 (80.7)	27 (87.1)	19 (73.1)	.182
Type of surgery				.384
Partial esophagectomy	36 (63.2)	18 (58.1)	18 (69.2)	
Total esophagectomy	21 (36.8)	13 (41.9)	8 (30.8)	
Type of conduit				.363
Stomach	47 (82.5)	24 (77.4)	23 (88.5)	
Small bowel	7 (12.3)	4 (12.9)	3 (11.5)	
Colon	3 (5.3)	3 (9.7)	0 (0.0)	
Mechanical ventilation (day)	4.7±5.4	6.2±6.6	2.9±2.5	.012
ASA class				.136
1	3 (5.3)	0 (0.0)	3 (11.5)	
2	34 (59.6)	21 (67.7)	13 (50.0)	
3	19 (33.3)	10 (32.3)	9 (34.6)	
4	1 (1.8)	0 (0.0)	1 (3.8)	
APACHEII	12.0±3.4	12.9±3.9	11.0±2.4	.029
Preoperative lab				
Albumin (g/dL)	4.0±0.5	4.0±0.5	3.9±0.5	.482
Hemoglobin (g/dL)	12.8±1.6	12.5±1.6	13.0±1.6	.277
White blood cell (cells/μL)	6614.4±3071.4	6111.0±1728.5	7214.6±4105.7	.210
Neutrophil (cells/μL)	4181.8±2880.1	3793.2±1524.1	4645.0±3922.2	.305
DNI (%)	0.6 (0–20.0)	0.8 (0–20.0)	0.4 (0–2.4)	.616
Postoperative lab				
Albumin (g/dL)	2.9±0.5	2.9±0.5	3.0±0.5	.722
Hemoglobin (g/dL)	12.4±1.4	12.0±1.5	12.9±1.1	.017
Base excess (mmol/L)	−3.7±3.8	−3.1±4.5	−4.3±2.6	.234
White blood cell (cells/μL)	12,042.3±4407.3	12,234.8±4591.5	11,812.7±4255.9	.722
Neutrophil (cells/μL)	10,327.4±4042.9	10,563.5±4276.7	10,045.8±3809.7	.634
DNI (%)	4.2 (0–40.3)	4.1 (0–40.3)	4.3 (0–15.5)	.927
CRP (mg/dL)	1.65 (0.29–12.9)	1.61 (0.29–8.55)	1.70 (0.29–12.9)	.920
Complications	31 (54.4)			
Surgical site infection	3 (5.3)			
Anastomotic stricture	4 (7.0)			
Anastomotic leakage	9 (15.8)			
Acute kidney injury	3 (5.3)			
Pneumonia	14 (24.6)			
Hospital stay (day)	33.4±19.4	38.7±20.9	27.2±15.6	.024
ICU stay (day)	9.4±11.4	13.3±14.2	4.9±3.1	.003
Mortality	9 (15.8)	9 (29.0)	0 (0.0)	.003*

APACHEII=acute physiology, age, chronic health evaluation II, ASA=American Society of Anesthesiologists physical status classification system, CRP=C-reactive protein, DNI=delta neutrophil index.
* Result of Fisher exact test.

Table 2

Postoperative serial labs.

	POD 0	POD 1	POD 2	POD 3
WBC	12,042.3±4407.3	11,099.5±4542.0	10,773.0±3607.2	9102.9±3647.5
Neutrophil	10,327.4±4042.9	9726.8±4338.0	9181.4±3435.6	7689.1±3359.6
DNI (%)	4.2 (0–40.3)	4.3 (0–27.2)	3.1 (0–25.0)	2.8 (0–38.7)
CRP	1.65 (0.29–12.9)	7.02 (0.34–23.4)	16.9 (5.97–30.1)	17.8 (4.13–30.7)

CRP=C-reactive protein, DNI=delta neutrophil index, POD=postoperative day, WBC=white blood cell.

Table 3

Comparison of postoperative serial labs between complication and noncomplication groups.

	Complication (n=31)	Noncomplication (n=26)	*P* value
WBC (cells/μL)			
POD 0	12234.8±4591.5	11812.7±4255.9	.722
POD 1	11206.8±4459.8	10971.5±4723.4	.848
POD 2	10445.0±3291.4	11151.5±3972.5	.470
POD 3	8421.0±3631.2	9889.6±3573.9	.134
Neutrophil (cells/μL)			
POD 0	10563.5±4276.7	10045.8±3809.7	.634
POD 1	9857.7±4272.2	9570.8±4494.8	.806
POD 2	9003.7±3213.9	9386.5±3728.7	.681
POD 3	7173.3±3430.0	8284.2±3239.9	.220
DNI (%)			
POD 0	4.1 (0–40.3)	4.3 (0–15.5)	.927
POD 1	4.6 (0–27.2)	4.0 (1–21.8)	.686
POD 2	4.3 (0–25.0)	1.7 (0–6.2)	.027
POD 3	3.9 (0–38.7)	1.6 (0–7.2)	.164
CRP (mg/dL)			
POD 0	1.61 (0.29–8.55)	1.70 (0.29–12.9)	.920
POD 1	7.03 (0.34–23.4)	7.01 (1.46–22.5)	.989
POD 2	17.31 (5.97–30.1)	16.47 (7.02–27.5)	.630
POD 3	17.98 (6.35–30.7)	17.58 (4.13–30.0)	.823

CRP=C-reactive protein, DNI=delta neutrophil index, POD=postoperative day, WBC=white blood cell.

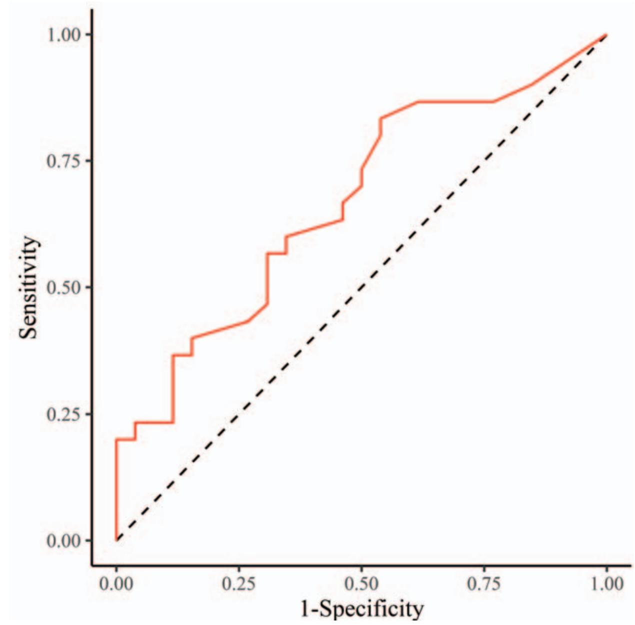

Figure 2. Receiver operating characteristic (ROC) curve analysis for delta neutrophil index (DNI) on postoperative day 2. Postoperative day 2 DNI: area under curve (AUC), 0.712 (95% CI: 0.567–0.856); cutoff DNI score, 2.15%; sensitivity, 61.5%; specificity, 70.8%; *P*=.01.

and liver abscess.[25–27] It has also recently been found that DNI is associated with disease severity or prognosis in noninfectious, inflammation-related diseases such as vasculitis, myocardial infarction, pulmonary embolism, AKI, and cardiac arrest.[28–32] A study on the usefulness of DNI in predicting the incidence of multiorgan dysfunction syndrome (MODS) and mortality in trauma patients was also reported.[33] In particular, studies conducted in the surgical field have shown that DNI could be useful for predicting disease severity, the necessity of surgical intervention, and prognosis.[11,15–17,34,35]

However, up to date, few studies have reported the efficacy of DNI for the postoperative complications or outcomes. Kim et al[17] reported that DNI is useful in predicting the postoperative mortality in patients with sepsis caused by secondary peritonitis, and the optimal cutoff value for predicting mortality is 7.8%. Our study showed that the optimal cutoff value for predicting the occurrence of postoperative complications was 2.15%, which is relatively low compared with the above study. In studies using DNI in inflammatory diseases such as acute cholecystitis, acute pancreatitis, acute rejection after kidney transplantation, and vasculitis, the optimal cutoff values of DNI are 0.65% to 3.5%, similar to those in this study.[14,28,36,37] The reason for this is as follows: first, the majority of the patients in this study have undergone elective surgery rather than emergency surgery; thus,

Table 4

Multivariate analysis of factors associated with complications in esophagectomy patients.

Variables	Risk factors for complications	
	OR (95% CI)	*P*-value
Sex	4.872 (0.383–61.947)	.380
Age (yr)	1.096 (1.019–1.178)	.013
APACHEII	1.195 (0.899–1.590)	.355
Postoperative hemoglobin (g/dL)	0.590 (0.333–1.043)	.069
POD 2 DNI (%)	1.451 (1.046–2.014)	.026

APACHEII=acute physiology, age, chronic health evaluation II, DNI=delta neutrophil index, POD=postoperative day.

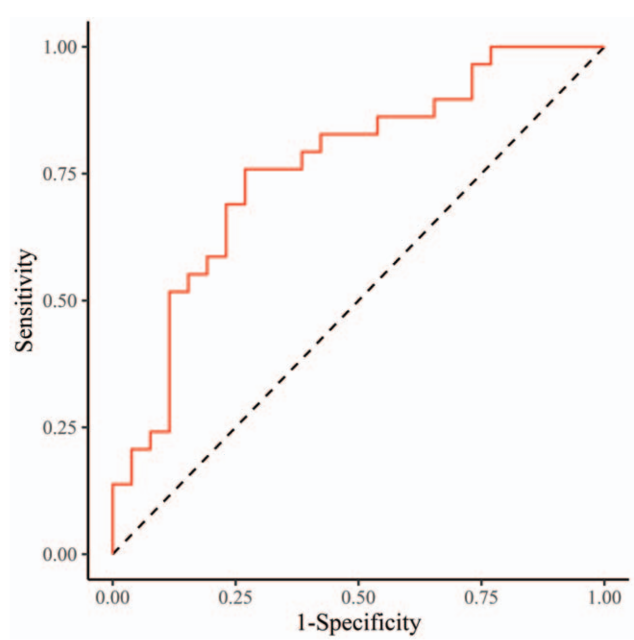

Figure 3. Receiver operating characteristic (ROC) curve analysis for delta neutrophil index (DNI) on postoperative day 2 combined with white blood cell (WBC) on postoperative day 3. Postoperative day 2 DNI with postoperative day 3 WBC: area under the curve (AUC), 0.763 (95% CI: 0.634–0.892); cutoff DNI score, 2.15%; cutoff WBC count, 8515 cells/μL; sensitivity, 75.9%; specificity, 73.1%; *P*<.01.

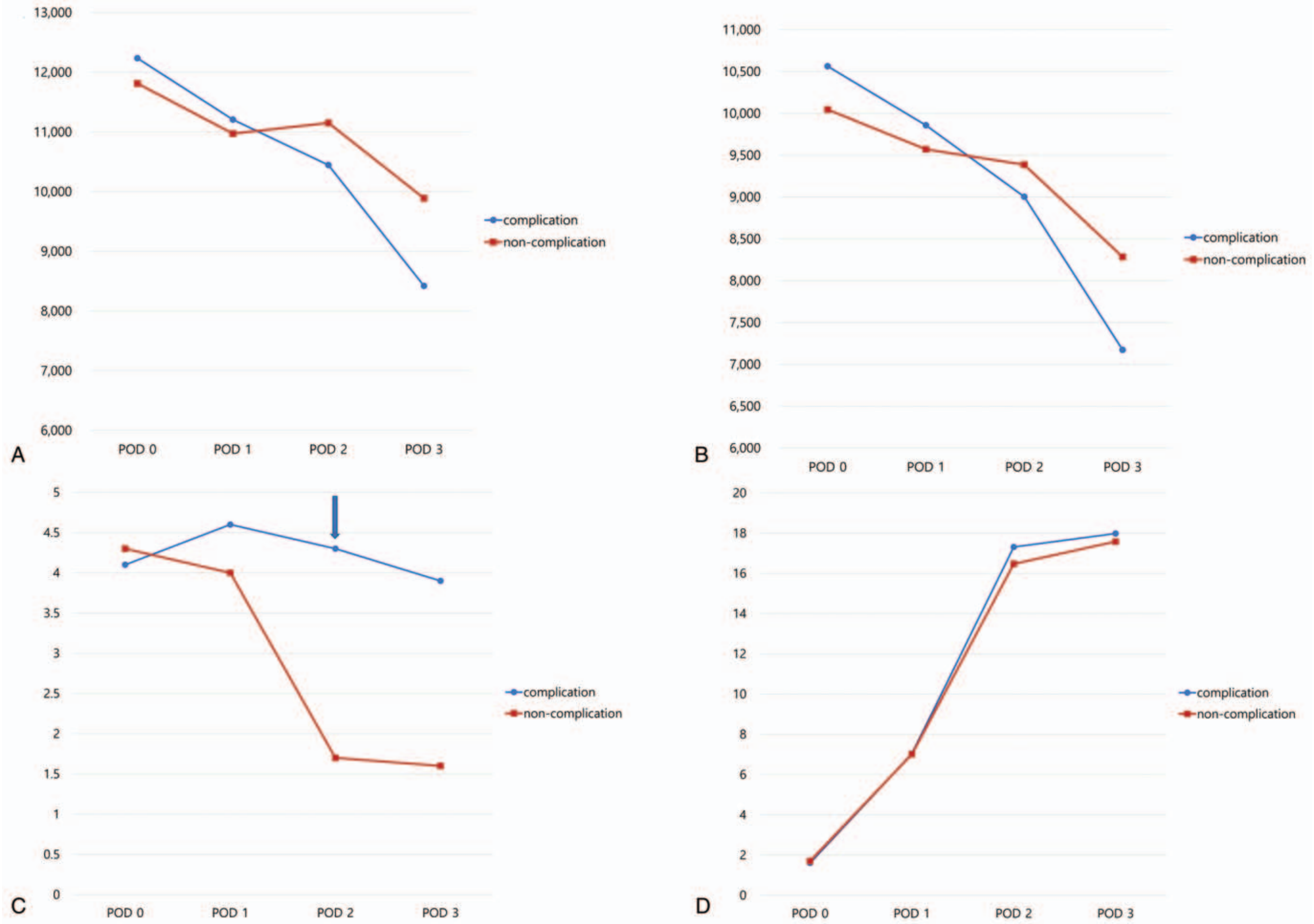

Figure 4. Changes in postoperative serial labs. (A) White blood cell (WBC) count during the postoperative period. (B) Neutrophil count during the postoperative period. (C) Delta neutrophil index (DNI) during the postoperative period. The mean DNI value of the complication group was significantly higher than that of the noncomplication group on postoperative day 2. (D) C-reactive protein (CRP) during the postoperative period.

the patients' condition might be relatively stable; second, unlike the study of Kim et al, this study did not target patients who are certainly diagnosed with sepsis; and third, this study was intended not to detect severe complications such as mortality, but to merely detect the occurrence of complications.

Several postoperative complications reported in this study can be classified as infectious conditions such as pneumonia, surgical site infection, and anastomotic leakage, as well as inflammatory conditions such as anastomotic stricture and AKI. These conditions activate the innate immune system comprising the neutrophils, monocytes, and complements, as in systemic inflammatory response syndrome. Activation of the immune cells and complements produces and releases inflammatory mediators like interleukins, resulting in a systemic inflammatory response, and consequently, organ dysfunction and immunoparesis. In this vicious cycle, neutrophils are initially activated, but over time, the function is markedly impaired, and this impairment is compensated by the recruitment and release of immature neutrophils.[38,39] Therefore, according to this mechanism, it can be estimated that DNI rises when postoperative complications occur. In other words, postoperative complications can be detected early by serially measuring DNI values.

Although this study did not show a significant difference in CRP values between the complication and noncomplication groups, a few studies have shown that CRP elevation can be used as a useful predictor of anastomotic leakage after esophagectomy and that it may indicate postoperative infectious complications.[4,6,8,23] However, it is difficult to use CRP as an early predictor of complications since it shows a relatively slow-changing pattern and is only reliable 48 hours after the onset of symptoms.[14,36] Additionally, although WBCs may be one of the indicators used to predict anastomotic leakage after esophagectomy and to exclude complications when it does not elevate rather than predict complications,[4,24] there was no significant difference in WBCs observed in this study. Since DNI is reported simultaneously with routine CBC, it has the advantages of being able to be measured without extra cost, time consumption, and additional blood collection. In addition, immature granulocytes circulate in the blood for about 6 to 10 hours and have a half-life of about 3 to 5 hours; therefore, DNI is more responsive than other biomarkers when complications occur.[14]

This study has some limitations. First, there may be a selection bias in this study because of its retrospective nature. Second, it is difficult to confirm the usefulness of DNI based on this study alone, because of the small sample size and single-center nature. Third, although all patients underwent esophagectomy, there may have been a difference in the surgical methods used depending on total or partial esophagectomy. However, as all the surgeries was performed by a single surgeon, the possible bias due to the surgeon may have been reduced. Finally, procalcitonin, which is an important biomarker of infection and sepsis, was not measured in a routine-serial manner because of insurance-related problems. Despite these limitations, this study may be meaningful in that it is the first study on the usefulness of DNI as a predictor of the complications in patients who underwent esophagectomy.

In conclusion, DNI can be useful as an early predictive biomarker of the complications after esophagectomy. In particular, it should be considered for close examination of whether the complications occur when the patient who underwent esophagectomy has a DNI value of 2.15% or higher in POD 2. In the future, the results of this study will be needed to be confirmed through multi-center, large-scale prospective studies.

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References

[1] Zick G, Boehle AS, Frerichs I, Both M, Scholz J, Weiler N. Tension pneumopericardium after esophagectomy: an extremely rare complication. J Cardiothorac Vasc Anesth 2008;22:267–9.
[2] Qiu ML, Lin JB, Li X, Luo RG, Liu B, Lin JW. Current state of esophageal cancer surgery in China: a national database analysis. BMC Cancer 2019;19:1064.
[3] Sato T, Fujita T, Fujiwara H, Daiko H. Internal hernia to the retrosternal space is a rare complication after minimally invasive esophagectomy: three case reports. Surg Case Rep 2019;5:26.
[4] de Mooij CM, Maassen van den Brink M, Merry A, Tweed T, Stoot J. Systematic review of the role of biomarkers in predicting anastomotic leakage following gastroesophageal cancer surgery. J Clin Med 2019;8:2005.
[5] Cetin DA, Gundes E, Ciyiltepe H, et al. Risk factors and laboratory markers used to predict leakage in esophagojejunal anastomotic leakage after total gastrectomy. Turk J Surg 2018;35:6–12.
[6] Asti E, Bonitta G, Melloni M, et al. Utility of C-reactive protein as predictive biomarker of anastomotic leak after minimally invasive esophagectomy. Langenbecks Arch Surg 2018;403:235–44.
[7] Ip B, Ng KT, Packer S, Paterson-Brown S, Couper GW. High serum lactate as an adjunct in the early prediction of anastomotic leak following oesophagectomy. Int J Surg 2017;46:7–10.
[8] Hoeboer SH, Groeneveld AB, Engels N, van Genderen M, Wijnhoven BP, van Bommel J. Rising C-reactive protein and procalcitonin levels precede early complications after esophagectomy. J Gastrointest Surg 2015;19:613–24.
[9] Findlay JM, Tilson RC, Harikrishnan A, et al. Attempted validation of the NUn score and inflammatory markers as predictors of esophageal anastomotic leak and major complications. Dis Esophagus 2015;28:626–33.
[10] Park JK, Kim JJ, Moon SW. C-reactive protein for the early prediction of anastomotic leak after esophagectomy in both neoadjuvant and non-neoadjuvant therapy case: a propensity score matching analysis. J Thorac Dis 2017;9:3693–702.
[11] Soh JS, Lim SW. Delta neutrophil index as a prognostic marker in emergent abdominal surgery. J Clin Lab Anal 2019;33:e22895.
[12] Park BH, Kang YA, Park MS, et al. Delta neutrophil index as an early marker of disease severity in critically ill patients with sepsis. BMC Infect Dis 2011;11:299.
[13] Nahm CH, Choi JW, Lee J. Delta neutrophil index in automated immature granulocyte counts for assessing disease severity of patients with sepsis. Ann Clin Lab Sci 2008;38:241–6.
[14] Lee SJ, Park EJ, Lee KJ, Cha YS. The delta neutrophil index is an early predictive marker of severe acute cholecystitis. Dig Liver Dis 2019;51:1593–8.
[15] Shin DH, Cho YS, Cho GC, et al. Delta neutrophil index as an early predictor of acute appendicitis and acute complicated appendicitis in adults. World J Emerg Surg 2017;12:32.
[16] Lee H, Kim IK, Ju MK. Which patients with intestinal obstruction need surgery? The delta neutrophil index as an early predictive marker. Ann Surg Treat Res 2017;93:272–6.
[17] Kim JW, Park JH, Kim DJ, Choi WH, Cheong JC, Kim JY. The delta neutrophil index is a prognostic factor for postoperative mortality in patients with sepsis caused by peritonitis. PLoS One 2017;12: e0182325.
[18] Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004;240:205–13.
[19] Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR. Guideline for prevention of surgical site infection, 1999. Hospital Infection Control Practices Advisory Committee. Infect Control Hosp Epidemiol 1999;20:250–78. quiz 279–80.
[20] Bellomo R, Ronco C, Kellum JA, Mehta RL, Palevsky P. Acute renal failure – definition, outcome measures, animal models, fluid therapy and information technology needs: the Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. Crit Care 2004;8:R204–212.
[21] Leone M, Bouadma L, Bouhemad B, et al. Hospital-acquired pneumonia in ICU. Anaesth Crit Care Pain Med 2018;37:83–98.
[22] Uhlenhopp DJ, Then EO, Sunkara T, Gaduputi V. Epidemiology of esophageal cancer: update in global trends, etiology and risk factors. Clin J Gastroenterol 2020;13:1010–21.
[23] McAnena P, Neary C, Doyle C, Kerin MJ, McAnena OJ, Collins C. Serial CRP levels following oesophagectomy: a marker for anastomotic dehiscence. Ir J Med Sci 2020;189:277–82.
[24] Tsujimoto H, Ono S, Takahata R, et al. Systemic inflammatory response syndrome as a predictor of anastomotic leakage after esophagectomy. Surg Today 2012;42:141–6.
[25] Kong T, Park YS, Lee HS, et al. The delta neutrophil index predicts the development of in-hospital hypotension in initially stable patients with pyogenic liver abscess. Sci Rep 2019;9:12105.
[26] Lee JW, Kim SH, Park SJ, et al. The value of delta neutrophil index in young infants with febrile urinary tract infection. Sci Rep 2017;7:41265.
[27] Kim H, Kim Y, Kim KH, Yeo CD, Kim JW, Lee HK. Use of delta neutrophil index for differentiating low-grade community-acquired pneumonia from upper respiratory infection. Ann Lab Med 2015;35:647–50.
[28] Yoo J, Ahn SS, Jung SM, Song JJ, Park YB, Lee SW. Delta neutrophil index is associated with vasculitis activity and risk of relapse in ANCA-associated vasculitis. Yonsei Med J 2018;59:397–405.
[29] Kong T, Kim TH, Park YS, et al. Usefulness of the delta neutrophil index to predict 30-day mortality in patients with ST segment elevation myocardial infarction. Sci Rep 2017;7:15718.
[30] Han IM, Yoon CY, Shin DH, et al. Delta neutrophil index is an independent predictor of mortality in septic acute kidney injury patients treated with continuous renal replacement therapy. BMC Nephrol 2017;18:94.
[31] Yune HY, Chung SP, Park YS, et al. Delta neutrophil index as a promising prognostic marker in out of hospital cardiac arrest. PLoS One 2015;10:e0120677.
[32] Kong T, Park YS, Lee HS, et al. Value of the delta neutrophil index for predicting 28-day mortality in patients with acute pulmonary embolism in the emergency department. Shock 2018;49:649–57.

[33] Kong T, Park YS, Lee HS, et al. The delta neutrophil index predicts development of multiple organ dysfunction syndrome and 30-day mortality in trauma patients admitted to an intensive care unit: a retrospective analysis. Sci Rep 2018;8:17515.
[34] Jung YT, Kim MJ, Lee JG, Lee SH. Predictors of early weaning failure from mechanical ventilation in critically ill patients after emergency gastrointestinal surgery: a retrospective study. Medicine (Baltimore) 2018;97:e12741.
[35] Kang HS, Cha YS, Park KH, Hwang SO. Delta neutrophil index as a promising prognostic marker of emergent surgical intervention for acute diverticulitis in the emergency department. PLoS One 2017;12:e0187629.
[36] Kim TY, Kim SJ, Kim YS, et al. Delta neutrophil index as an early predictive marker of severe acute pancreatitis in the emergency department. United European Gastroenterol J 2019;7:488–95.
[37] Lee JY, Han BG, Choi SO, et al. Increased delta neutrophil index is associated with poor prognosis in cadaver donor kidney transplantation. Transplant Proc 2019;51:2671–5.
[38] Brown KA, Brain SD, Pearson JD, Edgeworth JD, Lewis SM, Treacher DF. Neutrophils in development of multiple organ failure in sepsis. Lancet 2006;368:157–69.
[39] Lord JM, Midwinter MJ, Chen YF, et al. The systemic immune response to trauma: an overview of pathophysiology and treatment. Lancet 2014;384:1455–65.