Machine learning models for prediction of postoperative ileus in patients underwent laparoscopic colorectal surgery

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Abstract

Background: We aimed to assess the performance of machine learning algorithms for the prediction of risk factors of postoperative ileus (POI) in patients underwent laparoscopic colorectal surgery for malignant lesions.

Methods: We conducted analyses in a retrospective observational study with a total of 637 patients at Suzhou Hospital of Nanjing Medical University. Four machine learning algorithms (logistic regression, decision tree, random forest, gradient boosting decision tree) were considered to predict risk factors of POI. The total cases were randomly divided into training and testing data sets, with a ratio of 8:2. The performance of each model was evaluated by area under receiver operator characteristic curve (AUC), precision, recall and F1-score.

Results: The morbidity of POI in this study was 19.15% (122/637). Gradient boosting decision tree reached the highest AUC (0.76) and was the best model for POI risk prediction. In addition, the results of the importance matrix of gradient boosting decision tree showed that the five most important variables were time to first passage of flatus, opioids during POD3, duration of surgery, height and weight.

Conclusions: The gradient boosting decision tree was the optimal model to predict the risk of POI in patients underwent laparoscopic colorectal surgery for malignant lesions. And the results of our study could be useful for clinical guidelines in POI risk prediction.

Background

Postoperative ileus (POI) is temporary inhibition of gastrointestinal motility induced by abdominal or non-abdominal surgery, which is often described as postoperative functional ileus. Clinically, it is characterized by flatulence, pain, fecal delay, nausea and vomiting. Gastrointestinal motility usually goes through a stage of dysfunction after anesthesia and operation for 2-4d even longer than 7d. Its duration is related to the degree of surgical (especially colon surgery) trauma, the use of anesthetics, postoperative pain, inflammatory response, stress and many other factors [1]. A systematic review and meta-analysis showed that the incidence of POI in non-randomized controlled trials (non-RCTs) and RCTs was 10.3% and 10.2%, respectively [2]. In reality, not only patients in POI suffer significant discomfort, delay enteral nutrition, but also it boasts a high incidence of postoperative complications such as wound failure and pneumonia even prolongs length of postoperative hospitalization [3]. Therefore, prevention of POI is necessary for enhanced recovery and reduction of hospital expenses.

Recently, laparoscopic methods have been shown to be associated with less POI [4-5]. However, part of patients underwent laparoscopic surgery still have functional intestinal obstruction with incidence of >10%. Machine learning as one of the main ways of solving data mining problems is widely used in many areas, especially in the medical field. And the research relatively hot is the disease prediction. Traditionally, the assessment about possibility of disease development bases on basic information such as demography, existing medical conditions and lifestyle routines, but with a low accuracy. Now with the

development of big data and machine learning technology, disease prediction is becoming more and more accurate. Shanmuga et al. used a deep learning method to analyze colorectal polyps in images, the results showed that tumor detection accuracy of the method using in colon images is up to 95% through the existing algorithm evaluation [6]. At the same time, Xu et al. applied the machine learning methods like support vector machine, which can effectively classify colon cancer patients with different prognosis [7]. However, there is no research on predicting the risk factors of POI by machine learning.

In this study, we evaluated the performance of four machine learning algorithms and compared them with each other for the prediction of risk of POI by using clinical data with known outcomes, and provide a suitable guideline for clinic practise to prevent disease through early intervention.

Methods

To investigate the predict effect of machine learning on POI underwent laparoscopic colorectal cancer surgery, we conducted a retrospective observational study at Nanjing Medical University Affiliated Suzhou Hospital.

Participants

We performed a retrospective analysis of consecutive patients aged 18 years or older who underwent laparoscopic colorectal surgery for malignant lesions from April 2016 to January 2017. Exclusion criteria were patients who underwent surgery other than laparoscopic colorectal surgery, converted to open surgery, robot-assisted laparoscopic colorectal surgery, and parenteral nutrition surgery. POI was defined as flatulence and/or fecal pass delay or oral intake intolerance on the third day after surgery and confirmed with radiographs that small and/or large intestinal dilatation on abdominal X-ray films.

Anesthesia and operation management

The surgeries were performed by six different surgeons, each with more than 200 cases of surgical experiences in laparoscopic colorectal surgery. Laparoscopic surgery includes single incision and conventional laparoscopic colorectal surgery. Anesthesia techniques were similar in all cases. There was no thoracic epidural analgesia. Intravenous midazolam□sufentanil, propofol, and rocuronium were applied for induction of anesthesia, providing neuromuscular blockage for endotracheal intubation. Anesthesia was maintained with propofol, remifentanil, and sevoflurane. Opioids were routinely administered for postoperative pain 30 minutes prior to the end of surgery.

Variables collection

Several studies have shown that the risk factors for development of POI in patients who underwent colorectal surgery including the age, open approach, difficulty in operation, operative duration more than 3 hours, American Society of Anesthesiologists scores (ASA) 3 to 4, low-hematocrit and transfusion [8]. Therefore, we collected clinical data on 27 variables included the categories of demographics, social habits, comorbidities, intraoperative situation and postoperative management (**Table 1**). All doses of opioids were converted to equivalent intravenous morphine. The age-adjusted Charlson Comorbidity Index (ACCI), which has better predictive effects on hospital mortality and adverse events than other versions, was used to assess comorbidity. Events such as postoperative wound dehiscence were also recorded. The types of variables are shown in **Table 2**.

Modelling strategy

Four different algorithms were considered: logistic regression, decision tree, random forest, gradient boosting decision tree (Parameters see in **Table 3**). 637 cases were randomly split into a training (80%) and a testing (20%) data sets. The 20 times repeated to find the optimal hyper-parameters with a bootstrap procedure was performed in the training data set. The reason for using this method was its very low variance which appropriate to choose the goal between models [9]. Then models with the optimal hyper-parameters were run in the training set and used to predict the risk of cases in the testing data set.

The missing data were pre-processed using a nonparametric imputation method based on random forest that is good at coping with non-linear relations and complex interactions [10]. Meanwhile the categorical variables (ASA, type of surgery, operator, type of anesthesia) were transform into dummy variables.

The predictive performance was based on the area under ROC (receiver operator characteristic) curve (AUC), precision, recall and F1-score in testing data set. The drawing of AUC takes the false positive rate as x-axis and true positive rate as y-axis. Precision indicates the probability of the correctly predicted positive samples among all the samples predicted as positive samples. Recall indicates the probability of correctly predicted positive samples among all the original positive samples. And F1-score is the harmonic average of precision and recall, $F1 = 2rp / (r + p)$, where r is recall and p is precision. Finally, the variable importance was calculated for each risk factor by the optimal model. The flowchart of this study for prediction of risk factors of POI is showed in **Figure 1.**

Results

The ROC curve was used for quantitative validation of models with high prediction rates [11]. Based on the AUC, the gradient boosting decision tree (0.7631) was the model that obtained the best predictive performance in the testing data set, while random forest (0.7348) was the worst one (**Figure 2**). Also, the results of the precision, recall and F1-score are presented in **Table 4**. The recall of gradient boosting decision tree (0.32) was higher than that of the other three models, which of decision tree, logistic and

random forest was 0.24, 0.20, 0.16, respectively. While the precision of gradient boosting decision tree and random forest both were 0.67.

Obviously, the four models in this study have got a low recall but a high precision. One major reason for this problem is that the imbalance datasets, POI and non-POI accounting for 19.15% and 80.85%, respectively, affect the performance of machine learning models. And the another may be about highly critical value of dichotomies. Therefore, we used the comprehensive evaluation index, AUC and F1-score, to measure the performance of models. Overall, gradient boosting decision tree was systematically ranked among the best models.

The importance matrix of Gradient boosting decision tree was used to assess the variable importance of each risk factor. The three most important variables were time to first passage of flatus, opioids during POD3, duration of surgery for POI risk prediction (**Figure 3**). However, the first important factor was showed 100% correlation with POI because the postoperative patients all suffered delayed passage of flatus. Sometimes, even they have passed the flatus POI can occur again after food intake.

Discussion

In this study, we showed that among the different models, gradient boosting decision tree had the best performance for POI risk prediction. The AUC (0.76), precision (0.67) and recall (0.32) of it were the highest in the testing data set compared to the other three models. While decision tree was the second-best model with AUC=0.75.

Gradient boosting decision tree is a persistent model in machine learning which has the natural processing ability for mixed data and strong predictive ability in different fields. Its advantages of good training effect and uneasily over-fit make it obtain the optimal model through the iterative training of weak classifier (decision Tree). The classification and regression tree (CART) is applied to decision tree model which can result in poor generalization because of easily over-fit. We improved this situation by setting the minimum number of samples of nodes and limiting the depth of the decision tree. As a commonly used machine learning method, logistic regression has little calculation amount and short calculation time but it is liable to underfit to reduce the accuracy. When characteristic space is large the performance of it is not well. So small amount of interaction among the variables in this study give it a relatively good performance. However, random forest was the worst may be due to the fewer trees that can lead to over-fit.

The relative importance of 27 risk factors of POI was determined using gradient boosting decision tree. The results showed that time to first passage of flatus, opioids during POD3 and duration of surgery are of highest importance. The passage of flatus is an important indicator of recovery of gastroenteric function. A meta-analysis included 10 RCTs has showed that perioperative intravenous lidocaine could decrease the first flatus time and accelerate recovery of gastrointestinal function in patients underwent the laparoscopic colorectal surgery by alleviating acute pain and reducing opioid requirement [12]. Similarly, a systematic review of enhanced gastrointestinal function has found that the most commonly

recommended variation in interventions was magnesium-based laxative [13]. However, passage of flatus does not represent a complete recovery because parts of patients can develop into POI again after food or fluid intake.

The previous studies have shown that the application of opioids is an important factor in bowel movements [14]. Opioids such as morphine can bind to the gastrointestinal μ receptor and inhibit gastrointestinal motility. The study of Boelens et al has shown that the incidence of POI in patients administered with opioids after colorectal cancer surgery was significantly higher than that of patients who didn't use [15]. In recent years, ideal therapeutic effect had been obtained by pre-operatively administering to the patient with μ receptor agonist alvimopan for the prevention and treatment of POI [16]. Long operating time was also a risk factor for POI in colorectal surgery [17]. It may indicate prolongation, technical difficulties or severe inflammatory response, any of which can directly induce the occurrence of POI [18-19].

In addition, the obesity, perioperative fluid management and ACCI score were also showed in other studies as the risk factors of POI. A cohort study including nearly 28,000 patients has reported the POI incidence of 12.7% after colon surgery while the higher was in obese patients [20]. In a small series of reports, according to Parker *et al.* patients of POI are basically obese [21]. Maybe the reason is intestines of obese patients can contain more mesenteric fat which is so difficult to operate that damage to intestine during the surgery. Pillai *et al.* conducted a randomized controlled study of perioperative fluid management and esophageal ultrasound Doppler detection, and the results showed that optimizing perioperative fluid intake was correlated with enhanced rapidly restored intestinal function and reducing the incidence of other complications [22]. A recent retrospective study involving 11,397 patients who underwent open or laparoscopic colectomy showed that the high ACCI score was an independent predictor of POI prolongation [23].

Several limitations in this study should be acknowledged. Firstly, only a limited number of variables were considered that restricted analyses to predictive modelling with possible risk factors. Our conclusion cannot be widely applied to datasets with more predictors. Secondly, the influences on POI are not just the doses of opioids used in POD3. Moreover, we quantized the weight of each variable through machine learning methods but there are many variables cannot be intervened. Finally, this study performed only internal verification and no external verification. Therefore, we need to collect more perioperative data based on etiology and explore a more efficient predictive model in further study.

Conclusions

The common complication, POI, due to multiple risk factors after colorectal surgery indicates a need for a suitable and effective modelling for more effective protection. For accurate assessment of factors of POI, four machine learning algorithms have been studied. Based on the reviews of literature, 27 variables were used to analyze and predict. In this study, we demonstrate that gradient boosting decision tree was the

optimal model to predict the risk of POI underwent laparoscopic colorectal surgery for malignant lesions. The results could be useful for clinical guidelines in POI risk prediction.

Declarations

Ethics approval and consent to participate

Ethical approval for this study was waived by Suzhou Municipal Hospital Institutional Review Board , considering the retrospective design.

Consent for publication

Not applicable.

Availability of data and materials

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

Competing interests

The authors declare that they have no competing interests.

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Authers' contributions

CG conceived and designed the study. XL, GM, XQ, YW, and XH performed this study and analyzed the data. XL and GM wrote the manuscript. CG reviewed and edited the manuscript. All authors read and approved the final manuscript.

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Tables

Table 1. Baseline characteristics of the patients.

Variables	No POI (n=515)	POI (n=122)	P value
Age(years)	61.4 ± 11.6	63.7 ± 12.5	0.027
Weight(kg)	62.6 ± 10.9	60.6 ± 11.7	0.052
Height(cm)	162.5 ± 8.8	160.9 ± 9.9	0.077
BMI (kg/m^2)	23.7 ± 3.3	23.3 ± 3.3	0.088
Duration of surgery (min)	140.1 ± 49.0	160.2 ± 75.5	0.001
Duration of anesthesia (min)	185.5 ± 51.3	205.8 ± 74.4	<0.001
Lowest intraoperative core temperature (˚C)	35.5 ± 0.5	35.3 ± 0.5	0.004
Intravenous fluids (mL)	1058.5 ± 397.5	1181.7 ± 483.3	0.002
Tympanic temperature on PACU/ICU (˚C)	35.7 ± 0.6	35.6 ± 0.6	<0.001
Opioids during POD3 (morphine equivalents [mg])	16.3 ± 14.2	24.1 ± 19.2	<0.001
ACCI	4.1 ± 1.5	4.7 ± 1.8	0.003
Maximum pain during POD3*	5.6 ± 1.8	6.0 ± 1.7	0.014
Time to first passage of flatus (Day)	2.8 ± 0.9	3.9 ± 2.0	<0.001
Time to first solids (Day)	2.7 ± 1.1	3.6 ± 2.7	<0.001
Gender			0.570
female	247 (48.0%)	62 (50.8%)	
male	268 (52.0%)	60 (49.2%)	
ASA			<0.001
1	125 (24.3%)	9 (7.4%)	
2	264 (51.3%)	79 (64.8%)	
3	120 (23.3%)	31 (25.4%)	
4	6 (1.2%)	3 (2.5%)	
Drinking history			0.635
No	408 (79.2%)	99 (81.1%)	
Yes	107 (20.8%)	23 (18.9%)	
Smoking history			0.196
No	427 (82.9%)	107 (87.7%)	
Yes	88 (17.1%)	15 (12.3%)	
Type of surgery			0.242
left-sided colectomy	147 (28.5%)	35 (28.7%)	
right-sided colectomy	197 (38.3%)	36 (29.5%)	
rectal surgery	162 (31.5%)	48 (39.3%)	
others	9 (1.7%)	3 (2.5%)	
Presence of stomy			0.180
No	480 (93.2%)	109 (89.3%)	

Yes	35 (6.8%)	13 (10.7%)	
Operator			0.093
0	204 (39.6%)	37 (30.3%)	
1	74 (14.4%)	22 (18.0%)	
2	135 (26.2%)	26 (21.3%)	
3	61 (11.8%)	22 (18.0%)	
4	33 (6.4%)	13 (10.7%)	
5	8 (1.6%)	2 (1.6%)	
Type of anesthesia			1.000
Intravenous-inhalation combined anesthesia	444 (86.2%)	105 (86.1%)	
total intravenous anesthesia	30 (5.8%)	7 (5.7%)	
inhalation anesthesia	41 (8.0%)	10 (8.2%)	
Intraoperative hypothermia			0.044
No	94 (18.3%)	13 (10.7%)	
Yes	421 (81.7%)	109 (89.3%)	
Admission to ICU			0.256
No	469 (91.1%)	107 (87.7%)	
Yes	46 (8.9%)	15 (12.3%)	
Hypothermia on PACU or ICU			0.040
No	208 (40.4%)	37 (30.3%)	
Yes	307 (59.6%)	85 (69.7%)	
Refill iv-PCA			0.133
No	511 (99.2%)	119 (97.5%)	
Yes	4 (0.8%)	3 (2.5%)	
Wound dehiscence			0.028
No	512 (99.4%)	118 (96.7%)	
Yes	3 (0.6%)	4 (3.3%)	

P values refer to differences among the two groups, $p < 0.05$.

*Scores were measured on numerical rating scale (NRS)

Table 2. Types of variables at baseline.

Types	variables
Continuous	Age
	Weight
	Height
	BMI
	Duration of surgery
	Lowest intraoperative core temperature
	Intravenous fluids
	Tympanic temperature on PACU/ICU
	Intraoperative opioids (morphine equivalents)
	ACCI
	Maximum pain during POD3
	Time to first passage of flatus
	Time to first solids
Binary	Gender
	Drinking history
	Smoking history
	Presence of stomy
	Intraoperative hypothermia
	Admission to ICU
	Hypothermia on PACU or ICU
	Refill iv-PCA
	Wound dehiscence

	ASA
Categorical	Type of surgery
	Operator
	Type of anesthesia

Table 3. Classifier, packages, and tuning parameters in the Anaconda software used for machine learning

Algorithm	Classifier	Package	Tuning Parameters
LR	LR	Sklearn 0.19.1	penalty='l2', tol=0.000001, C=0.1, fit_intercept=True, intercept_scaling=1, class_weight=None, max_iter=100, multi_class='ovr', verbose=0, warm_start=False, n_jobs=1
DT	DT	Sklearn 0.19.1	splitter='best', max_depth=3, min_samples_split=30, min_samples_leaf=2, min weight_fraction_leaf=0.01
RF	RF	Sklearn 0.19.1	n_estimators=50, n_jobs=1, min_samples_split=20, min_samples_leaf=2, random_state=41
GBDT	GBDT	Sklearn 0.19.1	learning_rate=0.1, n_estimators=20, max_depth=3, min_samples_split=30, min_samples_leaf=5

*LR: logistic regression; DT: decision tree; RF: random forest; GBDT: gradient boosting decision tree.

Table 4. Forecast results of the testing group

models	precision	recall	f1_score	AUC
Logistic regression	0.5556	0.2000	0.2941	0.7445
Decision tree	0.4615	0.2400	0.3158	0.7512
Random forest	0.6667	0.1600	0.2581	0.7348
Gradient boosting decision tree	0.6667	0.3200	0.4324	0.7631

Figures

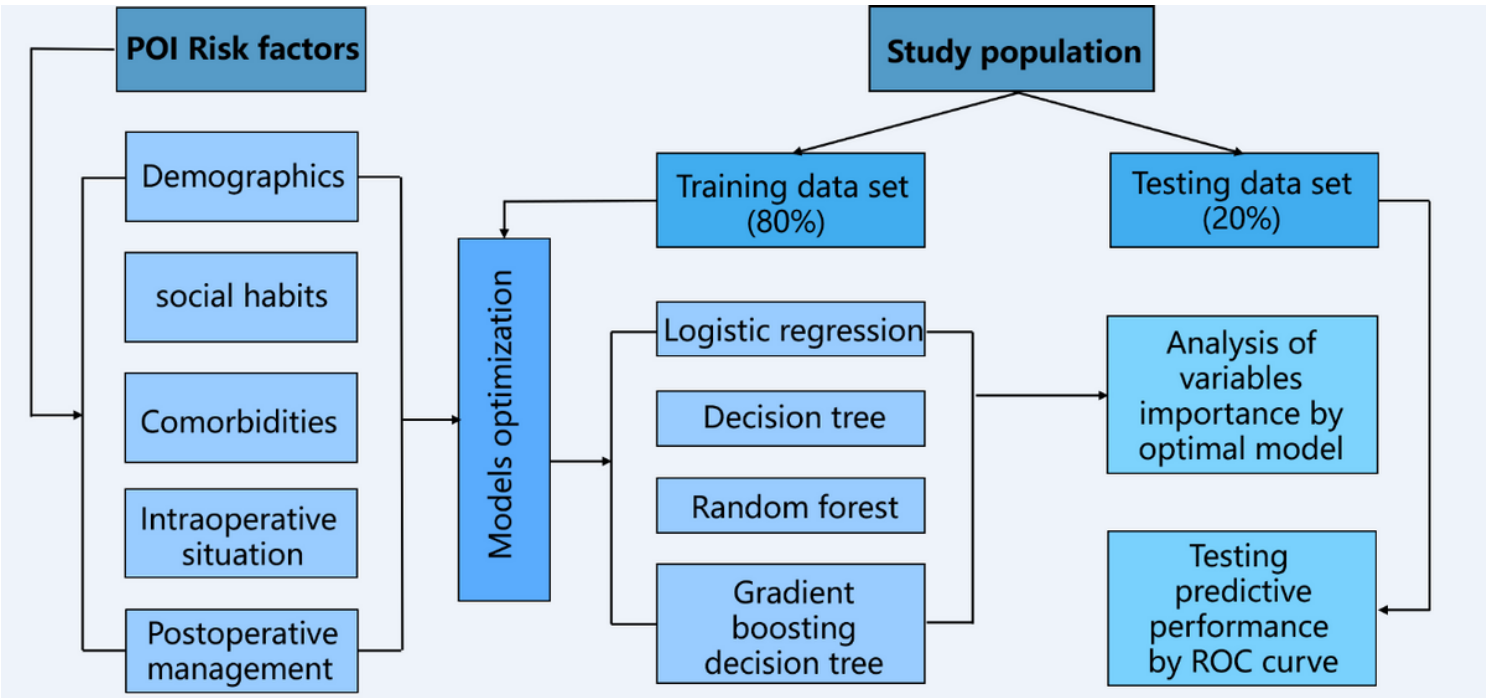

Figure 1

Flowchart of this study for prediction of risk factors of POI.

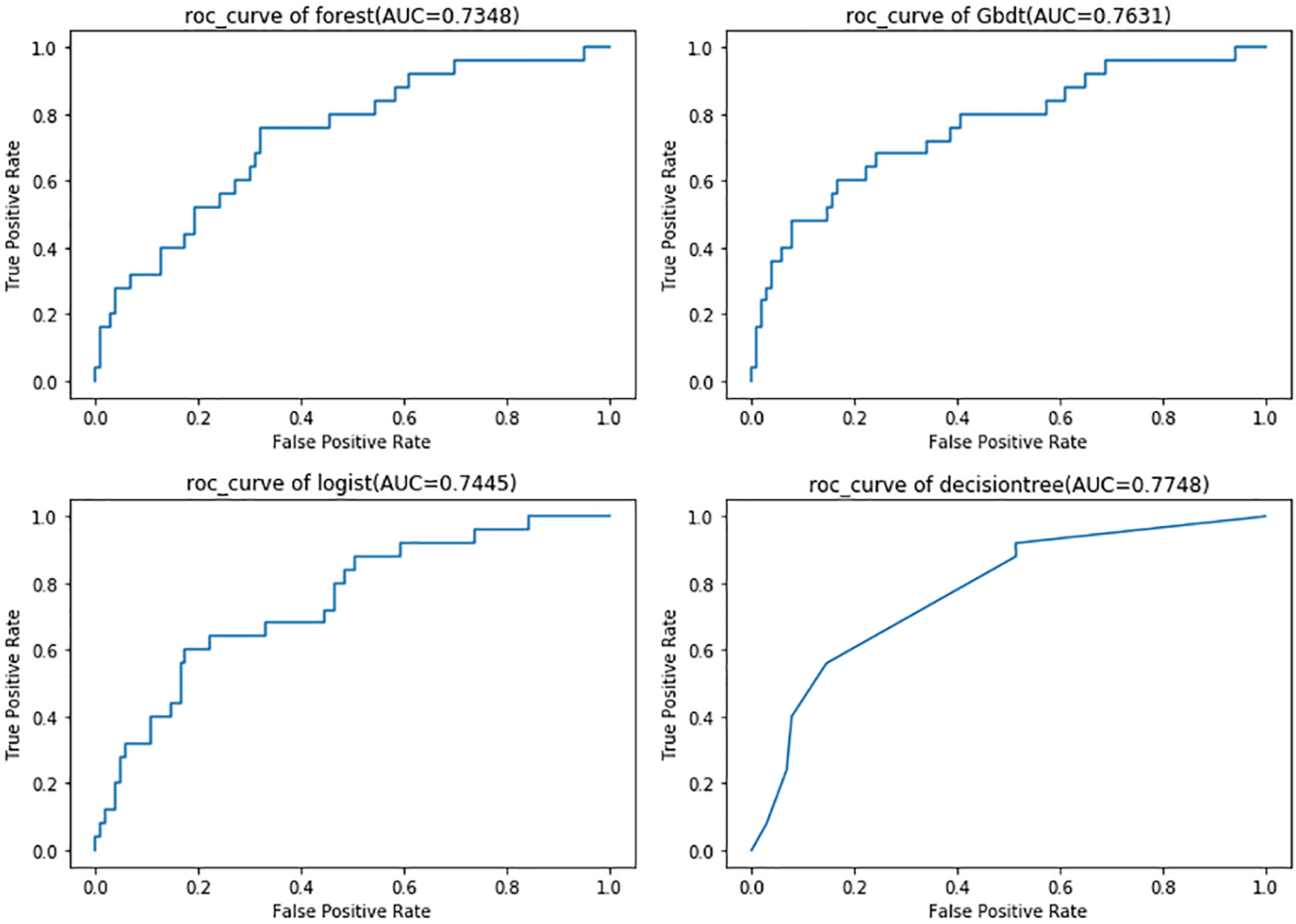

Figure 2

ROC curve showing four difference models AUC values based on testing datasets.

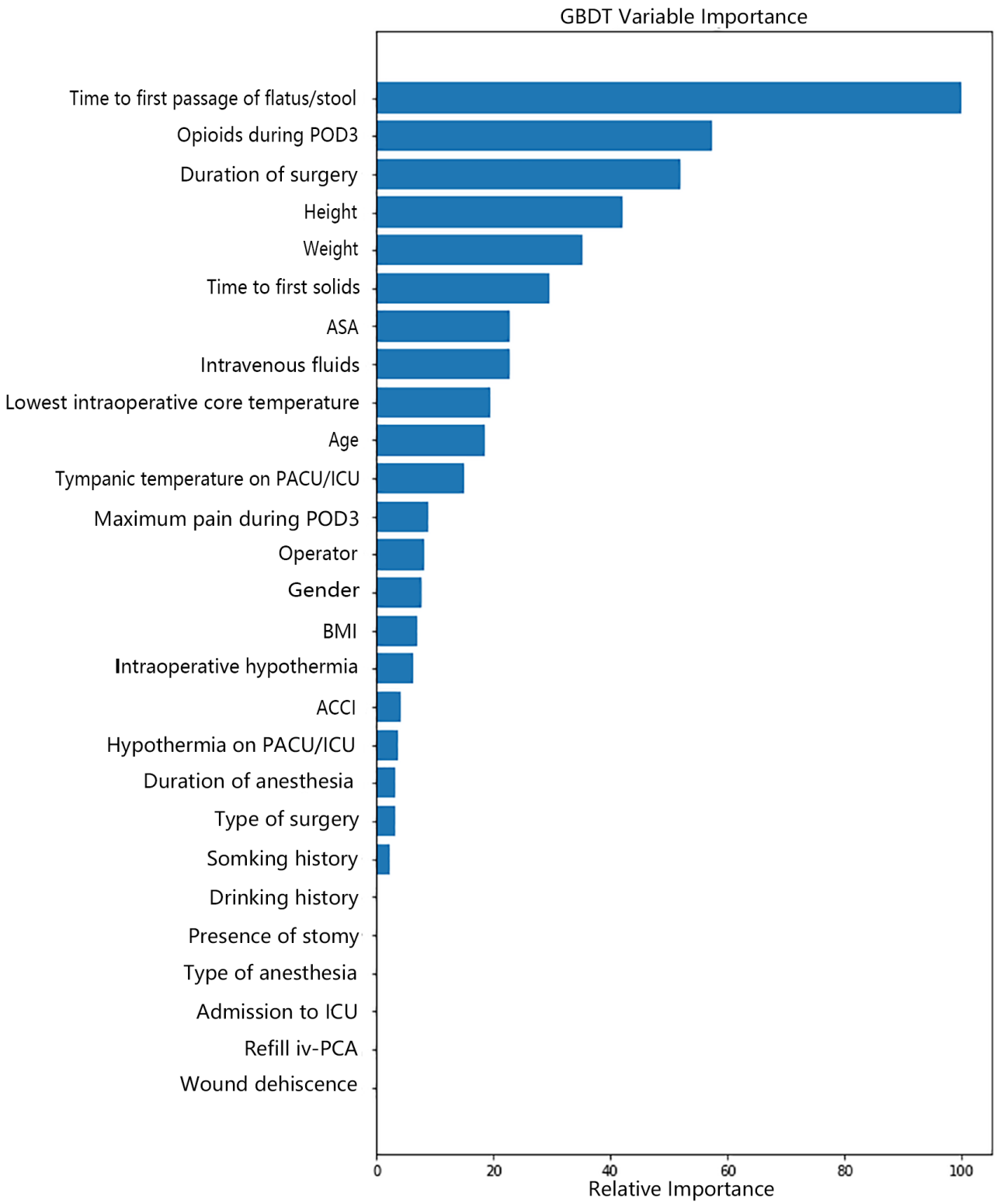

Figure 3

Variable importance of the risk factors for gradient boosting decision tree of POI.