Machine learning applications for the prediction of surgical site infection in neurological operations

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OBJECTIVE Surgical site infection (SSI) following a neurosurgical operation is a complication that impacts morbidity, mortality, and economics. Currently, machine learning (ML) algorithms are used for outcome prediction in various neurosurgical aspects. The implementation of ML algorithms to learn from medical data may help in obtaining prognostic information on diseases, especially SSIs. The purpose of this study was to compare the performance of various ML models for predicting surgical infection after neurosurgical operations.

METHODS A retrospective cohort study was conducted on patients who had undergone neurosurgical operations at tertiary care hospitals between 2010 and 2017. Supervised ML algorithms, which included decision tree, naive Bayes with Laplace correction, k-nearest neighbors, and artificial neural networks, were trained and tested as binary classifiers (infection or no infection). To evaluate the ML models from the testing data set, their sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV), as well as their accuracy, receiver operating characteristic curve, and area under the receiver operating characteristic curve (AUC) were analyzed.

RESULTS Data were available for 1471 patients in the study period. The SSI rate was 4.6%, and the type of SSI was superficial, deep, and organ/space in 1.2%, 0.8%, and 2.6% of cases, respectively. Using the backward stepwise method, the authors determined that the significant predictors of SSI in the multivariable Cox regression analysis were postoperative CSF leakage/subgaleal collection (HR 4.24, $p < 0.001$) and postoperative fever (HR 1.67, $p = 0.04$). Compared with other ML algorithms, the naive Bayes had the highest performance with sensitivity at 63%, specificity at 87%, PPV at 29%, NPV at 96%, and AUC at 76%.

CONCLUSIONS The naive Bayes algorithm is highlighted as an accurate ML method for predicting SSI after neurosurgical operations because of its reasonable accuracy. Thus, it can be used to effectively predict SSI in individual neurosurgical patients. Therefore, close monitoring and allocation of treatment strategies can be informed by ML predictions in general practice.

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KEYWORDS surgical site infection; survival analysis; machine learning; neural network

SURGICAL site infection (SSI) following neurosurgical operations is a burdensome complication in the field. Such complications can impact morbidity, mortality, and economics.^{4,5,25} O’Keeffe et al. conducted a cost analysis of craniotomy infections, identifying an estimated cost per case of infection at £9283. The financial burden caused by craniotomy infections is often compounded by

the direct costs incurred by prolonged hospitalization of the patient, diagnostic tests, treatment, and reoperation.^{4,18}

Machine learning (ML) is used for outcome prediction in the neurosurgical field. Several ML algorithms have been developed using complex mathematical models that can learn from clinical data from, for example, neuro-oncology, neurovascular surgery, traumatic brain injury,

ABBREVIATIONS ANN = artificial neural network; ASA = American Society of Anesthesiologists; AUC = area under the receiver operating characteristic curve; CSF = cerebrospinal fluid; DT = decision tree; k-NN = k-nearest neighbors; ML = machine learning; NB = naive Bayes; NPV = negative predictive value; PPV = positive predictive value; ROC = receiver operating characteristic; SAH = subarachnoid hemorrhage; SSI = surgical site infection.

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FIG. 1. Workflow of training and testing the ML algorithms. Using random sampling without replacement, each sample was divided into five subsets. Therefore, 80% of each subset (white boxes) was used for training various algorithms, and 20% of the subset (gray boxes) was used to test the performance of each ML model.

and epilepsy.^{3,14,17,19,23,24,26} Memarian et al. reported that the multimodality of ML, including linear discriminant analysis, naïve Bayes (NB), and support vector machines, has high accuracy in surgical outcome prediction in patients with mesial temporal lobe epilepsy.^{15,17} Moreover, Armañanzas et al. demonstrated that ML algorithms such as NB, logistic regression, and k-nearest neighbors (k-NN) may be powerful methods of selecting surgical candidates who have a high likelihood of remaining free from seizures in temporal lobe epilepsy.³

From literature reviews we find evidence that ML has been applied in predicting neurosurgical complications, particularly SSI. Habibi et al. compared artificial neural networks (ANNs) and traditional logistic regression models for predicting ventriculoperitoneal shunt infections in childhood hydrocephalus.¹² The ANNs and logistic models predicted shunt infection with an accuracy of 83.1% and 55.7%, respectively.¹² The implementation of ML algorithms to learn from medical data may help in obtaining prognostic information on diseases. It also has potential use in predicting which patients will be in the high-risk group as well as allocating treatment strategies in general practice.¹¹ Given the burden of SSI, the purpose of this study was to compare the performance of various ML models in terms of predicting surgical infection after neurosurgical operations.

Methods

Study Design and Population

This study was performed with the approval of the Ethics Committee of the Faculty of Medicine, Songklanagarind Hospital, Prince of Songkla University. We conducted a retrospective review of patients who had undergone neurosurgical operations at Songklanagarind Hospital between 2010 and 2017 and who had at least 3 months of follow-up data after surgery. Patients without available operative data and spine surgery patients were not included in our analysis. Demographic data were collected, as were baseline clinical characteristics, operative details, American Society of Anesthesiologists (ASA) classifications, and postoperative outcomes.

The initial operation was counted as the first operation performed at Songklanagarind Hospital, whereas any subsequent operations were counted as a reoperation variable in the same patient. Operative time was defined as the time from skin incision to skin closure, which was documented in the anesthesia records by an anesthesiologist. Postoperative cerebrospinal fluid (CSF) leakage was defined as visible leaking from a surgical wound, nasal cavity (transphenoidal operation), or subgaleal/subcutaneous collection as observed after craniotomy or spinal operations in the same admission. Postoperative ventriculostomy was

TABLE 1. Baseline characteristics of 1471 patients who underwent neurosurgical operations between 2010 and 2017

Factor	No. (%)
Sex	
Male	839 (57.0)
Female	632 (43.0)
Age in yrs	
<60	1079 (73.4)
≥60	392 (26.6)
Disease	
Tumor	698 (47.5)
Trauma	300 (20.4)
Vascular	337 (22.9)
Congenital	49 (3.3)
Primary infection	44 (3.0)
Other	43 (2.9)
Location	
Supratentorial	1365 (92.8)
Infratentorial	106 (7.2)
Underlying disease	
Diabetes mellitus	154 (10.5)
Previous infection	95 (6.5)
Coagulation	46 (3.1)
Preop hair removal	668 (45.4)
Dexamethasone injection	293 (19.9)
Antibiotic drug prophylaxis	1397 (95.0)
Type of wound	
Clean	1320 (89.7)
Clean-contaminated	57 (3.9)
Contaminated	84 (5.7)
Dirty	10 (0.7)
ASA classification	
I	16 (1.1)
II	288 (19.6)
III	1015 (69.0)
IV	142 (9.7)
V	10 (0.7)
Type of op	
Emergency	751 (51.1)
Elective	720 (48.9)
Procedure	
Craniotomy	588 (40.0)
Craniectomy	270 (18.4)
Shunt	179 (12.2)
Burr hole	94 (6.4)
Ventriculostomy	92 (6.3)
ICP monitoring	8 (0.5)
Transsphenoidal op	85 (5.8)
Cranioplasty	15 (1.0)
Debridement for trauma	6 (0.4)
Debridement for SSI	2 (0.1)

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TABLE 1. Baseline characteristics of 1471 patients who underwent neurosurgical operations between 2010 and 2017

Factor	No. (%)
Procedure (<i>continued</i>)	
Other	125 (8.5)
Intraop ventricular exposure	155 (10.5)
Finding insect in op room	31 (2.1)
Postop ventriculostomy	92 (6.3)
Postop CSF leakage/subgaleal collection	68 (4.6)
Postop fever	51 (3.5)
Bacteremia	51 (3.5)
Urinary tract infection	93 (6.3)
Pneumonia	102 (6.9)
Reop in same admission (excluding reop due to SSI)	85 (5.8)
Postop drain	561 (38.1)
SSI	67 (4.6)
Type of infection	
Superficial	17 (1.2)
Deep	12 (0.8)
Organ/space	38 (2.6)
Meningitis or ventriculitis	30 (2.0)
Brain abscess	6 (0.4)
Subdural empyema	2 (0.1)

ICP = intracranial pressure.

defined as the ventriculostomy catheter inserted after the primary procedure but during the same operative case. Postoperative fever was defined as such when a patient developed a body temperature of 38°C or higher during the same admission.^{6,7} Bacteremia, urinary tract infection, and pneumonia were defined as any organism identified by culture or by evidence of infection involving a specific organ detected on an imaging test in the same admission. Previous infection was defined as such when a patient had a history of an SSI from a procedure at another hospital before having an operation at our hospital.

According to the SSI criteria defined by the Centers for Disease Control and Prevention (CDC), the primary outcomes were reviewed and routinely determined at hospital discharge, every follow-up appointment, and at outpatient clinics until December 31, 2018, using outpatient medical records. Additionally, SSIs were classified as superficial incisional SSI, deep incisional SSI, and organ/space SSI.^{6,7}

Superficial incisional SSI is defined as purulent drainage from a superficial incision or as organisms identified by a culture. Deep incisional SSI is defined as purulent drainage from the deep soft tissue of an incision (e.g., fascial and muscle layers), an organism identified by a culture, or evidence of infection involving the deep incision that is detected on gross anatomical or histopathological exam or an imaging test.^{6,7} Moreover, organ/space SSIs include brain abscess, subdural or epidural infection, encephalitis, meningitis, and ventriculitis.^{6,7} An organ/space SSI is defined as such when purulent drainage comes from a drain

FIG. 2. The Kaplan-Meier curve for infection-free neurosurgical operations. **A:** Kaplan-Meier curve for all cases shows that the overall median infection-free time has not been reached yet. **B:** Kaplan-Meier curves for infection-free probability in patients with preoperative hair removal or no hair removal. Infection-free probability was significantly lower in the patients with hair removal than in those with no hair removal ($p = 0.008$, log-rank test). **C:** Kaplan-Meier curves for postoperative fever or no fever. Infection-free probability was significantly lower in the patients with fever than in those without ($p = 0.009$, log-rank test). **D:** Kaplan-Meier curves for postoperative CSF leakage/subgaleal collection or no CSF leakage/subgaleal collection. Infection-free probability was significantly lower in patients with CSF leakage/subgaleal collection than in those without ($p < 0.001$, log-rank test).

that is placed into the organ/space (e.g., ventriculostomy); the main part of an abscess/other infection deeper than the fascial/muscle layers is present; organisms are identified from an aseptically obtained fluid or tissue in the organ/space by a culture; or there is evidence of infection involving the organ/space that is detected on gross anatomical or histopathological exam or on imaging.^{6,7}

Descriptive Statistics and Survival Analysis

Clinical characteristics and therapeutic factors were first described using descriptive statistics. A survival curve was constructed from the total data using the Kaplan-Meier method. A Cox proportional-hazards regression model was used to identify the univariate and multivariate predictors of survival. In the multivariate analysis, a stepwise method with the Akaike information criterion (AIC) was used to check whether the variable deserved to be included in the model and stratification factors. A p value less than 0.05 was considered statistically significant. Statistical analysis was performed using R version 3.5.0 software (R Foundation for Statistical Computing) with the 'survival' package.

Machine Learning

Using random sampling without replacement, all data were divided into five subsets, as shown in Fig. 1. There-

fore, 80% of each subset was used for training the ML model, while the remaining 20% was used for testing the ML model. Data preprocessing included the dichotomization of independent variables to between 0 and 1.

Supervised ML algorithms included decision tree (DT), NB with Laplace correction, k-NN with $k = 5$, and ANNs. The network was trained 200 times using different random weights and tested as binary outcomes (SSI or no SSI). To validate the models from the testing data set, the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of the models were determined for the predictive efficacy of each ML algorithm. Furthermore, the receiver operating characteristic (ROC) curve and the area under the ROC curve (AUC) were plotted. Additionally, AUCs revealed that values ≥ 0.9 were "excellent," ≥ 0.80 were "good," ≥ 0.70 were "fair," and < 0.70 were "poor."²⁷ All mathematical analyses were done using RapidMiner Studio version 9.0 with an academic license. Moreover, the ROC curves and AUCs were created using the 'plotROC' package (R Foundation for Statistical Computing).

Results

The clinical characteristics of the 1471 eligible patients who underwent neurosurgical operations in the study

TABLE 2. Cox proportional-hazards regression analysis for SSI

Factor	Univariate Analysis HR (95% CI)	p Value	Multivariable Analysis† HR (95% CI)	p Value
Sex				
Male	Reference			
Female	0.61 (0.35–1.03)	0.06		
Age in yrs				
<60	Reference			
≥60	1.94 (0.96–3.93)	0.06		
Preop KPS score				
<80	Reference			
≥80	1.01 (0.98–1.01)	0.91		
Preop GCS score				
13–15	Reference			
9–12	0.74 (0.34–1.60)	0.45		
3–8	1.14 (0.58–2.24)	0.68		
Diabetes mellitus*	0.74 (0.31–1.73)	0.48		
Preop coagulopathy*	1.34 (0.48–3.72)	0.56		
Preop dexamethasone*	1.38 (0.79–2.40)	0.24		
History of previous SSI*	0.57 (0.31–1.03)	0.06		
ASA classification				
I–II	Reference			
≥III	1.09 (0.63–1.88)	0.74		
Tumor op*	1.13 (0.69–1.86)	0.62		
Vascular op*	0.85 (0.40–1.79)	0.67		
Shunt op*	0.68 (0.36–1.29)	0.24		
Trauma op*	1.14 (0.57–2.27)	0.69		
Primary infectious op*	1.21 (0.61–2.41)	0.57		
Type of surgical wound				
Clean	Reference			
Contaminated	1.36 (0.69–2.68)	0.36		
Clean-contaminated	0.70 (0.32–1.52)	0.37		
Dirty	2.40 (0.93–6.18)	0.07		
Region of op				
Supratentorial	Reference			
Infratentorial	0.62 (0.23–2.38)	0.62		
Preop hair removal*	1.84 (1.10–3.08)	0.01	1.66 (0.99–2.78)	0.054
Antibiotic prophylaxis*	1.12 (0.34–3.57)	0.85		
Insect in op room*	0.71 (0.36–1.42)	0.34		
Emergency op*	1.33 (0.79–2.26)	0.27		
Op time in mins				
<240	Reference			
≥240	0.98 (0.54–1.76)	0.94		
Postop ventriculostomy*‡	0.57 (0.25–1.27)	0.17		
Postop CSF/subgaleal collection*§	4.60 (2.08–10.17)	<0.001	4.24 (1.89–9.49)	<0.001
Postop subgaleal drain*‡	0.99 (0.56–1.76)	0.99		
Postop fever§				
No	Reference		Reference	
Fever	1.79 (1.09–2.94)	0.02	1.67 (1.01–2.76)	0.04
Bacteremia*§	1.51 (0.89–2.56)	0.12		
Urinary tract infection*§	0.79 (0.24–2.53)	0.70		
Pneumonia*§	0.95 (0.37–2.38)	0.95		

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TABLE 2. Cox proportional-hazards regression analysis for SSI

Factor	Univariate Analysis HR (95% CI)	p Value	Multivariable Analysis† HR (95% CI)	p Value
Reop*§¶	1.35 (0.80–2.26)	0.25		
Postop KPS score				
<80	Reference			
≥80	1.08 (0.67–1.72)	0.74		

GCS = Glasgow Coma Scale; KPS = Karnofsky Performance Scale.

* Data show only “yes group” while reference groups (no group) are hidden.

† Backward stepwise method.

‡ In the same procedure.

§ In the same admission.

¶ Excluded reoperation due to SSI.

period are listed in Table 1. More than half of the study population were males. The mean age was 45.07 years (SD 21.1), and 10.5% of the patients presented with diabetes mellitus. Almost all patients (95%) received the antibiotic prophylaxis, while 19.9% received preoperative dexamethasone. Additionally, hair shaving occurred in 45.4% of cases. Common diseases in the cohort included tumors, trauma, and vascular conditions, while the most frequently performed procedures were cranial operations.

TABLE 3. Performance data on ML algorithms

Data Set & Algorithm	Sensitivity	Specificity	PPV	NPV	Accuracy	AUC
1st data set						
DT	0.31	0.97	0.41	0.96	0.93	0.64
NB	0.56	0.80	0.14	0.96	0.79	0.69
k-NN	0.06	0.83	0.01	0.94	0.80	0.53
ANN	0.18	0.99	0.60	0.95	0.94	0.59
2nd data set						
DT	0.31	0.95	0.35	0.94	0.90	0.64
NB	0.63	0.87	0.29	0.96	0.86	0.76
k-NN	0.09	1.0	1.0	0.93	0.93	0.55
ANN	0.27	0.98	0.66	0.94	0.93	0.63
3rd data set						
DT	0.25	0.97	0.30	0.96	0.94	0.61
NB	0.58	0.97	0.50	0.97	0.95	0.71
k-NN	0.16	0.98	0.33	0.96	0.95	0.58
ANN	0.25	0.97	0.30	0.96	0.94	0.61
4th data set						
DT	0.40	0.99	0.84	0.97	0.96	0.70
NB	0.53	0.90	0.20	0.97	0.88	0.72
k-NN	0.08	0.99	0.60	0.95	0.95	0.54
ANN	0.37	0.99	0.86	0.97	0.96	0.69
5th data set						
DT	0.43	0.99	0.87	0.97	0.97	0.71
NB	0.53	0.93	0.28	0.97	0.91	0.74
k-NN	0.13	0.99	0.69	0.96	0.95	0.57
ANN	0.41	0.99	0.82	0.97	0.96	0.71

The SSI rate was 4.6%, while the types of SSIs were superficial, deep, or organ/space in 1.2%, 0.8%, and 2.6% of cases, respectively. Among the organ/space SSIs, postoperative brain abscess was found in 0.4% cases, while meningitis or ventriculitis was found in 2.0% of all cases.

Survival Analysis

Time-to-event statistical analysis was possible using the Kaplan-Meier curve shown in Fig. 2A. Mean follow-up time was 313.3 weeks (SD 137.4). Also, the overall median infection-free time was not yet reached in the cohort, while the 1-, 3-, and 12-month infection-free probabilities were 97.4%, 96.4%, and 95.5%, respectively.

According to the Cox proportional-hazards regression analysis (Table 2), the significant parameters for an increased risk of SSI included preoperative hair removal (HR 1.84, $p = 0.01$), postoperative fever (HR 1.79, $p = 0.02$), and postoperative CSF leakage/subgaleal collection (HR 4.60, $p < 0.001$) on univariate analysis. Using the backward stepwise method, we determined that the significant predictors of SSI in the multivariable analysis were postoperative fever (HR 1.67, $p = 0.04$) and postoperative CSF leakage/subgaleal collection (HR 4.24, $p < 0.001$).

For subgroup analysis of the Kaplan-Meier curve in Fig. 2B–D, infection-free probability was significantly lower in patients with hair removal than in those with no hair removal ($p = 0.008$, log-rank test). Infection-free probability was also significantly lower in patients with postoperative fever in the same admission than in those without ($p = 0.009$, log-rank test). Moreover, the patients with postoperative CSF leakage/subgaleal collection had a significantly lower infection-free probability than the patients without ($p < 0.001$, log-rank test).

Machine Learning Algorithms

After training the four algorithms, we used the test data set with each ML algorithm to obtain the performance data shown in Table 3. The NB algorithm had the highest performance with the largest AUC at 76%, sensitivity at 63%, specificity at 87%, PPV at 29%, NPV at 96%, and accuracy at 86%, whereas the other algorithms exhibited lower performance for predicting SSI with the cohort data. The ROC curve and AUC for all data sets are summarized graphically in Fig. 3. Overall, the data suggest that NB is

FIG. 3. The ROC curve and AUC of the five data sets, with the NB algorithm having the largest AUC. First data subset (A), second data subset (B), third data subset (C), fourth data subset (D), and fifth data subset (E).

the most effective methodology for predicting SSI in neurosurgical operations.

Discussion

The rate of diagnosed SSIs has a reported range of 1.1%–6.2%. In the present study, SSI was observed at 4.6%, which is similar to rates in previous studies. Moreover, we observed postoperative fever and postoperative CSF leakage/subgaleal collection in the same admission as being associated with an increased rate of SSI. Similarly, Chiang et al. reported that CSF leakage was a significant variable associated with SSI (OR 3.5, 95% CI 1.4–8.5).⁸ Other independent risk factors for SSI have included meningioma, longer operation time, craniotomy, dural substitute, staples in wound closure, operation performed by a specialist or senior medical officer, surgery conducted for infectious causes, ASA physical status II, and clean-contaminated wound,^{1,5,8–10,16,25} depending on the cohorts, although these factors were not associated with SSI in the present study.

Cranial surgery without hair removal is a modifiable risk factor that has been discussed in prior studies. Ratanalert et al. recommended not shaving hair for intracranial procedures in nonemergency neurosurgical procedures because shaving significantly increased the risk of SSI compared with not shaving. Further, Adeleye et al. mentioned that cranial surgery without hair removal is safe and does not increase the risk of surgical wound infection.^{2,20} In our cohort, 45.4% of cases were shaved at the discretion of the attending neurosurgeon. The patients with preopera-

tive hair removal had a significantly increased risk of SSI on univariate analysis; however, the results were limited to interpretation of the nonrandomized data.

ML algorithms such as DT, NB, k-NN, and ANN can provide strong predictive clinical outcomes in neurosurgical practice. The DT is a ML model composed of decision rules based on optimal feature cutoff values that recursively divide independent variables into different groups in order to predict an outcome. Hostettler et al. used DT for predicting outcomes in patients with aneurysmal subarachnoid hemorrhage (SAH). The prediction accuracy of the DT models for survival on day 1 was 75.2% for Hostettler et al.,¹⁵ whereas Rau et al. reported that DT achieved an accuracy of 97.9% for the prediction of death in patients with traumatic SAH.²¹

NB, k-NN, and ANN are the algorithms used in ML for predicting classification. Hale et al. studied the prediction of types of meningioma using several ML algorithms, reporting that ANN had the highest performance for predicting meningioma grade (AUC = 0.8895) compared with other algorithms.¹⁴ ANNs have been adopted widely in clinical medicine; however, their use in such settings is subject to translation. Rughani et al. demonstrated that ANNs had significantly higher performance in predicting survival following traumatic brain injury compared with regression models.²² Recently, Hale et al. used ANN to predict 6-month outcomes for pediatric head injury. The results showed profound accuracy (AUC = 0.9462 ± 0.0422).¹³ Moreover, Shi et al. used an ANN for the prediction of in-hospital mortality after traumatic

brain injury surgery. The ANN model achieved high accuracy in 95.15% of cases and a better AUC in 89.14% of cases.²⁶ Conversely, in the present study we found that NB was an effective ML algorithm for predicting SSI, which achieved a good AUC at 78% and good accuracy at 88.5%. The results were likely affected by imbalances between the prevalence of SSI and the lack of SSI. Moreover, this study is the first to harness the utility of ML to predict SSI, meaning that continued study is needed in the future.

Finally, certain limitations in the present study should be acknowledged. Firstly, its retrospective design may have led to bias and an inability to control for confounding factors. Secondly, the imbalance of outcomes was probably the reason why performance failed to reach an excellent level. However, a future aim is to conduct a prospective study to evaluate ML performance for the increase in SSI prevalence in order to correct the imbalance problem.

Conclusions

In summary, in this study we found that NB algorithms have potential as a tool for predicting SSI after a neurosurgical operation with reasonable accuracy, meaning that they could be applied in effectively predicting serious complications. Therefore, close monitoring and allocation of treatment strategies can be informed by ML predictions in general practice.

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Disclosures

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Author Contributions

Conception and design: Tunthanathip. Acquisition of data: Tunthanathip, Taweksomboonyat. Analysis and interpretation of data: Tunthanathip. Drafting the article: Tunthanathip, Sakarunchai,

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