RESEARCH ARTICLE

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F-18 FDG PET/CT based Preoperative Machine Learning Prediction Models for Evaluating Regional Lymph Node Metastasis Status of Patients with Colon Cancer

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Abstract

Objective: This study aimed to develop a simple machine-learning model incorporating lymph node metastasis status with F-18 Fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT) and clinical information for predicting regional lymph node metastasis in patients with colon cancer. **Methods:** This retrospective study included 193 patients diagnosed with colon cancer between January 2014 and December 2017. All patients underwent F-18 FDG PET/CT and blood test before surgery. One categorical variable (lymph node FDG uptake [LNFDG]) and six continuous variables (age, neutrophil-to-lymphocyte ratio [NLR], carcinoembryonic antigen [CEA], carbohydrate antigen 19-9 [CA19-9], C-reactive protein, and maximal standardized uptake value (SUVmax) of the primary tumor) were used as input variables. Four supervised machine learning methods were used to build predictive models: logistic regression (LR), random forest (RF), gradient boosting machine (GBM), and support vector machine (SVM). Area under the receiver operating characteristic curve (AUC) of the validation set were used for evaluating and comparing model performance. **Results:** The number of patients with lymph node metastasis were 63 (33%). The mean number of harvested lymph nodes was 28.8 ± 11.4. The mean CEA, CA19-9, and CRP levels were 4.8 ± 9.3 ng/ml, 15.6 ± 42.8 U/ml, and 1.0 ± 3.0 mg/dl, respectively. The mean NLR was 2.2 ± 1.2. The mean SUVmax levels of the primary tumor were 15.2 ± 7.9. Fifty-one (26%) patients showed FDG uptake in the pericolic lymph nodes. The mean AUC of the LR, RF, GBM, and SVM methods for the LNFDG model was 0.7046, 0.7047, 0.7040, and 0.7058, respectively. The mean AUC of the LR, RF, GBM, and SVM methods for the LNFDG plus clinical information model was 0.7046, 0.7302, 0.7444, and 0.7097, respectively. **Conclusion:** Machine learning methods using LNFDG and clinical information could predict the lymph node metastasis status in patients with colon cancer with higher accuracy than a model using only FDG uptake of the lymph nodes.

Keywords: Lymph node metastasis- colon cancer- machine learning- F-18 FDG PET/CT

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Introduction

Approximately 52,000 deaths were reported in 150,000 patients newly diagnosed with colorectal cancer, making colorectal cancer the third leading cause of death in the United States in 2022 [1]. Lymph node metastasis status is a crucial factor for determining the treatment plan and predicting the prognosis of patients with colon cancer. Patients with colon cancer and lymph node metastasis could achieve survival benefit from adjuvant chemotherapy [2]. Five-year survival rates of 30–60% and 70–80% and have been reported in patients with and without lymph node metastasis, respectively [3].

Although computed tomography (CT) and F-18 Fluorodeoxyglucose positron emission tomography/CT (F-18 FDG PET/CT) have been employed to assess the lymph node metastasis status before surgery, relatively low diagnostic accuracies in patients with colon cancer have been reported in previous meta-analyses, thereby making the precise prediction of the lymph node metastases status challenging. Pooled sensitivity and specificity of CT and F-18 FDG PET/CT for detecting lymph node metastases in patients with colon cancer were 71%, and 67% [4], and 72% and 71%, respectively [5]. For CT, the size of the lymph node was used to predict the lymph node metastasis status [4], whereas the maximal standardized uptake value (SUV_{max}) was commonly used for F-18 FDG PET/CT to predict the lymph node metastasis status [5].

Machine learning models utilizing radiomic features, which have been developed to ensure more precise

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prediction, have demonstrated superior accuracy compared to methods relying solely on lymph node size or SUV_{max} [6, 7]. However, the process of extracting radiomic features requires drawing regions of interest around the tumor, which can be labor-intensive and time consuming. Moreover, the application of these methods in clinical settings is challenging. Therefore, we aimed to develop a simple machine-learning model incorporating lymph node metastasis status with FDG PET/CT and clinical information to predict regional lymph node metastasis in patients with colon cancer.

Materials and Methods

Patients

This retrospective study included 193 patients diagnosed with colon cancer between January 2014 and December 2017. All the patients underwent F-18 FDG PET/CT before surgery. Differential white blood cell (WBC) counts and serum carcinoembryonic antigen (CEA), carbohydrate antigen 19-9 (CA19-9), and C-reactive protein (CRP) levels were recorded within 30 days of surgery. The serum neutrophil-to-lymphocyte ratio (NLR) was calculated from the differential WBC counts. Patients with a history of cancer were excluded from the study. The pathological stages of colon cancer were determined according to the American Joint Committee on Cancer Manual, 8th edition [8].

FDG PET/CT imaging

Oral intake and intravenous glucose injection were prohibited for at least 6 h before undergoing PET/CT scan. Blood glucose levels were measured before F-18 FDG administration, and PET/CT scans were conducted only if the blood glucose levels were below 200 mg/dl. A whole-body scan covering the area from the head to the thigh (torso) was performed 60 min after intravenous injection of approximately 370 MBq of F-18 FDG. The PET/CT examinations were performed using PET/CT scanners (Discovery STE or Discovery 690; GE Healthcare, Milwaukee, WI, USA). CT images were acquired using multi-detector CT equipment with a standard protocol comprising 140 kV, 60–80 mA, and a section thickness of 3.75 mm. The PET emission data were acquired for 2 min per bed position. The PET images were reconstructed using an ordered-subset expectation maximization iterative reconstruction algorithm with three iterations, 18 subsets, a matrix size of 256 × 256, and a transaxial field of view of 50 cm. The PET images were subsequently fused with the CT images.

Image evaluation

Semi-quantitative analysis was independently performed by two experienced nuclear medicine physicians who were blinded to the clinicopathological results. For semi-quantitative analysis, a three-dimensional volume of interest (3D VOI) was drawn on the primary tumor and lymph nodes, and SUV_{max} was calculated for the pixels within the 3D VOI. Lymph nodes with an SUV_{max} higher than 2.0 were classified as metastatic lymph nodes.

Machine learning models

One categorical variable (lymph node FDG uptake [LNFDG]) and six continuous variables (age, LNR, CEA, CA19-9, CRP, and SUV_{max} of the primary tumor) were used as input variables.

Four supervised machine learning methods were used to build predictive models: logistic regression (LR), random forest (RF), gradient boosting machine (GBM), and support vector machine (SVM). The Scikit-learn package (version 1.3.0) was used to train and test the machine learning models in Python (version 3.11); 20 times 5-fold-cross-validation technique was employed to reduce overfitting. The patients were split into training and validation sets using stratified random sampling; 156 (80%) patients were assigned to the training set and 39 (20%) patients were assigned to the validation set. The average results of 100 independent tests were used to reduce variability in the model performance.

Evaluation and comparison of model performance

Area under the receiver operating characteristic curve (AUC) of the validation set were used for evaluating and comparing model performance [9].

Statistical analysis

Statistical analyses were performed using MedCalc for Windows, version 22.013 (MedCalc Software, Ostend, Belgium). The chi-square test or Mann–Whitney U test was used to compare the differences in the clinical variables. The optimal cutoff values for predicting regional lymph node metastasis were calculated using the receiver operating characteristic analysis. Univariable and multivariable analyses were performed using the following clinical variables: age; sex; LNFDG, CEA, CA19-9, and CRP levels; NLR; and SUV_{max} levels of the primary tumor. Statistical significance was set at $P < 0.05$.

Results

Characteristics of the study population

The patient characteristics are shown in Table 1. A total of 193 patients were included in this study (104 male and 89 female patients; mean age, 66.8 ± 11.3 years). The number of patients with lymph node metastasis were 63 (33%). The mean number of harvested lymph nodes was 28.8 ± 11.4. The mean CEA, CA19-9, and CRP levels were 4.8 ± 9.3 ng/ml, 15.6 ± 42.8 U/ml, and 1.0 ± 3.0 mg/dl, respectively. The mean NLR was 2.2 ± 1.2. The mean SUV_{max} levels of the primary tumor were 15.2 ± 7.9. Fifty-one (26%) patients showed FDG uptake in the pericolic lymph nodes. Among the 193 patients, 47 were diagnosed with stage I, 83 with stage II, 62 with stage III, and one with stage IV disease. The optimal cut-off values for age, CEA, CA19-9, CRP, NLR, and SUV_{max} levels of the primary tumor were 65, 4.7, 7.5, 0.5, 1.6, and 13.7, respectively. In the univariable analysis, the LNFDG, CEA, and SUV_{max} levels of the primary tumor were significantly associated with regional lymph node metastasis (Table 2). In the multivariable analysis, the LNFDG and SUV_{max} levels of the primary tumor were significantly associated with regional lymph node

Table 1. Patient Characteristics. SD, standard deviation; LNFDG, lymph node fluorodeoxyglucose; CEA, carcinoembryonic antigen; CA19-9, carbohydrate antigen 19-9; CRP, c-reactive protein; NLR, neutrophil-lymphocyte ratio; SUVmax, maximum standardized uptake value.

Characteristics	Total (n = 193)	LNM- (n = 130)	LNM+ (n = 63)	P value
Age (years) mean±SD	66.8±11.3	66.6±11.5	67.3±11.2	0.5889
Sex				0.9873
Female	89 (46)	60	29	
Male	104 (54)	70	34	
Stage				
I	47 (24)	47	0	
II	83 (43)	83	0	
III	62 (32)	0	62	
IV	1 (1)	0	1	
LNFDG				<0.0001
Positive	53	18	35	
Negative	140	112	28	
Harvested lymph nodes	28.8±11.4	29.5±11.6	27.6±10.9	0.1900
CEA (ng/mL)	6.6±16.4	4.8±9.2	10.3±25.2	0.0388
CA19-9 (U/mL)	23.2±111.5	15.4±42.5	39.2±185.4	0.0366
CRP (mg/dL)	1.0±3.0	1.2±3.2	0.8±2.3	0.1684
NLR	2.2±1.2	2.2±1.2	2.2±1.1	0.6964
SUV_{max} of primary tumor	15.2±7.9	15.3±7.8	14.9±8.1	0.5418

Table 2. Univariable Analyses for Lymph Node Metastasis. LNFDG, lymph node fluorodeoxyglucose; CEA, carcinoembryonic antigen; CA19-9, carbohydrate antigen 19-9; CRP, c-reactive protein; NLR, neutrophil-lymphocyte ratio; SUV_{max}, maximum standardized uptake value.

Characteristics	Odds ratio (95% CI)	P value
Age (years)		0.3907
<65	1.0000	
≥65	1.3090 (0.7078-2.4211)	
Sex		0.7460
Female	1.0000	
Male	1.1051 (0.6037-2.0230)	
LNFDG		<0.0001
Negative	1.0000	
Positive	7.7778 (3.8495-15.7149)	
CEA (ng/mL)		0.0207
<4.7	1.0000	
≥4.7	2.1935 (1.1277-4.2666)	
CA19-9 (U/mL)		0.9609
<7.5	1.0000	
≥7.5	1.0156 (0.5468-1.8865)	
CRP (mg/dL)		0.4177
<0.5	1.0000	
≥0.5	1.3133 (0.6794-2.5386)	
NLR		0.4110
<1.6	1.0000	
≥1.6	1.3114 (0.6872-2.5023)	
SUVmax of primary tumor		0.0413
<13.7	1.0000	
≥13.7	1.8958 (1.0256-3.5045)	

metastasis (Table 3).

Correlations between clinical factors

A strong positive correlation was observed between the CEA and CA19-9 levels, while a weak positive correlation was noted between the other clinical factors (Figure 1).

Model performances

The mean AUC for each method is presented in Table 4. All model performance values are expressed as means and standard deviations of the 100 cross-validations. The mean AUC of the LR, RF, GBM, and SVM methods for the LNFDG model was 0.7046, 0.7047,

Table 3. Multivariable Analyses for Lymph Node Metastasis. LNFDG, lymph node fluorodeoxyglucose; CEA, carcinoembryonic antigen; CA19-9, carbohydrate antigen 19-9; SUV_{max}, maximum standardized uptake value.

Characteristics	Odds ratio (95% CI)	P value
LNFDG		<0.0001
Negative	1.0000	
Positive	7.2869 (3.5082-15.1355)	
CEA (ng/mL)		0.2613
<4.7	1.0000	
≥4.7	1.5634 (0.7169-3.4095)	
CA19-9 (U/mL)		0.6137
<7.5	1.0000	
≥7.5	1.2029 (0.5871-2.4645)	
SUV_{max} of primary tumor		0.0389
<13.7	1.0000	
≥13.7	2.0781 (1.0380-4.1605)	

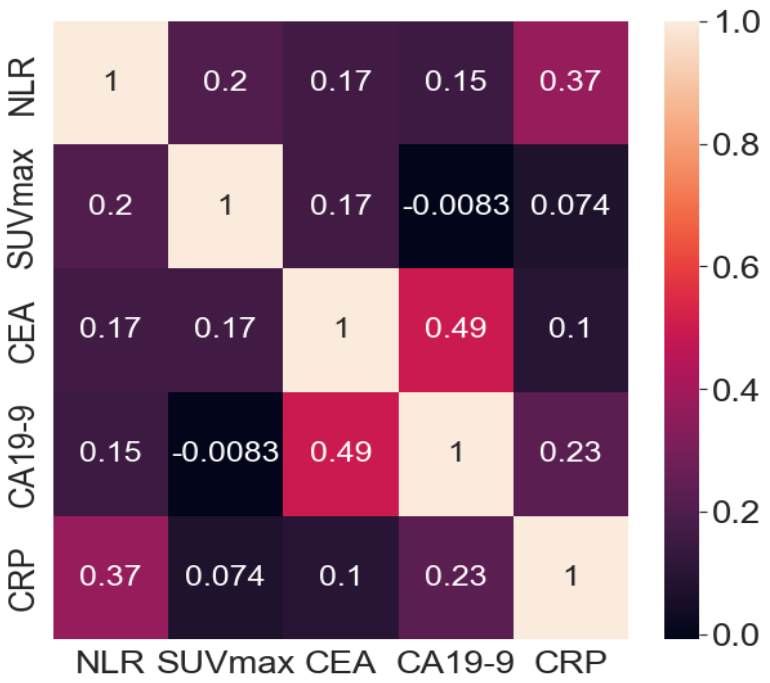

Figure 1. Correlations between Clinical Factors. NLR, neutrophil-lymphocyte ratio; SUV_{max}, maximum standardized uptake value; CEA, carcinoembryonic antigen; CA19-9, carbohydrate antigen 19-9; CRP, c-reactive protein.

Table 4. AUC of the Machine Learning Models. LNFDG, lymph node fluorodeoxyglucose; LR, SD, standard deviation; linear regression; RF, random forest; GBM, gradient boosting machine; SVM, support vector machine.

Methods	LNFDG	LNFDG +clinical information	P value
LR mean±SD	0.7046±0.0641	0.7046±0.0821	0.7927
RF mean±SD	0.7047±0.0676	0.7302±0.0810	0.0140
GBM mean±SD	0.7040±0.0695	0.7444±0.0773	0.0004
SVM mean±SD	0.7048±0.0778	0.7097±0.0808	0.4284

0.7040, and 0.7058, respectively. The mean AUC of the LR, RF, GBM, and SVM methods in the LNFDG plus clinical information model was 0.7046, 0.7302, 0.7444, and 0.7097, respectively. The mean AUC was significantly higher in the LNFDG plus clinical information model than in the LNFDG model using the RF and GBM methods. Among the machine learning models, the GBM method had the highest score for predicting regional lymph node metastasis in the LNFDG plus clinical information model.

Discussion

Accurate prediction of the regional lymph node metastasis status in patients with colon cancer is important for facilitating treatment strategies. Imaging examinations, such as CT and F-18 FDG PET/CT, have been conventionally used to predict regional lymph node metastasis status. Although the usefulness of CT and F-18 FDG PET/CT in lymph node metastasis detection in patients with colon cancer is well established, the diagnostic accuracy reported in previous studies was relatively low [4, 5]. Several factors, such as micrometastasis, limited spatial resolution of PET, and low FDG avidity, may contribute to the false-negative results of lymph node metastasis in colon cancer [10, 11]. Furthermore, reactive lymphadenopathy could result in false-positive findings of lymph node metastasis [12].

Recently, several studies have used machine learning methods to evaluate lymph node metastasis in colon cancer. These studies reported more accurate results with machine learning methods than those with conventional imaging methods. However, most previous studies have incorporated radiomic features, which can be labor-intensive and time-consuming [7, 13, 14]. To address these challenges, we have utilized relatively simple machine learning methods. Machine learning models incorporating LNFDG status and clinical information showed good scores for predicting the preoperative status of regional lymph node metastasis in our study. We used four machine-learning techniques (LR, RF, GBM, and SVM). LR is a widely used machine learning technique for binary classification [15, 16]. RF is an ensemble technique that combines multiple decision tree models that classify the given datasets into two groups based on a certain criterion [17]. GBM is also an ensemble technique that leverages weak learners to minimize loss function, thereby building a robust predictive model [18]. SVM is a machine learning algorithm that determines an optimal hyperplane to separate classes of data [19].

No significant differences were observed in the AUC

among the machine learning methods in the LNFDG model. To assess supplementary advantages in the performance of the LNFDG plus clinical information models upon comparison with the LNFDG model, we used only one variable in the LNFDG model, which could account for the similar model performance among the machine learning methods in the LNFDG model. However, the RF and GBM methods had a significantly higher AUC in the LNFDG plus clinical information model than the LR and SVM methods. Furthermore, the AUC for RF and GBM in the LNFDG plus clinical information model were significantly higher than those in the LNFDG model. Among these methods, RF and GBM are decision tree-based and ensemble methods that have demonstrated high accuracy in predicting clinical outcomes in studies across the medical field [20, 21].

In this study, only the LNFDG and SUV_{max} levels of the primary tumor were significantly associated with lymph node metastasis in the multivariable analysis. No significant association was observed between other clinical factors and lymph node metastasis. The LNFDG plus clinical information model included age, NLR, and CEA, CA19-9, CRP, and SUV_{max} levels of the primary tumor. However, NLR was not associated with lymph node metastasis [22, 23]. CRP was also not associated with lymph node metastasis [23, 24]. Several previous studies reported that preoperative CEA and CA19-9 levels were significantly associated with lymph node metastasis [22, 25-28]. The SUV_{max} levels of the primary tumor are significantly correlated with lymph node metastasis [29]. Machine learning models predict the most accurate results by adjusting the weights assigned to each included factor. In this way, a combination of clinically relevant factors can improve the diagnostic accuracy of regional lymph node metastasis in patients with colon cancer, which could be have contributed to the better performance of the LNFDG plus clinical information model in predicting lymph node metastasis.

This study has certain limitations. First, the number of patients included in the machine learning training set was low. Generally, the accuracy of the model tends to improve with increase in the amount of data. Thus, future studies with larger data sizes could improve the accuracy of the prediction models. Second, deep learning models, such as convoluted neural networks (CNN), which are mostly used for image data, have demonstrated improved accuracy compared with conventional machine learning models. In this study, we employed conventional machine-learning models for the sake of simplicity and convenience. However, studies utilizing automated CNNs and deep learning are warranted to develop more powerful tools for predicting lymph node metastasis in the future.

In conclusion, FDG uptake in the lymph nodes could accurately predict lymph node metastasis in patients with colon cancer. Furthermore, machine learning methods using LNFDG and clinical information could predict the lymph node metastasis status in patients with colon cancer with higher accuracy than a model using only FDG uptake of the lymph nodes.

Author Contribution Statement

Author contribution statement: SJ contributed to the study design, data analysis, and writing of the manuscript. JS, HJ, MS, and KB contributed to data collection and analysis. SS contributed to data analysis and interpretation and supervised the finding of this work. All authors discussed the results and contributed to final manuscript.

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This study was not approved by any scientific Body and is not part of an approved student thesis.

Ethics statement

The study was approved by the Institutional Review Board of Inje University Busan Paik Hospital (IRB No. 2023-10-056) and was performed in accordance with the ethical standards proposed in the 1964 Declaration of Helsinki and its later amendments.

Availability of data

Data is available upon request.

Conflict of Interest

The authors declare no other potential conflicts of interest relevant to this article

References

1. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer statistics, 2022. CA Cancer J Clin. 2022;72(1):7-33. https://doi.org/10.3322/caac.21708.
2. Chau I, Cunningham D. Adjuvant therapy in colon cancer--what, when and how? Ann Oncol. 2006;17(9):1347-59. https://doi.org/10.1093/annonc/mdl029.
3. Ong ML, Schofield JB. Assessment of lymph node involvement in colorectal cancer. World J Gastrointest Surg. 2016;8(3):179-92. https://doi.org/10.4240/wjgs.v8.i3.179.
4. Nerad E, Lahaye MJ, Maas M, Nelemans P, Bakers FCH, Beets GL, Beets-Tan RGH. Diagnostic Accuracy of CT for Local Staging of Colon Cancer: A Systematic Review and Meta-Analysis. AJR Am J Roentgenol. 2016;207(5):984-95. https://doi.org/10.2214/AJR.15.15785.
5. Lu YY, Chen JH, Ding HJ, Chien CR, Lin WY, Kao CH. A systematic review and meta-analysis of pretherapeutic lymph node staging of colorectal cancer by 18F-FDG PET or PET/CT. Nucl Med Commun. 2012;33(11):1127-33. https://doi.org/10.1097/MNM.0b013e328357b2d9.
6. Li M, Zhang J, Dan Y, Yao Y, Dai W, Cai G, Yang G, Tong T. A clinical-radiomics nomogram for the preoperative prediction of lymph node metastasis in colorectal cancer. J Transl Med. 2020;18(1):46. https://doi.org/10.1186/s12967-020-02215-0.
7. He J, Wang Q, Zhang Y, Wu H, Zhou Y, Zhao S. Preoperative prediction of regional lymph node metastasis of colorectal cancer based on 18F-FDG PET/CT and machine learning. Ann Nucl Med. 2021;35(5):617-27. https://doi.org/10.1007/s12149-021-01605-8.
8. Edition S, Edge S, Byrd D. AJCC cancer staging manual. AJCC cancer staging manual. 8th ed. Springer. 2017.
9. Erickson BJ, Kitamura F. Magician's Corner: 9. Performance Metrics for Machine Learning Models. Radiol Artif Intell. 2021;3(3):e200126. https://doi.org/10.1148/

ryai.2021200126.
10. Nomori H, Watanabe K, Ohtsuka T, Naruke T, Suemasu K, Uno K. The size of metastatic foci and lymph nodes yielding false-negative and false-positive lymph node staging with positron emission tomography in patients with lung cancer. J Thorac Cardiovasc Surg. 2004;127(4):1087-92. https://doi.org/https://doi.org/10.1016/j.jtcvs.2003.08.010.
11. Shin SS, Jeong YY, Min JJ, Kim HR, Chung TW, Kang HK. Preoperative staging of colorectal cancer: CT vs. integrated FDG PET/CT. Abdom Imaging. 2008;33(3):270-7. https://doi.org/10.1007/s00261-007-9262-9.
12. Zeman MN, Green C, Akin EA. Spectrum of [18F]FDG-PET/CT Findings in Benign Lymph Node Pathology. Mol Imaging Biol. 2021;23(4):469-80. https://doi.org/10.1007/s11307-020-01576-8.
13. Eresen A, Li Y, Yang J, Shangguan J, Velichko Y, Yaghmai V, Benson AB, Zhang Z. Preoperative assessment of lymph node metastasis in Colon Cancer patients using machine learning: a pilot study. Cancer Imaging. 2020;20:1-9. https://doi.org/10.1186/s40644-020-00308-z
14. Bedrikovetski S, Dudi-Venkata NN, Kroon HM, Seow W, Vather R, Carneiro G, et al. Artificial intelligence for pre-operative lymph node staging in colorectal cancer: a systematic review and meta-analysis. BMC Cancer. 2021;21(1):1058. https://doi.org/10.1186/s12885-021-08773-w.
15. Zou X, Hu Y, Tian Z, Shen K. Logistic regression model optimization and case analysis. In2019 IEEE 7th international conference on computer science and network technology (ICCSNT) 2019 Oct 19 (pp. 135-139). IEEE.
16. Sperandei S. Understanding logistic regression analysis. Biochem Med (Zagreb). 2014;24(1):12-18. https://doi.org/10.11613/bm.2014.003.
17. Schonlau M, Zou RY. The random forest algorithm for statistical learning. Stata J. 2020;20(1):3-29. https://doi.org/10.1177/1536867x20909688.
18. Natekin A, Knoll A. Gradient boosting machines, a tutorial. Front Neurorobot. 2013;7. https://doi.org/10.3389/fnbot.2013.00021.
19. Karatzoglou A, Meyer D, Hornik K. Support vector machines in R. Journal of statistical software. 2006;15:1-28.
20. Alam MZ, Rahman MS, Rahman MS. A Random Forest based predictor for medical data classification using feature ranking. Inform Med Unlocked. 2019;15:100180. https://doi.org/10.1016/j.imu.2019.100180.
21. Zhang Z, Zhao Y, Canes A, Steinberg D, Lyashevska O. Predictive analytics with gradient boosting in clinical medicine. Ann Transl Med. 2019;7(7):152. https://doi.org/10.21037/atm.2019.03.29.
22. Xu Y, Chen Y, Long C, Zhong H, Liang F, Huang Lx, et al. Preoperative Predictors of Lymph Node Metastasis in Colon Cancer. Front Oncol. 2021;11:667477. https://doi.org/10.3389/fonc.2021.667477.
23. Lale A, Sahin E, Aslan A, Can OF, Ebiloglu MF, Aygen E. The Relation Between Serum-based Systemic Inflammatory Biomarkers and Locoregional Lymph Node Metastasis in Clinical Stages I to II Right-sided Colon Cancers: The Role of Platelet-to-Lymphocyte Ratio. Surg Laparosc Endosc Percutan Tech. 2023;33(6):603-7. https://doi.org/10.1097/sle.0000000000001228.
24. Kwon KA, Kim SH, Oh SY, Lee S, Han JY, Kim KH, et al. Clinical significance of preoperative serum vascular endothelial growth factor, interleukin-6, and C-reactive protein level in colorectal cancer. BMC Cancer. 2010;10(1):203. https://doi.org/10.1186/1471-2407-10-203.
25. Marchena J, Acosta MA, Garcia-Anguiano F, Simpson H, Cruz F. Use of the preoperative levels of CEA in patients with colorectal cancer. Hepatogastroenterology. 2003;50(52):1017-20.
26. Gao Y, Wang J, Zhou Y, Sheng S, Qian SY, Huo X. Evaluation of Serum CEA, CA19-9, CA72-4, CA125 and Ferritin as Diagnostic Markers and Factors of Clinical Parameters for Colorectal Cancer. Sci Rep. 2018;8(1):2732. https://doi.org/10.1038/s41598-018-21048-y.
27. Yu H, Son GM, Joh YG. The clinical significance of preoperative serum levels of carbohydrate antigen 19-9 in colorectal cancer. JKSS. 2013;84(4):231-7. https://doi.org/10.4174/jkss.2013.84.4.231.
28. Luo H, Shen K, Li B, Li R, Wang Z, Xie Z. Clinical significance and diagnostic value of serum NSE, CEA, CA19-9, CA125 and CA242 levels in colorectal cancer. Oncol Lett. 2020;20(1):742-50. https://doi.org/10.3892/ol.2020.11633.
29. Li D, Wang Y, Liu W, Chen Q, Cai L, Xing X, Gao S. The Correlation between 18F-FDG PET/CT Imaging SUV_{max} of Preoperative Colon Cancer Primary Lesions and Clinicopathological Factors. J Oncol. 2021;2021:4312296. https://doi.org/10.1155/2021/4312296.