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A Study on the Artificial Intelligence Model of White Blood Cell Counts Prediction Using Gan

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Abstract: In this paper, an artificial intelligence model for predicting white blood cell counts that required conventional blood tests were studied using deep learning. White blood cell counts are crucial human information for knowing inflammatory levels in the body and septic shock. However, white blood cell counts require a blood test, and two hours of medical waiting time is required to confirm the test results. Therefore, emergency patients may find it difficult to receive a sufficient medical response while waiting for blood test results that can reliably confirm white blood cell counts. As a process to solve this problem, medical responses are performed based on other bio-signals and information in the medical field. However, responses differ from responses according to quantitatively provided white blood cell counts. Therefore, in this study, we conducted a study on an artificial intelligence model that predicts white blood cell counts by receiving patient bio-signals and information based on Generative Adversarial Networks (GAN) of artificial intelligence. The artificial intelligence model of this study learns non-missing data and quantitatively predicts when the data with missing white blood cell counts act as input. The verification of the model consisted of the performance when input into the artificial intelligence model by mixing the original data and missing data. The verification results showed that the mixed data group, including white blood cell counts generated through the white blood cell prediction model, had better detection performance for sepsis patients than the original data group.

Keywords*: WBC, Sepsis, GAN, Artificial Intelligence, Prediction Model*

1. Introduction

White Blood Cell (WBC) Count is a clinical indicator of the body's inflammation level quantitatively.[1] These white blood cell counts are essential for diagnosing and preventing inflammatory diseases.[2] This is useful for diagnosing sepsis, a fatal inflammatory disease. [3, 4] Sepsis is a systemic inflammatory reaction caused by microbial infection and causes acute septic shock. [5] Sepsis shock affects 30 million patients annually and is the highest medical cost. In addition, septic shock requires a quick medical response, such as antibiotic administration and acute treatment within 3 hours of occurrence. Therefore, white blood cell counts are significant for emergency or critically ill patients who are fatal to the inflammatory response. [1,6] These white blood cell counts can be obtained by blood tests performed by extracting the patient's blood. In the hospital's blood test, the shape of blood cells is analyzed and counted in the extracted blood to quantify white and red blood cell levels.

The clinical pathology department mainly performs this process, and automatic analysis and counting methods have been continuously developed to reduce analysis time. [7] This analysis is a technology that automatically classifies blood cells through image analysis and the morphology of blood cells that blood experts have performed through microscopic cells. In addition, since this technology finds and distinguishes various types of blood cell cells through a microscope, it is necessary to introduce automation with high expertise and time-consuming tasks. Despite such efforts, sufficiently advanced blood tests take an average of two hours. However, blood tests take an average of two hours. [8 This can lead to a lack of response time for critical and emergency patients needing an immediate medical response. [9] In order to solve this problem in hospitals, medical responses are performed based on the patient's bio-signals and information before blood tests.[10] This minimizes time consumption for a medical response but is based on practical learning by medical staff. Therefore, medical staff with relatively little experience have difficulty actively responding. [11] In addition, it is difficult to expect an active effect of the medical staff's active response than the medical response using the quantitative value of the white blood cell level, which is the result of the blood test. [12] Therefore, in this paper, we study an artificial intelligence model for predicting quantitative white blood cell counts for active response by medical staff. The artificial intelligence model predicts white blood cell counts through Generative

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Adversarial Networks (GANs) after model input based on patient bio-signals and information. The leukocyte level prediction model was verified with the performance to diagnose sepsis according to the composition of the data.

2. Related Works

Related research can be explained in two directions. The first is a technology that automatically analyzes white blood cell levels at a microscope stage and counts them. These technologies use CNN (Convolutional Neural Networks) of advanced artificial intelligence technologies. Red blood cell phenotyping from 3D confocal images using artificial neural networks (Simionato, G.,) Using CNN, the paper studied an artificial intelligence model that performs extraction and counting of red blood cell features.[7] This highlighted the stain of doctors' 2D Cell Image manual classification, constructing a two-stage neural network architecture in 3D Images. It also confirmed that features of the feature appear in high-frequency spectra and utilized them to enable unbiased feature recognition. In addition, the extracted features of 3D images were applied to actual clinical practice to study the process of diagnosis and analysis. CNN-SSPSO: a hybrid and optimized CNN approach for peripheral blood cell image recognition and classification (Kumar, R.,). This paper developed a clustered CNN model by applying a clustering algorithm to shorten the long process of image processing technology. [13] In addition, VGG19 Net was used in the training course of the model, which showed 98% accuracy. However, the SSPSO-CNN Model studied in this paper showed 99% accuracy by applying actual clinical data. This shortened the process, a chronic problem of image processing, and showed about 1% higher performance. WBC-Net: A white blood cell segmentation network based on UNet++ and ResNet. (Lu, Y.,) This paper discusses the problem of automated WBC image segmentation due to factors such as background complexity and appearance changes caused by histological staining conditions. [14] To address this, we propose a deep learning network called WBC-Net based on UNet++ and ResNet to increase the accuracy of WBC image segmentation. Furthermore, experiments on four image datasets show that the proposed WBC-Net achieves better WBC segmentation performance than several state-of-the-art methods. This shows that experiments on image datasets obtained under fast and standard staining conditions show that WBC-Net has better segmentation accuracy than several state-of-the-art methods. Second, there is a paper that calculates important indicators of blood levels based on various biometric information. A significant indicator for diagnosing sepsis is the neutrophil-derived by calculating the number of white blood cells. A novel scoring system combining Modified Early Warning Score with biomarkers of monocyte distribution width, white blood cell counts, and neutrophil-to-lymphocyte ratio to improve early sepsis prediction in older adults. (Lin, S. F.) [15] In this paper, we aim to investigate whether it is helpful to combine the scoring system with the mononuclear sphere distribution width (MDW) for early detection of sepsis in the elderly in the emergency room (ED). Based on several calculated data, three scoring systems were evaluated: qSOFA, Modified Early Warning Score (MEWS), National Early Warning Score (NEWS), MDW, neutrophil-to-Lymphocyte Ratio (NLR), and Creative Protein (CRP) for early detection of sepsis. The artificial intelligence model constructed a sepsis prediction model using a logistic regression model. However, all of these studies require patient information and blood test information or are organized to increase the efficiency of the blood test itself.

3. Methods And Details

3.1. Data organization and analysis

In this paper, PhysioNet's 'Early Prediction of Sepsis from Clinical Data the PhysioNet Computing in Cardiology Challenge 2019' was used as a dataset. [16] This data was from an open database organized by the Research Resource Center of the National Institutes of Health. [17] Since medical data containing patient personal and biometric information is expensive, such as direct knowledge intervention by experts, public data was used in this study because it was difficult to obtain. This data is related to sepsis acquired in several hospital intensive care units. In this study, among 41 items of the data, data on bio-signal, bio-information, patient information, and annotation were extracted and used. The data items used include systolic blood pressure, general blood pressure, heart rate, body temperature, respiratory rate, white blood cell level, base level in the body, oxygen saturation level, carbon salt level, arterial blood gas, creatine, and patient age. All data items selected in this study are closely related to white blood cell counts. [18] The criteria for selecting these data items followed the contents of Systemic Infrared Response Syndrome (SIRS), which was constructed for diagnostic reference according to rapid changes in inflammatory levels. [2,19]

Table. 1: Missing Data Table.

Data Factor		Normal (779,079)		Sepsis (17,136)	
		Count	Rate (%)	Count	Rate (%)
Vital Sign	HR	60,084	7.712	1,105	6.448
	O2Sat	93,447	11.995	1,632	9.524
	Temp	511,616	65.669	11,698	68.266
	SBP	117,194	15.043	3,007	17.548
	MAP	79,477	10.201	1,381	8.059
	DBP	373,195	47.902	7,102	41.445
	Resp	75,922	9.745	1,336	7.796
Patient & Vital Info	Age	0	0	0	0
	pH	685,258	84.5	14,342	83.7
	HCO3	711,108	91.3	15,490	90.4
	PaCO2	705,999	90.6	14,928	87.1
	Creatin	721,877	92.5	15,851	92.5
	WBC	715,201	91.8	15,666	91.422

In this study, patient (approximately 40,000 people) data from the corresponding public dataset were classified as cases based on time series. This is to use biometric signals and information, which are data items of this study, as a case based on measurement time, and it was derived as about 800,000 cases. However, all items in the public data do not exist. As mentioned above, there are cases in which data missing due to practical difficulties in obtaining public data is included. Therefore, 1.1 Data Composition and Analysis describes how to distinguish missing data, select it, and use it for research. First, the missing data is more concentrated in biometric information than in biometric signals. This occurs due to biometric information characteristics that require processes such as blood collection and urine tests rather than bio-signals that can be directly obtained through medical devices. Table 1 shows the number and ratio of missing data items used in this study. The data are divided into normal and septicemia; the total data is 796,215 cases. The items shown in the Data Factor in the table are systolic blood pressure, general blood pressure, heart rate, body temperature, respiratory rate, white blood cell level, body base level, oxygen saturation level, carbon salt level, arterial blood gas, creatine, and patient age. As seen in the table, data with high missing data correspond to patient information, and in particular, items corresponding to blood tests (Creatin, WBC) showed more missing rates. In addition, the missing ratio is zero for the age data that cannot be omitted. This study was conducted to predict by inputting 91.8% of the data missing white blood cell count items into an artificial intelligence model. The data screening process is shown in Figure 1 below.

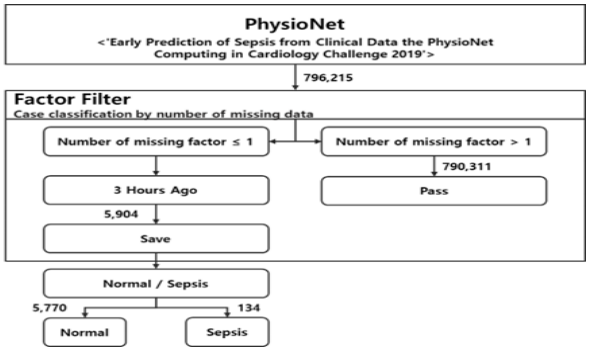

Fig. 1: Data Screening Process.

Table 1 is a data screening process, and in this study, data from 796,215 cases were selected using a factor filter. The screening criteria include the number of missing data in 12 items, excluding patient age. All 12 data items exist for the selected data, or one item is missing. In addition, for an appropriate medical response to critical and emergency patients, steps 3 hours before inflammatory levels were added to the data screening criteria. Therefore, 790,311 data need to include two or more items from the 796,215 and 5,904 data used in this study. It is used by dividing it into 5,770 normal and 134 Sepsis cases. In this study, data 5,904 were used by dividing the learning data set and the test set by a ratio of 8 to 2, and in the case of sepsis, 25 were used as tests.

3.2. Data Preprocessing

Data preprocessing describes the Factor Filter that could be seen during the screening process. Factor Filter is the data screening process used in this study and is described in Figure 2.

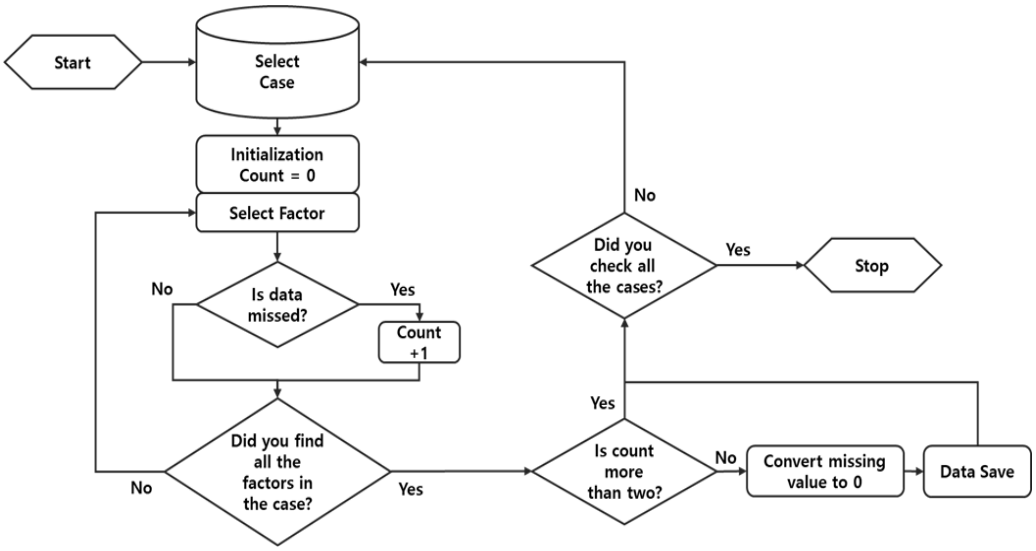

Fig. 2: Factor Filter Process.

As can be seen in Figure 2, the Factor Filter starts in the process of selecting a case. After that, the count variable is initialized to confirm the number of missing data items. Next, the data item is selected, the state (existence/missing) is checked, and the Count variable is increased accordingly. The Factor Filter checks missing data by rotating all data items in the selected case. When the verification of the item of the finally selected case is completed, the case is ignored or stored according to the Count variable. This procedure was performed for a single case, but it was performed for all 796,215 cases in this study.

Table. 2: Factor Filter Sample.

HR	O2	Temp	SBP	~	Resp	WBC	State
68	91	36.4	131	~	16.1	81	Pass
71	98	36.8	145	~	16.8	0	Pass
66	95	36.5	138	~	0	0	Ignore

Table 2 is an example of a Factor Filter. For one case, the State is determined through filtering, and there is no missing item or less for the above two cases. However, in the last case, the number of missing items is more than one, so it is ignored.

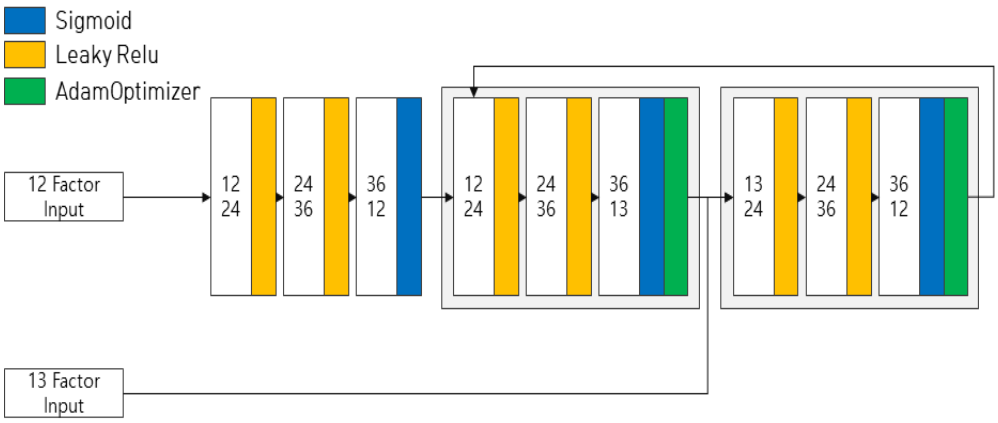

Fig. 3: White blood cell count prediction model

Figure 3 shows the composition of the leukocyte level prediction model. This model consists of a Generative Adversarial Network (GAN) of deep learning, and there are producers and discriminators. In addition, in this model, data in which the missing data item is a white blood cell number is used as an input, which is written as a 12 Factor Input in Figure 3. Based on the data entered in the model, the white blood cell level, which is one data item, is predicted. This means that the 12 Factor Input is input to the generator of the GAN, and the data generated by the generator and the 13 Factor Input are used as the input of the discriminator. The artificial neural network of the leukocyte-level prediction model consists of a fully connected network structure (FC). In Figure 3, the number represented by one square is an FC-type layer, which means neurons inside the layer. Thus, the 12 Factor Input received in the model is output to 24 neurons in the first FC layer. The second layer then consisted of 36 neurons. Since the third layer is a layer just before input as a constructor, it has the same neuron structure as the output of the discriminator.

In addition, the third layer used a different active function than the previous layer. The Leaky Relu function was used in the previous two layers, but the Sigmoid function was used in the third layer. This is because the role of the threshold in the artificial neural network of the Relu activity function was utilized. Since the leukocyte prediction model in this study was studied to enable proper medical response of critical and emergency patients, the operation time of the prediction model is of great importance. Therefore, the model of this study can be configured with relatively little complexity to secure real-time, but classification and prediction performance for complex data may need improvement. Therefore, in this paper, to improve this prediction performance, we focused on weight control between layers. As a result, the Leaky Relu function, which can significantly reduce the probability while maintaining the diversity of data, was used for the first and second layers. This is like Relu, which plays the role of criticality, but is suitable for use in low-complexity models because it maintains negative values of weights.

$$G_{epoch} = Sigmoid\left(W_g * x_g + b_g\right) - (n * \frac{\Delta E}{\Delta W})_{epoch} \quad (1)$$

$$D_{epoch} = Sigmoid(W_d * x_d + b_d) - (n * \frac{\Delta E}{\Delta W})_{epoch} \quad (2)$$

Equations 1 to 2 shows the optimization function of the leukocyte prediction model. In the equation, epoch means the number of times the model is learned, and Sigmoid is the activation function of the last layer. In addition, △E/△W is a vector having a directionality for the weight, and unlike Gradient, it has a directionality. This represents the model direction in one learning. The constructor of the leukocyte prediction model learned in this way outputs white blood cell counts. In this study, the leukocyte level prediction is performed by calculating the minimum difference value of the output leukocyte level. Calculating the minimum difference value is an algorithm that finds the most appropriate number of white blood cell counts produced by the constructor for one case. It is used as a postprocessing of the model and follows the calculation method of the standard deviation.

4. A Discussion Of The Result

In this paper, an artificial intelligence model was studied for an early medical response to predict white blood cell levels that require blood tests for critical and emergency patients. The model's leukocyte level prediction results are expressed in quantitative numbers. This paper compared them with cases where all data items, including white blood cell counts, exist. In addition, the predicted data were mixed with unforeseen data, and sepsis prediction performance by mixing ratio was compared. First, it compares a case in which all data items exist and a case in which white blood cell levels are predicted. In this paper, a case in which all data items exist is defined as a measurement case, and a case in

which white blood cell levels are predicted is called a prediction case. Five measurement cases were not involved in the learning and testing of the predictive model. Table 3 below is a case comparison sample.

Table. 3: Case Comparison Sample.

Case Factor	Measurement Case	Predictive Case
HR	94	92
O2Sat	100	99
Temp	36.7	36.6
SBP	138	131
MAP	67	65
DBP	44	45
Resp	16.5	16.2
pH	7.43	7.4
HCO3	26.3	26.1
PaCO2	42.4	40.8
Creatin	0.97	1.01
Age	74	78
WBC	88	81

The WBC of the Predictive Case in Table 3 is the value predicted by this paper's leukocyte level prediction model. It was compared using the standard deviation error degree to compare it with the measurement case. The standard deviation error degree compares all items in the two case groups. Figure 4 below shows the calculation method of the standard deviation error. Here, P is a data item of the prediction case, and M is a data item of the measurement case.

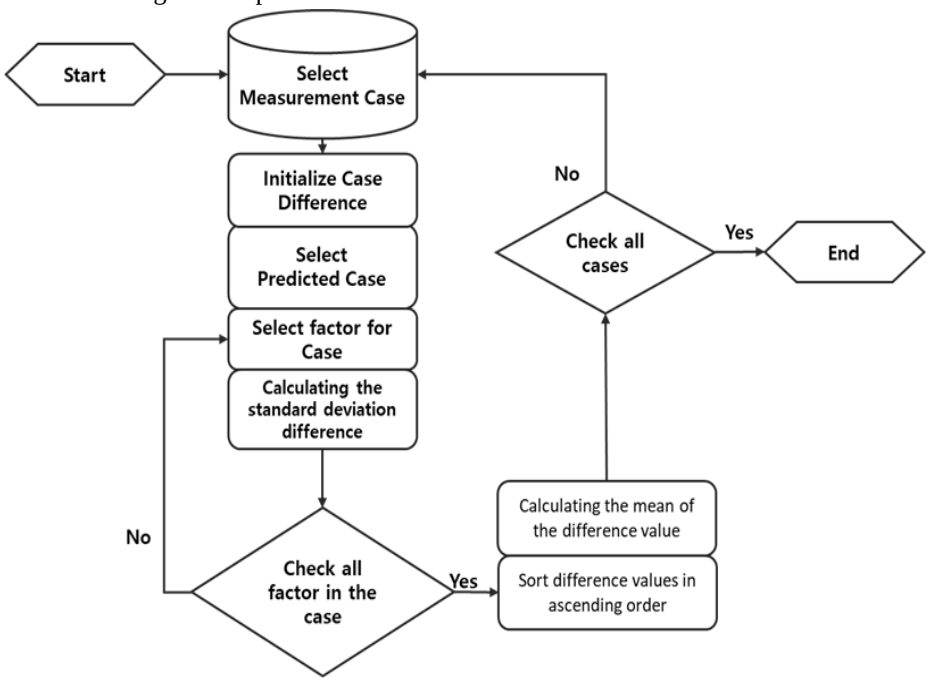

Fig. 4: Standard deviation error calculation procedure

As can be seen in Figure 4, after selecting the measurement case, the difference value of each data element is compared with the prediction case. This includes predicted leukocyte counts, and the different values of all data elements are extracted to calculate the error range of the median and average values after ascending alignment. This is for calculating the standard deviation of the difference value. These results are shown in Table 4 below.

Table. 4: Standard deviation result.

Case Factor	Measurement Case (5)	Predictive Case (5)
WBC	12.7	-
Non-WBC	16.5	13.4

The standard deviation of all data elements in the measurement case is 12.7 for cases with white blood cell count and 16.5 for cases without white blood cell count. In addition, in the case where white blood cell levels were predicted, it was 13.4. This shows that the standard deviation of the measurement case in which the white blood cell level exists and the standard deviation of the predicted case became similar by 3.1. The following method compares sepsis prediction performance for each mixing ratio by mixing the predicted data with unexpected data. It used a previous study, a septic prediction model. [20] The comparison was conducted by mixing the unforeseen and predicted data groups at a constant ratio of 10%.

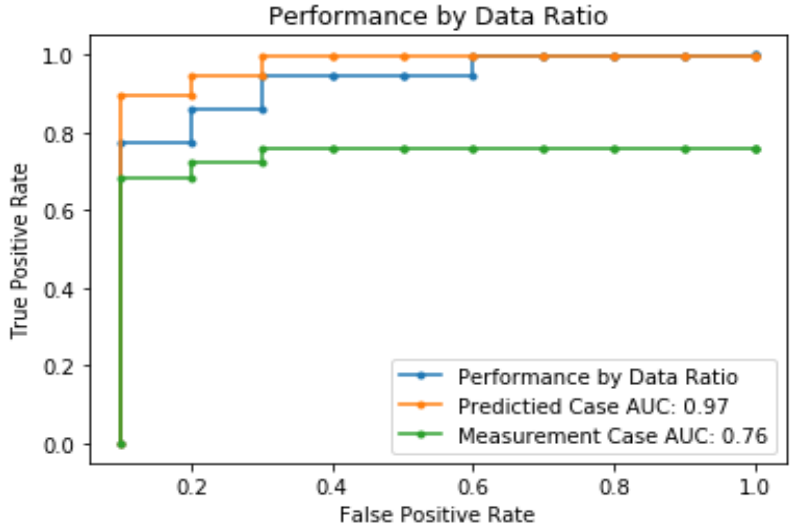

Fig. 5: Performance by Data Ration

Figure 5 is a performance comparison according to the ratio of the unforeseen data group and the predicted data group. Performance indicators are based on AUC (Area Under the Curve). The blue graph in the figure talks about the mixing performance of the predicted data group. This was done by mixing a 10% predicted data group with a measurement data group. In addition, there was no performance improvement from when the predicted data was mixed by more than 60%. These can be seen in the orange and green graphs of the figure. Orange is the performance calculated only from the predicted data, and the green graph is the result of using only the measured data. Since the classification performance is excellent according to the mixing ratio of the predicted data, the prediction performance of the white blood cell level prediction model is significant. This can be seen as 0.21 unit, which is the difference between the AUC of the measurement case and the prediction case. In addition, these results are shown for data in which the prediction case is mixed with 60% or more.

5. Conclusion

In this paper, a study was conducted to predict white blood cell levels that can be obtained through blood tests using artificial intelligence's GAN. The white blood cell level is derived from a blood test based on the patient's blood, which takes an average of two hours. However, the time required for blood tests can be difficult for medical staff to respond sufficiently. In addition, medical responses that proceed without quantitative values may differ according to the medical staff's experience. Therefore, to solve this problem, we studied an artificial intelligence model that can predict white blood cell levels based on patients' bio-signals and bio-information. This study uses a public dataset, and 5,904 cases were used through the data screening process. An FC-type model with a GAN structure was constructed as an

artificial intelligence model, and research was conducted. The data in this study are structured data, and only excellent quality data that was not missing through the data screening and preprocessing process were used. This is to secure timelessness to ensure the rapidity of medical responses in this study. Therefore, this study's leukocyte level prediction model also focused on real-time. The model of this study has a model structure with a slight complexity with less than 2 seconds to process one case. In addition, two experiments were conducted to compare studies in this study. First, the standard deviation error was performed on the white blood cell level prediction case and the original case, and the difference was quantitatively compared. In addition, the effectiveness of predicting white blood cell levels was confirmed by mixing and inputting data groups into the sepsis prediction model. In the standard deviation error method, the standard deviation of all data elements in the measurement case is 12.7 for the white blood cell count and 16.5 for the white blood cell count. In addition, the predicted white blood cell level was 13.4. This shows that the standard deviation of the measurement cases in which white blood cells exist and the standard deviation of the prediction cases became similar by 3.1. The second data mix verification is based on AUC. The performance increase trend of artificial intelligence models is confirmed according to the ratio of mixing white blood cell number correction data. The results showed no performance improvement compared to when the predicted data were mixed by more than 60%. It was also confirmed that there was a 0.21 performance improvement. Since the classification performance according to the mixing ratio of the predicted data is excellent, the prediction performance of the white blood cell level prediction model is significant.

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