Machine learning with interpretability predict surgical site infection after posterior cervical surgery

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Research Article

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Abstract

Background:

Ideal tools should not only investigate risk factors, but also provide explicit auxiliary answer for whether a patient will develop surgical site infection (SSI) or not. Machine learning (ML) models have ability to carry out complicated predictive medical tasks. We intend to develop ML models to predict SSI after posterior cervical surgery and interpret the outcome.

Methods:

We retrospectively analyzed 235 patients who had undergone posterior cervical surgery between June 2013 to April 2019 at Zhongda Hospital Affiliated to Southeast University. We established Artificial neural networks (ANN), XGBClassifier (xgboost), KNeighborsClassifier (KNN), Decision tree classifier (decision tree), Random forest classifier (random forest) and support vector classifier (SVC). Receiver operating characteristic (ROC) curve, area under the curve (AUC) score, accuracy score, recall score, F1 score and precision score were calculated to measure models' performance. Shapley values were calculated using SHapley Additive exPlanations (SHAP) to determine relative feature importance of xgboost model.

Results:

The incidence of SSI was 7.23%. With AUC of 0.9972, 0.9923, 0.9865, 0.9615, 0.9540, 0.8934, the xgboost, random forest, ANN, KNN, decision tree, SCV accurately predicted SSI. Xgboost, ANN, decision tree and random forest achieved excellent performance in testing set. Top 10 variables with high predictive contribution of xgboost including, drainage volume, body mass index (BMI), drainage duration, operation blooding, cholesterin, sex, prognostic nutritional index (PNI), albumin, hypertension, operation time.

Conclusion:

We had successful established ML models in individualized predicting SSI after posterior cervical surgery. Xgboost, ANN, decision tree and random forest achieved excellent performance which could provide auxiliary information for clinical decision makers. The interpretable model focuses on contribution of important features to the predictive result. It can improve the acceptance of clinicians on ML and promote ML's application in the actual clinical work.

Background:

Posterior cervical surgery is the major surgical approach for the treatment of cervical diseases. Surgical site infection (SSI) is one of most common severe postoperative complications following spinal surgery.

[1] The rates of SSI after spinal surgery had been reported ranging from 0.7–12.0%[2]. The SSI can induce devastating complications including neurological injury, paralysis, pseudarthrosis, sepsis and death, with prolonging the length of hospital stay and increasing costs[1, 3, 4]. Identifying risk factors associated with SSI is a significant focus in past researches.

Previous studies had identified many risk factors of SSI after spinal surgery, including age, diabetes, body mass index (BMI), malnutrition, American Society of Anesthesiologists score (ASA score), smoking status, revision, posterior approach, operative time, osteotomy, and fusion length.[2, 5, 6] Although many studies had investigated factors associating with SSI, it mainly based on clinicians' analytical judgment, that recognizing whether a patient will develop SSI or not and deciding subsequent treatment. Ideal tools are needed to provide explicit auxiliary answer to doctors.

Though logistic regression analysis had been developed to predict SSI after instrumented thoracolumbar spine surgery and showed reasonable discriminative ability and calibration.[7] But logistic regression analysis is static and often relies on predefined relationships (eg, linear), which makes it less robust for large data sets with complex relationships between patient characteristics and outcomes.[8] In recent years, artificial intelligence (AI) has made great progress in medical management. As a major branch of AI, machine learning (ML) has ability to learn from complicated data and nonlinear relationships[8], and achieves better performance from big data. To our best knowledge, no studies have been conducted to use ML models predicting SSI after posterior cervical surgery. Therefore, the purpose of this study is to develop ML models for predicting SSI and interpret the outcome.

Methods:

1. Patient population and data processing

We retrospectively analyzed 235 patients who had undergone posterior cervical surgery for cervical spondylosis, ossification of the posterior longitudinal ligament (OPLL), cervical stenosis, cervical acute trauma, cervical tumors and atlantoaxial disorder between June 2013 to April 2019 at Zhongda Hospital Affiliated to Southeast University. The Diagnostic criteria of SSI were as follows[9]: (1)Purulent drainage, with or without laboratory confirmation, from the superficial incision or deep incision; (2) Organisms isolated from an aseptically obtained culture of fluid or tissue from the incision; (3) The incision spontaneously dehisces or is deliberately opened by a surgeon when the patient has at least one of following signs or symptoms: fever (>38ºC), localized pain, or tenderness, localized swelling, redness, or heat, unless site is culture-negative; (4) An abscess or other evidence of infection is found on direct examination, during reoperation, or by histopathologic or radiologic examination; (5) Diagnosis of SSI by the surgeon or attending physician. The detailed exclusion criteria were as follows: (1) Primary spinal infection; (2) Previous history of spinal surgery; (3) Combined with other operations, such as anterior cervical surgery or thoracic surgery; (4) Posterior cervical minimally invasive surgery; (5) Incomplete clinical data.

The following variables were analyzed as input: sex, age, BMI, diabetes, hypertension, preoperative nutritional status (including serum albumin, serum total cholesterol, total blood lymphocyte count), the prognostic nutritional index (PNI) (10 × serum albumin [g/dL] + 0.005 × total lymphocyte count [/μL]), [5] operation time, intraoperative blood loss, incision length, postoperative drainage and drainage time. BMI≥25 is overweight. Parameters used to train models were shown in Table 1. To overcome the low sample size for SSI cohorts, the SMOTE approach, confirmed in previous research[10], was utilized to generate SSI sample for reducing class imbalance. Then the dataset was randomly divided into training set and test set at 7:3.

Table.1 Variables identified and used for final training models.

Categorical variables	Continuous variables	Target variable
Sex	Age	Infection
Diabetes	BMI	
Hypertension	Albumin	
	Cholesterin	
	Lymphocyte	
	PNI	
	Operation time	
	Operation blooding	
	Incision length	
	Drainage	
	Drainage duration	

PNI (prognostic nutritional index)

2. Machine Learning construction and evaluation

Machine learning analysis was conducted in Python (version 3.7.6) with the Sci-Kit Learn package's XGBClassifier (xgboost), KNeighborsClassifier (KNN), Decision tree classifier (decision tree), Random forest classifier (random forest) and support vector classifier (SVC). Artificial neural networks were conducted in Tensorflow (version 2.3) keras package. Grid searching of various parameters was performed and training was evaluated by tenfold cross-validation for decision tree and random forest. Gradient descent method was used to reduce loss of the ANN, and dropout was added to inhibit overfitting. The training was performed for 1300 epochs and the learning rate was 0.0005. Receiver operating characteristic (ROC) curve, area under the curve (AUC) score, accuracy score, recall score, F1 score and precision score were calculated to measure models' performance. Shapley values were

calculated using SHapley Additive exPlanations (SHAP) to determine relative feature importance, for improving interpretability of our xgboost model.[11]

Results:

There were 58 females and 177 males who underwent posterior cervical surgery, in which 17 patients were diagnosed as SSI and the incidence of SSI was 7.23%. Total patients had a mean age of 60.10 (SD: ± 11.29) years, BMI of 24.36 (SD: ± 3.20) kg/m^2, which shown in Table 2.

Table.2 Baseline patient characteristics.

	Total patients n = 235		Non-SSI patients n = 218		SSI Patients n = 17	
Female gender, n (%)	58(24.7)		53(24.3)		5(29.4)	
Diabetes	42(17.9)		34(15.6)		8(47.1)	
Hypertension	84(35.7)		77(35.3)		7(41.2)	
	Mean	Std	Mean	Std	Mean	Std
Age	60.10	11.29	60.16	11.40	59.35	9.94
BMI	24.36	3.20	24.14	3.14	27.22	2.61
Albumin	39.67	4.45	39.48	4.45	42.13	3.80
Cholesterin	4.54	1.03	4.53	1.04	4.73	0.91
Lymphocyte	1.77	0.62	1.76	0.63	1.96	0.45
PNI	48.53	5.62	48.26	5.66	51.95	3.82
Operation time	169.32	45.94	167.27	44.21	195.59	59.74
Operation blooding	342.47	315.32	336.15	316.85	423.53	291.61
Incision length	10.84	2.52	10.72	2.52	12.41	1.84
Drainage volume	609.85	756.70	580.85	753.80	981.76	713.61
Drainage duration	82.06	54.81	80.95	53.98	96.32	64.64

PNI (prognostic nutritional index)

Validation demonstrated AUC of models, which were shown in Fig 1. With AUC of 0.9972, 0.9923, 0.9865, 0.9615, 0.9540, 0.8934, the xgboost, random forest, ANN, KNN, decision tree, SCV accurately predicted SSI. Performance of models on accuracy score, recall score, F1 score and precision score were shown in Table 3. Xgboost, ANN, decision tree and random forest achieved excellent prediction result in testing set.

xgboost (XGBClassifier), KNN (KNeighborsClassifier), decision tree (Decision tree classifier), random forest (Random forest classifier) and SVC (support vector classifier)

Table.3 Performance of models on accuracy score, recall score, F1 score and precision score.

	xgboost	KNN	decision tree	random forest	ANN	SVC
ACC	0.9695	0.855	0.9542	0.9924	0.9618	0.8931
Recall	0.9697	0.8333	0.9848	1	0.9545	0.8636
F1-score	0.9697	0.8527	0.9559	0.9925	0.9618	0.8906
Precesion	0.9697	0.873	0.9286	0.9851	0.9692	0.9194

xgboost (XGBClassifier), KNN (KNeighborsClassifier), decision tree (Decision tree classifier), random forest (Random forest classifier) and SVC (support vector classifier). ROC (Receiver operating characteristic curve), AUC (area under the curve score), ACC (accuracy score)

Model features and feature importance

All categorical variables and continuous variables for training xgboost were listed in Table 1. The baseline demographic data of SSI group and non-SSI group are shown in Table 2. SSI group had higher rates for female, diabetes, hypertension and higher means for BMI, albumin, cholesterin, lymphocyte, PNI, operation time, operation blooding, incision length, drainage volume and drainage duration than non-SSI group, but lower age than controls.

Top 10 variables with high predictive contribution in xgboost, were ranked on Fig 2. The xgboost model identified drainage volume, BMI, drainage duration, operation blooding, cholesterin, sex, PNI, albumin, hypertension and operation time as the important predictors of SSI.

Discussion:

Plenty of studies had investigated risk factors of SSI after spinal surgery.[2, 5, 6] However, when a patient with several factors needs spine surgery, the exact SSI incidence possibility is ambiguous and the treatment decision still depended on clinicians' experience. While intelligent algorithms based on previous complicated patient data will provided a wealth of information. A paper had applied a Deep Neural Network model using 35 unique variables to predict SSIs after posterior spinal fusions.[12] They mainly pay attention on demographics, combined disease and operation type.[12] We hold that more specific variables are necessary to improve ML predictive models. To our best knowledge, no study had yet explored ML models to predict SSI after posterior cervical surgery.

Our models shown reliably predive performance based on patient data from this institution. Xgboost, random forest, ANN and decision tree got predictive accuracy more than 90% in test set. The ability to predict SSI may assist surgeons in identifying potential risk patients, better selecting candidates for

posterior cervical surgery, managing patient expectations and timely intervene to improve outcomes. These lends to precision-based spine care and more bespoke management to optimize patient outcomes and improve daily function, with decreasing healthcare-related costs.[11]

We established sex different models to find the most robust one, which contain one deep learning and two model ensembles. Deep learning has superior fitting ability than traditional models, suitable to big data. Model ensembles, like xgboost and random forest, combines plenty weak classifiers to increase accuracy on ML tasks. However, in this study xgboost and random forest got slightly better predictive ability than ANN, the deep learning algorithm, which may explain by the low order of magnitude data. Interestingly, the decision tree also achieved satisfactory result after grid searching for best parameters. This may due to our fine-tuning work and well feature selection.

We input more individual features like, nutritional status and operation data, differing from national level database taking into account plenty demographic and general management variables. We thought these may better providing personalized preoperative status and provide more individual information. However, these variables were all manual inputted and laborious.

A main challenge of ML needed to overcome is Black box, that limits application of ML in medicine. It is that most AI technologies operate based on opaque logic and hardly understandable to users. Interpretation of xgboost based on SHAP is a solution of Black box. Beyond get an unexplainable prediction, we could examine contribution of each valuable on the individual prediction. Two examples are shown in Fig 3 and Fig 4.

Drainage volume and drainage duration were identified as predictors in the present study. Prolonged drainage duration has frequently been cited as independent risk factors for SSI.[4, 13, 14] Liu et al used multivariable analysis to confirm that prolonged drainage duration was a risk factor for SSI after lumbar spinal surgery.[4] Moreover, Rao et al suggested to remove the drain as early as possible for reducing infection rate following spinal fusion.[17] Drains may induce local tissue inflammation and become direct access for bacteria by ascending the drain tube, thus increasing the risk of infection.[18] Also, a study demonstrated two-fold reduction of SSI with implementation of prolonged prophylactic systemic antibiotics regimen for the duration of drain.[15]

Previous researches had suggested a positive relationship between BMI and SSI. Pesenti et al confirmed that obesity is a significant risk factor for SSI after spinal arthrodesis and BMI > 30 kg m^{-2} as a significant risk factor in most of studies.[6] Another meta-analysis found 21 % increase in risk of spinal SSI for every 5-unit increase in BMI, after adjusting for diabetes and other confounders.[16] It has been reported that increasing subcutaneous adipose tissue raises the likelihood of fat necrosis and thus increases infection risk.[17]

A multivariate analysis found that perioperative blood loss≥500 mL was a risk factor for SSI in spine surgery.[18] Zhou et al indicated that the SSI incidence of blood loss500 mL was twice those blood loss<500 mL.[19] Meanwhile, they found surgical time≥3 hours have higher incidence of spinal SSI,

which may be explained by that prolonging operative duration increases the chance of contamination in surgical wounds.[19] However, some studies found no relation between the surgical time and SSI.[20] Besides “operative time”, total anesthetic time is also an independent predictor of SSI, when patient remains in the operative room environment.[21]

Our model identifies cholesterin, PNI and albumin as risk factors, while the total cholesterol had no signature between SSI and non-SSI in previous researchs.[22, 23] Lower preoperative PNI and lower serum albumin were found be risk factor for SSI after spine surgery.[4, 5, 24] However, PNI and albumin are higher in SSI(51.95±3.82 and 42.13±3.80 g/dL) than non-SSI(48.26±5.66 and 39.48±4.45) among this cohort, which opposite to previous studies. And the relationship between sex and SSI is controversial in some studies. Ogihara et al found male sex were risk factors for deep SSI after thoracolumbar instrumented fusion.[25] While sex was not significantly associated with SSI in a cohort of over 1000 consecutive spinal fusions.[21] Next, hypertension had been found as risk factors for SSI in spine surgery by a few studies.[23]

Although performance of ML models on SSI after posterior cervical surgery are robust, this study has noteworthy limitations. First, the sample of this study is small, and further larger sample inputting may improve prediction results. Also, the data retrieved from a single institution, and further external validation is necessary to elevate models’ expansibility.

Conclusions:

We had successful established ML models in individualized predicting SSI after posterior cervical surgery. Xgboost, ANN, decision tree and random forest achieved excellent performance which could provide auxiliary information for clinical decision makers. The interpretable model focuses on contribution of important features to the predictive result. It can improve the acceptance of clinicians on ML and promote ML’s application in the actual clinical work.

Abbreviations

Surgical site infection (SSI), Machine learning (ML), Artificial neural networks (ANN), XGBClassifier (xgboost), KNeighborsClassifier (KNN), Decision tree classifier (decision tree), Random forest classifier (random forest), support vector classifier (SVC), Receiver operating characteristic (ROC) curve, area under the curve (AUC), SHapley Additive exPlanations (SHAP), American Society of Anesthesiologists score (ASA score), artificial intelligence (AI), ossification of the posterior longitudinal ligament (OPLL).

Declarations

Ethics approval and consent to participate: The study had been approved by Zhongda Hospital Affiliated to Southeast University ethics committee and the reference number was 2021ZDSYLL222-P01. This

study had met the requirements for exemption from informed consent, and approved to exemption from informed consent by Zhongda Hospital Affiliated to Southeast University ethics committee.

Consent for publication: Not Applicable.

Availability of data and materials: The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

Competing interests: The authors have no relevant financial or non-financial interests to disclose.

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Authors' contributions: GuanRui Ren and ZhiYang Xie contributed to the study conception and design. Data collection were performed by YiYang Wang, PeiYang Wang and Wei Zhang. Analysis was performed by GuanRui Ren. The first draft of the manuscript was written by GuanRui Ren and ZhiYang Xie. Lei Liu, YunTao Wang, and XiaoTao Wu commented on previous versions of the manuscript. All authors read and approved the final submitted version.

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Figures

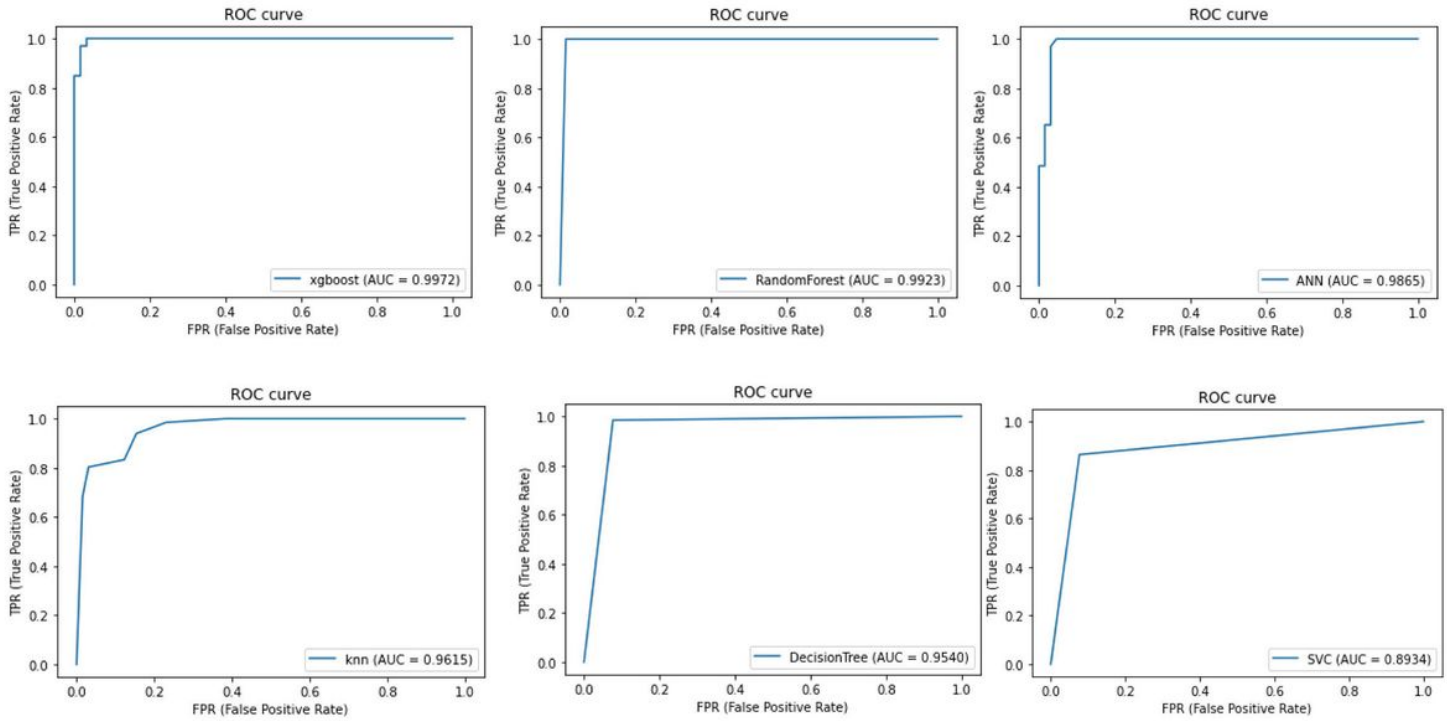

Figure 1

AUC results of models. xgboost (XGBClassifier), KNN (KNeighborsClassifier), decision tree (Decision tree classifier), random forest (Random forest classifier) and SVC (support vector classifier)

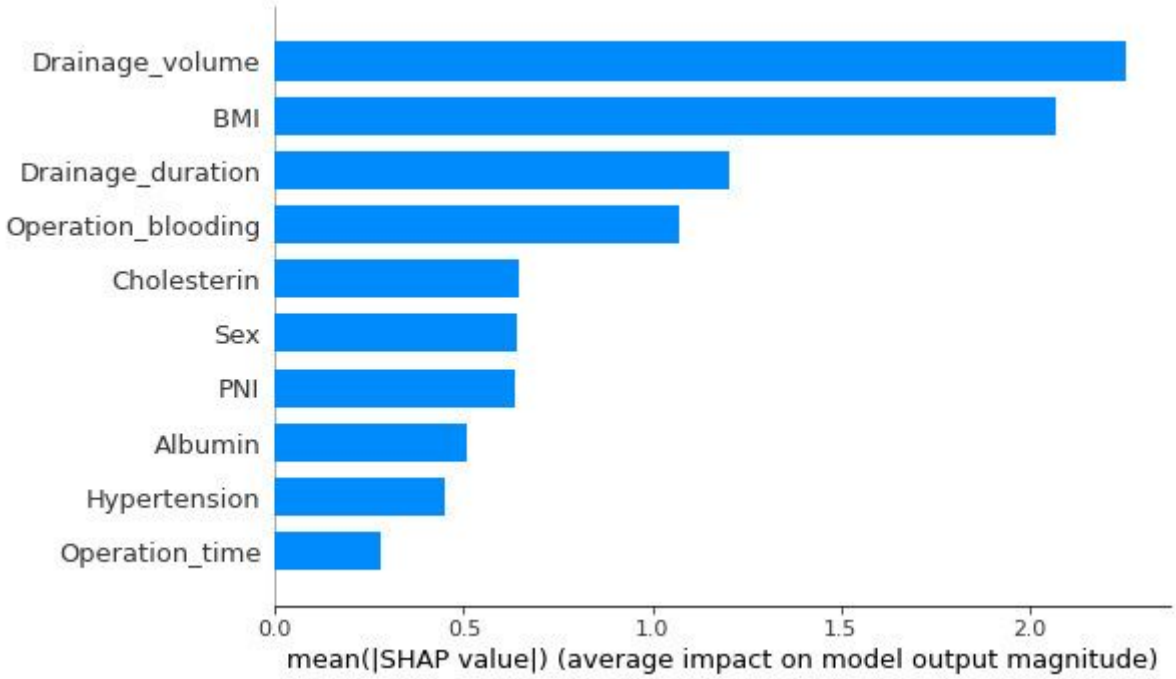

Figure 2

Feature importance ranking based on strength of relation to SSI. PNI (prognostic nutritional index)

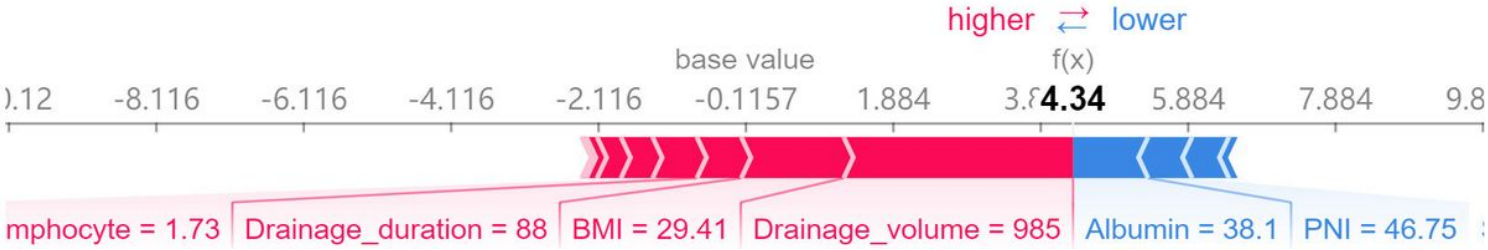

Figure 3

Patient Example 1. High probability of SSI. PNI (prognostic nutritional index)

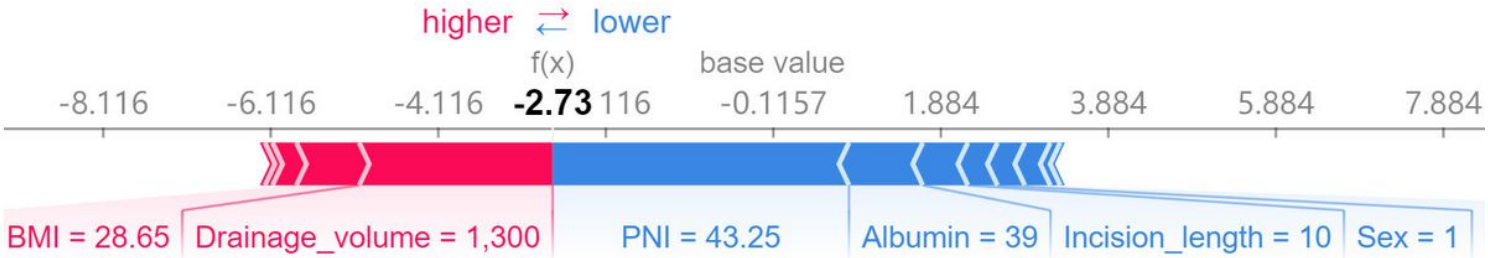

Figure 4

Patient Example 2. Low probability of non-SSI. PNI (prognostic nutritional index)