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Predicting central line-associated bloodstream infections and mortality using supervised machine learning

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ABSTRACT

Purpose: The purpose of this study was to compare machine learning techniques for predicting central line-associated bloodstream infection (CLABSI).
Materials and methods: The Multiparameter Intelligent Monitoring in Intensive Care III database was queried for all ICU admissions. The variables included six different severities of illness scores calculated on the first day of ICU admission with their components and comorbidities. The outcomes of interest were in-hospital mortality, central line placement, and CLABSI. Predictive models were created for these outcomes using classifiers with different algorithms: logistic regression, gradient boosted trees, and deep learning.
Results: There were 57,786 total hospital admissions and the mortality rate was 10.1%. There were 38.4% patients with a central line and the rate of CLABSI was 1.5%. The classifiers using deep learning performed with the highest AUC for mortality, 0.885 ± 0.010 ($p < 0.01$) and central line placement, 0.816 ± 0.006 ($p < 0.01$). The classifier using logistic regression for predicting CLABSI performed with an AUC of 0.722 ± 0.048 ($p < 0.01$).
Conclusions: This study demonstrates models for identifying patients who will develop CLABSI. Early identification of these patients has implications for quality, cost, and outcome improvements.

1. Introduction

In the 1990s, it was reported that nosocomial bloodstream infections in the intensive care unit (ICU) had an attributable mortality rate of 35% and were associated with doubling the ICU length of stay [1]. The early 2000s saw many randomized controlled trials focused on preventing central line-associated bloodstream infections (CLABSI) and a 50% decrease in CLABSIs was seen between 2008 and 2014 [2]. Beginning in 2015, the Centers for Medicare and Medicaid Services has been reducing payments to hospitals performing the poorly on hospital-acquired infections [3]. Despite this, an estimated 30,100 CLABSIs still occur in the US each year [2].

Most outcomes in medicine are determined by a large number of variables and classifying these outcomes can be highly complex. Conventional statistical approaches to creating predictive models attempt to use simple algorithms to solve complex problems. For example, conventional statistical models for predicting suicide attempts have been created for over 50 years and have never progressed beyond predictions that are near chance [4]. However, more modern predictive models created using machine learning have proved to be highly accurate [5].

Machine learning refers to a field of artificial intelligence in computer science that allows computers to "learn" without explicitly being programmed [6]. The two main types of machine learning are supervised and unsupervised. Supervised refers to using a training set of data to produce a function that can be used to predict a labeled outcome. Unsupervised machine learning infers a function from unlabeled data and describes a hidden structure. Applications of supervised machine learning have shown to be highly-accurate for various predictions including outcomes in surgery and burn wound healing [7-9]. Applying machine learning concepts to the ICU has also proven useful for discerning clinically relevant vital sign alarms and predicting clinical deterioration [10,11].

The purpose of this study was to use supervised machine learning to predict central line placement, central line-associated bloodstream infections, and mortality in patients admitted to the intensive care unit. It was hypothesized that predictive models could be developed for

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these outcomes using conventional severity of illness scores and comorbidities. This would allow for additional comparisons to be made of different machine learning algorithms across a range of related outcomes.

2. Materials and methods

2.1. Datasource

The Multiparameter Intelligent Monitoring in Intensive Care III (MIMIC-III) database contains the medical records of 46,520 admissions at Beth Israel Deaconess Medical Center from 2001 to 2012. The database contains detailed information on patient stays including International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) codes, laboratory data, vital signs, medication administrations and mortality data from the Social Security Death Index (SSDI) [12]. The database also provides severity of illness scores for the first day of each ICU admission.

2.2. Variable selection

For this study, the MIMIC-III database was queried for all hospital admissions. Six different severity of illness scores were calculated on the first day of the first ICU admission for each hospital admission. The individual components of each score were also obtained. The severity of illness scores were: Oxford Acute Severity of Illness Score (OASIS), Sequential Organ Failure Assessment (SOFA), Simplified Acute Physiology Score (SAPS), Simplified Acute Physiology Score II (SAPS II), Acute Physiology Score III (APS III), and Logistic Organ Dysfunction Score (LODS). The database was also queried for thirty Elixhauser comorbidities for each patient. Patients who had antibiotics ordered during the first day of ICU admission were identified. Patients who had a central venous catheter placed during the admission were identified by ICD-9 procedure code (38.93, 38.95, 38.97). Additional patients with central venous access present during the admission were identified by the presence of documented events such as line dressing change or medication administration through the line. The patients with a CLABSI were determined by the presence of ICD-9 diagnosis codes 999.31 and 999.32 associated with the hospital admission.

2.3. Data modeling

The outcomes of interest were death during the current admission, central line placement, and CLABSI. Patients were excluded from the analysis of CLABSI if they did not have a central line placed during the admission. Three different machine learning classifiers using different algorithms were created for each outcome. The different algorithms used were: logistic regression, gradient boosted trees, and deep learning. Gradient boosting sequentially applies weak classification algorithms and creates a series of decision trees. This results in an ensemble of classification tree models that predict results through gradually improved estimations [13]. The deep learning algorithm uses a multi-layered artificial neural network to extract simple features and applies advanced gradient descents [14]. This algorithm mimics the communication and interpretation of information that occurs in biological nervous systems [15].

Cross validation was performed by dividing the datasets into ten subsets. One of the subsets was retained as the testing subset and the remaining nine subsets were used to train the learning classifiers. This process was repeated ten times using each one of the subsets as the testing subsets once. The means were calculated for receiver operating characteristic (ROC) curves and variable importance was quantified. Categorical variables were compared using a Chi-squared test and continuous variables were compared using Student's *t*-test. The classifiers were compared with an ANOVA test on the mean results of performance for each outcome and F-statistics were calculated with significance set at 0.05 [16]. Statistical analysis was performed using SPSS Statistics

Table 1
Categorical variables used by the machine learning classifiers presented as number with (percentage). CLABSI = central line-associated bloodstream infection, OASIS = Oxford Acute Severity of Illness Score, SOFA = Sequential Organ Failure Assessment, SAPS = Simplified Acute Physiology Score, SAPS II = Simplified Acute Physiology Score II, APS III = Acute Physiology Score III, LODS = Logistic Organ Dysfunction Score.

	Total	Mortality	p	Central line	p	CLABSI	p
Total	57,786 (100.0)	5813 (10.1)	–	22,201 (38.4)	–	322 (1.5)	–
Antibiotics on admission	16,263 (28.1)	2205 (13.6)	<0.01	8835 (54.3)	<0.01	171 (1.9)	<0.01
Congestive heart failure	8073 (14.0)	1484 (18.4)	<0.01	4566 (56.6)	<0.01	91 (2.0)	<0.01
Cardiac arrhythmias	8917 (15.4)	1714 (19.2)	<0.01	4672 (52.4)	<0.01	96 (2.1)	<0.01
Valvular disease	2936 (5.1)	445 (15.2)	<0.01	1476 (50.3)	<0.01	23 (1.6)	0.72
Pulmonary circulation	1925 (3.3)	333 (17.3)	<0.01	1107 (57.5)	<0.01	33 (3.0)	<0.01
Peripheral vascular disease	4290 (7.4)	536 (12.5)	<0.01	2244 (52.3)	<0.01	42 (1.9)	0.08
Hypertension	5965 (10.3)	839 (14.1)	<0.01	3326 (55.8)	<0.01	86 (2.6)	<0.01
Paralysis	1462 (2.5)	156 (10.7)	0.43	846 (57.9)	<0.01	14 (1.7)	0.61
Other neurological conditions	4014 (6.9)	511 (12.7)	<0.01	2229 (55.5)	<0.01	55 (2.5)	<0.01
COPD	9471 (16.4)	1122 (11.8)	<0.01	4409 (46.6)	<0.01	63 (1.4)	0.89
Diabetes, uncomplicated	10,003 (17.3)	1165 (11.6)	<0.01	4619 (46.2)	<0.01	72 (1.6)	0.49
Diabetes, complicated	3285 (5.7)	335 (10.2)	0.79	1808 (55.0)	<0.01	43 (2.4)	<0.01
Hypothyroidism	5122 (8.9)	590 (11.5)	<0.01	2414 (47.1)	<0.01	51 (2.1)	<0.01
Renal failure	7258 (12.6)	1074 (14.8)	<0.01	4058 (55.9)	<0.01	99 (2.4)	<0.01
Liver disease	3298 (5.7)	536 (16.3)	<0.01	1905 (57.8)	<0.01	37 (1.9)	0.06
Peptic ulcer disease	44 (0.1)	4 (9.1)	0.83	19 (43.2)	0.52	1 (5.3)	0.16
AIDS	267 (0.5)	22 (8.2)	0.32	118 (44.2)	0.05	6 (5.1)	<0.01
Lymphoma	688 (1.2)	141 (20.5)	<0.01	381 (55.4)	<0.01	12 (3.1)	<0.01
Metastatic cancer	2113 (3.7)	523 (24.8)	<0.01	1047 (49.6)	<0.01	15 (1.4)	0.96
Solid tumor	1343 (2.3)	211 (15.7)	<0.01	666 (49.6)	<0.01	5 (0.8)	0.13
Rheumatoid arthritis	1428 (2.5)	161 (11.3)	0.12	765 (53.6)	<0.01	14 (1.8)	0.37
Coagulopathy	5495 (9.5)	1254 (22.8)	<0.01	3646 (66.4)	<0.01	93 (2.6)	<0.01
Obesity	2618 (4.5)	191 (7.3)	<0.01	1550 (59.2)	<0.01	28 (1.8)	0.22
Weight loss	1841 (3.2)	306 (16.6)	<0.01	1361 (73.9)	<0.01	44 (3.2)	<0.01
Fluid and electrolyte disorders	14,744 (25.5)	2581 (17.5)	<0.01	8511 (57.7)	<0.01	180 (2.1)	<0.01
Blood loss anemia	1037 (1.8)	101 (9.7)	0.73	528 (50.9)	<0.01	11 (2.1)	0.22
Deficiency anemia	9409 (16.3)	889 (9.4)	0.03	5215 (55.4)	<0.01	117 (2.2)	<0.01
Alcohol abuse	3387 (5.9)	365 (10.8)	0.15	1481 (43.7)	<0.01	32 (2.2)	0.02
Drug abuse	1612 (2.8)	105 (6.5)	<0.01	740 (45.9)	<0.01	19 (2.6)	0.01
Psychosis	2038 (3.5)	144 (7.1)	<0.01	830 (40.7)	0.03	20 (2.4)	0.02
Depression	4530 (7.8)	321 (7.1)	<0.01	2141 (47.3)	<0.01	41 (1.9)	0.06

Table 2
Severity of injury scores with their components used by the machine learning classifiers presented as mean with (standard deviation). CLABSI = central line-associated bloodstream infection, OASIS = Oxford Acute Severity of Illness Score, SOFA = Sequential Organ Failure Assessment, SAPS = Simplified Acute Physiology Score, SAPS II = Simplified Acute Physiology Score II, APS III = Acute Physiology Score III, LODS = Logistic Organ Dysfunction Score.

	Overall	Mortality	p	Central line	p	CLABSI	p
OASIS	29.63 ± 9.80	39.35 ± 9.61	<0.01	33.49 ± 9.05	<0.01	34.02 ± 9.82	0.30
Age	4.95 ± 2.85	6.40 ± 2.17	<0.01	5.61 ± 2.34	<0.01	5.40 ± 2.10	0.10
Pre ICU LOS	3.37 ± 1.92	3.68 ± 1.88	<0.01	3.26 ± 2.00	<0.01	3.44 ± 1.90	0.11
GCS	1.59 ± 2.53	2.35 ± 3.36	<0.01	1.80 ± 2.75	<0.01	2.04 ± 2.65	0.11
Heart rate	2.45 ± 2.23	2.86 ± 2.25	<0.01	2.42 ± 2.13	0.02	2.74 ± 2.04	<0.01
Mean BP	1.53 ± 1.26	2.07 ± 1.23	<0.01	1.75 ± 1.24	<0.01	1.84 ± 1.23	0.21
Respiratory rate	2.42 ± 2.64	3.27 ± 2.96	<0.01	2.71 ± 2.77	<0.01	3.10 ± 2.87	0.01
Temperature	2.71 ± 1.06	2.99 ± 1.12	<0.01	2.79 ± 1.07	<0.01	2.82 ± 1.13	0.66
Urine output	3.52 ± 3.66	5.34 ± 3.89	<0.01	3.68 ± 3.66	<0.01	4.32 ± 4.03	<0.01
Elective surgery	5.35 ± 1.86	5.84 ± 0.97	<0.01	5.30 ± 1.93	<0.01	5.78 ± 1.14	<0.01
SOFA	3.89 ± 3.11	6.78 ± 4.05	<0.01	5.30 ± 3.37	<0.01	6.02 ± 3.55	<0.01
Respiration	1.68 ± 1.35	1.99 ± 1.49	<0.01	1.82 ± 1.43	<0.01	1.98 ± 1.42	0.21
Coagulation	0.43 ± 0.79	0.76 ± 1.09	<0.01	0.58 ± 0.90	<0.01	0.81 ± 1.19	<0.01
Liver	0.72 ± 1.11	0.89 ± 1.25	<0.01	0.72 ± 1.10	0.75	0.65 ± 1.02	0.36
Cardiovascular	1.22 ± 1.06	1.86 ± 1.43	<0.01	1.53 ± 1.26	<0.01	1.60 ± 1.33	0.32
CNS	0.61 ± 1.01	0.93 ± 1.33	<0.01	0.70 ± 1.10	<0.01	0.84 ± 1.11	0.03
Renal	1.04 ± 1.41	1.57 ± 1.49	<0.01	1.18 ± 1.42	<0.01	1.60 ± 1.56	<0.01
SAPS	16.36 ± 6.30	22.35 ± 5.88	<0.01	19.27 ± 5.43	<0.01	19.77 ± 5.48	0.09
Age	2.06 ± 1.56	2.86 ± 1.32	<0.01	2.35 ± 1.43	<0.01	2.05 ± 1.43	<0.01
HR	1.84 ± 1.07	2.01 ± 1.08	<0.01	1.77 ± 1.06	<0.01	1.71 ± 1.01	0.31
Systolic BP	1.34 ± 1.24	1.78 ± 1.33	<0.01	1.43 ± 1.24	<0.01	1.39 ± 1.20	0.63
Respiratory	1.30 ± 1.00	1.51 ± 1.12	<0.01	1.40 ± 1.03	<0.01	1.53 ± 1.05	0.03
Temperature	0.58 ± 0.73	0.85 ± 0.86	<0.01	0.69 ± 0.81	<0.01	0.77 ± 0.88	0.09
Urine output	0.76 ± 1.34	1.23 ± 1.57	<0.01	0.75 ± 1.32	0.51	1.08 ± 1.47	<0.01
BUN	1.62 ± 1.08	2.19 ± 1.24	<0.01	1.83 ± 1.17	<0.01	2.10 ± 1.24	<0.01
Hematocrit	1.21 ± 1.14	1.27 ± 1.16	<0.01	1.40 ± 1.14	<0.01	1.47 ± 1.14	0.27
Glucose	4.00 ± 0.07	4.00 ± 0.04	0.02	4.00 ± 0.04	<0.01	4.00 ± 0.00	0.77
Potassium	0.69 ± 1.07	0.84 ± 1.17	<0.01	0.79 ± 1.12	<0.01	0.79 ± 1.16	0.91
Sodium	0.16 ± 0.57	0.32 ± 0.76	<0.01	0.20 ± 0.63	<0.01	0.16 ± 0.56	0.23
Bicarbonate	0.38 ± 0.60	0.64 ± 0.71	<0.01	0.46 ± 0.63	<0.01	0.51 ± 0.63	0.17
GCS	0.28 ± 0.82	0.59 ± 1.18	<0.01	0.36 ± 0.92	<0.01	0.41 ± 0.91	0.31
SAPS II	32.40 ± 14.87	49.67 ± 16.09	<0.01	38.97 ± 14.43	<0.01	39.43 ± 15.22	0.57
Age	9.75 ± 6.49	13.16 ± 5.18	<0.01	11.13 ± 5.66	<0.01	10.21 ± 5.50	<0.01
HR	2.28 ± 2.21	2.76 ± 2.70	<0.01	2.11 ± 2.12	<0.01	1.87 ± 1.84	0.04
Systolic BP	4.13 ± 3.45	6.08 ± 4.44	<0.01	4.76 ± 3.57	<0.01	4.58 ± 3.45	0.35
Temperature	0.00 ± 0.05	0.00 ± 0.12	<0.01	0.00 ± 0.06	0.40	0.00 ± 0.00	0.74
PAO2 FIO2	7.45 ± 1.79	8.10 ± 2.01	<0.01	7.71 ± 1.86	<0.01	8.02 ± 1.90	0.08
Urine output	2.18 ± 3.90	3.91 ± 4.62	<0.01	2.26 ± 3.90	<0.01	3.06 ± 4.44	<0.01
BUN	2.13 ± 3.11	3.73 ± 3.41	<0.01	2.72 ± 3.32	<0.01	3.43 ± 3.35	<0.01
WBC	0.50 ± 1.37	0.96 ± 2.03	<0.01	0.68 ± 1.66	<0.01	1.21 ± 2.88	<0.01
Potassium	1.03 ± 1.42	1.20 ± 1.47	<0.01	1.16 ± 1.46	<0.01	1.02 ± 1.42	0.07
Sodium	0.20 ± 0.70	0.37 ± 0.92	<0.01	0.25 ± 0.77	<0.01	0.20 ± 0.69	0.28
Bicarbonate	0.75 ± 1.48	1.62 ± 1.96	<0.01	1.01 ± 1.66	<0.01	1.05 ± 1.65	0.72
Bilirubin	1.08 ± 2.66	1.35 ± 3.04	<0.01	0.96 ± 2.55	<0.01	0.77 ± 2.29	0.26
GCS	1.94 ± 5.17	3.89 ± 7.55	<0.01	2.41 ± 5.86	<0.01	2.43 ± 5.25	0.96
Comorbidity	0.86 ± 2.91	1.87 ± 3.94	<0.01	1.14 ± 3.33	<0.01	1.80 ± 4.08	<0.01
Admission type	5.68 ± 2.02	6.18 ± 1.22	<0.01	5.71 ± 2.14	<0.01	6.10 ± 1.41	<0.01
APS III	40.00 ± 20.34	62.66 ± 26.06	<0.01	48.57 ± 21.23	<0.01	54.81 ± 21.11	<0.01
HR	4.35 ± 5.34	4.97 ± 4.90	<0.01	3.97 ± 4.71	<0.01	4.31 ± 4.25	0.19
Mean BP	11.34 ± 5.06	13.56 ± 5.70	<0.01	12.15 ± 5.13	<0.01	12.65 ± 5.25	0.08
Temperature	1.22 ± 2.50	2.41 ± 4.21	<0.01	1.43 ± 2.85	<0.01	1.17 ± 2.29	0.12
Respiratory rate	5.36 ± 3.70	5.59 ± 3.97	<0.01	5.20 ± 3.82	<0.01	6.33 ± 3.52	<0.01
PAO2/P(A-a)O2	0.63 ± 2.13	0.93 ± 2.65	<0.01	0.57 ± 2.06	<0.01	0.97 ± 2.56	0.06
Hematocrit	2.76 ± 0.81	2.88 ± 0.58	<0.01	2.90 ± 0.55	<0.01	2.91 ± 0.52	0.71
WBC	0.61 ± 1.96	1.35 ± 3.12	<0.01	0.92 ± 2.51	<0.01	1.96 ± 4.54	<0.01
Creatinine	1.90 ± 3.00	3.56 ± 3.81	<0.01	2.57 ± 3.31	<0.01	3.48 ± 3.48	<0.01
Urine output	4.64 ± 4.72	6.75 ± 5.14	<0.01	4.77 ± 4.63	<0.01	5.58 ± 5.20	<0.01
BUN	4.74 ± 4.32	7.07 ± 4.06	<0.01	5.58 ± 4.37	<0.01	6.14 ± 4.54	0.02
Sodium	0.58 ± 0.95	0.76 ± 1.09	<0.01	0.70 ± 1.01	<0.01	0.67 ± 0.97	0.67
Albumin	1.45 ± 3.01	2.75 ± 3.99	<0.01	1.95 ± 3.45	<0.01	2.81 ± 3.99	<0.01
Bilirubin	2.09 ± 4.17	2.73 ± 4.97	<0.01	2.05 ± 4.14	0.08	1.72 ± 3.73	0.22
Glucose	1.34 ± 2.18	1.85 ± 2.32	<0.01	1.48 ± 2.18	<0.01	1.41 ± 2.19	0.59
Acid base	3.07 ± 3.35	4.75 ± 4.19	<0.01	3.57 ± 3.61	<0.01	3.66 ± 3.57	0.71
GCS	3.39 ± 9.24	6.93 ± 13.57	<0.01	4.23 ± 10.46	<0.01	4.65 ± 9.99	0.47
LODS	3.58 ± 2.74	6.49 ± 3.47	<0.01	4.81 ± 2.91	<0.01	5.18 ± 2.92	0.02
Neurologic	0.38 ± 1.03	0.77 ± 1.50	<0.01	0.47 ± 1.16	<0.01	0.48 ± 1.06	0.95
Cardiovascular	0.68 ± 0.89	1.31 ± 1.40	<0.01	0.82 ± 0.98	<0.01	0.79 ± 0.86	0.52
Renal	2.11 ± 1.53	3.15 ± 1.67	<0.01	2.40 ± 1.62	<0.01	2.89 ± 1.72	<0.01
Pulmonary	0.48 ± 0.85	0.90 ± 1.13	<0.01	0.78 ± 1.02	<0.01	0.56 ± 0.97	<0.01
Hematologic	0.06 ± 0.29	0.18 ± 0.51	<0.01	0.09 ± 0.39	<0.01	0.29 ± 0.74	<0.01
Hepatic	0.44 ± 0.50	0.59 ± 0.49	<0.01	0.52 ± 0.50	<0.01	0.59 ± 0.49	0.02

version 24 (IBM Corp., Armonk, NY). Data modeling was performed with RapidMiner Studio version 7.4 (RapidMiner, Inc., Boston, MA).

3. Results

There were 57,786 total hospital admissions and 38.4% of patients had a central line. In patients with a central line, the rate of CLABSI was 1.5%. The overall mortality rate was 10.1% while the mortality rate for patients with a central line was 16.2% and patients without a central line had a 6.2% mortality rate ($p < 0.01$). Patients diagnosed with CLABSI had an 18.0% mortality rate versus 16.2% without CLABSI ($p = 0.38$). The categorical variables used by the classifiers for each outcome are shown in Table 1 and the continuous variables are shown in Table 2. Patients on antibiotics at admission had a higher rate of mortality, central line, and CLABSI than the overall rates (Table 1).

3.1. Mortality

Comparison of the classifiers for predicting mortality revealed an F-statistic of 36.09 with p-value <0.01. Fig. 1 shows the ROC plot and Table 3 shows the results of classifier performance for mortality. Deep learning had the highest AUC however logistic regression had the highest accuracy and precision. Deep learning also had the highest negative predictive value while logistic regression had the highest positive predictive value (Table 3). The gradient boosted trees algorithm reported the variables with the highest importance were SAPS II (46.7%), APS III (10.3%), and OASIS (7.8%).

3.2. Central line placement

The classifiers for predicting central line placement had an F-statistic of 28.08 and a p-value of <0.01. Table 4 shows the results of classifier performance for predicting central line and Fig. 2 shows the ROC comparison. Deep learning again performed with the highest AUC. Logistic regression had the highest specificity and positive predictive value. Gradient boosted trees had the highest sensitivity and negative predictive value (Table 4). The variables with highest importance for the gradient boosted trees algorithm predicting central line were: SAPS (17.7%), SOFA (12.0%), and APS III (10.7%).

3.3. CLABSI

Comparing the classifiers for predicting CLABSI in patients with a central line revealed an F-statistic of 22.25 and a p-value of <0.01. Table 5 contains the results of classifier performance for predicting CLABSI and Fig. 3 shows the ROC comparison. Logistic regression had the highest AUC for predicting CLABSI (Table 5). However, logistic regression had a 0% sensitivity and negative predictive value. Gradient boosted trees had the highest accuracy, precision, sensitivity, and negative predictive value (Table 5). The variables with the highest importance for predicting CLABSI with the gradient boosted trees algorithm were: APS III respiratory rate (6.2%), OASIS pre ICU length of stay (LOS) (3.9%), and LODS (3.3%). The OASIS respiratory rate was the 7th most important variable 2.3%.

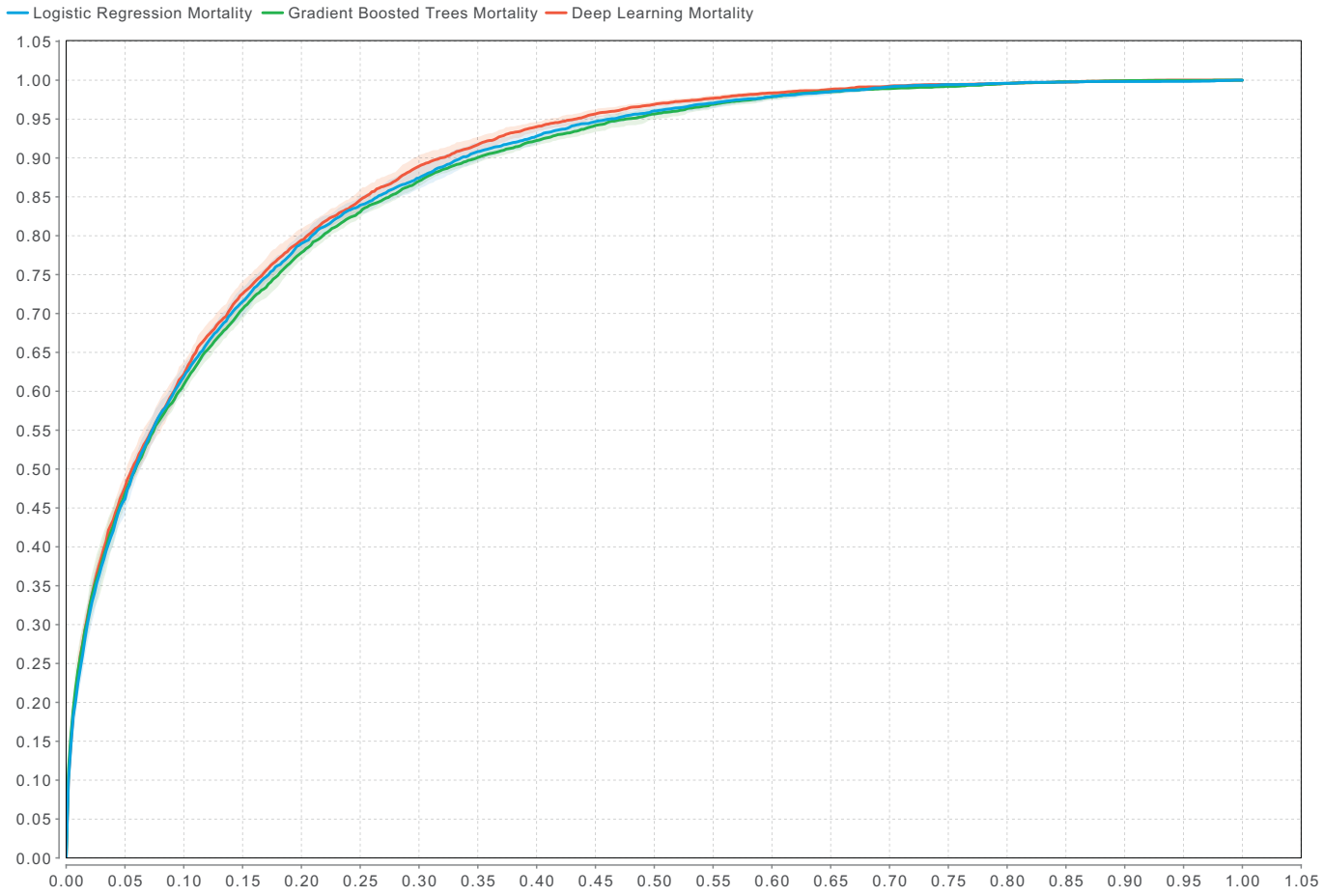

Fig. 1. Mortality classifier performance receiver operating characteristic curve of 10 fold cross validation. Shaded portion represents the range while solid line represents the mean. The x-axis is the false positive rate and the y-axis is the true positive rate.

Table 3
Results of mortality classifier performance presented as mean with standard deviation. AUC = area under the curve, PPV = positive predictive value, NPV = negative predictive value.

	Logistic regression	Gradient boosted trees	Deep learning	F	p
AUC	0.878 ± 0.005	0.874 ± 0.005	0.885 ± 0.010	6.40	<0.01
Accuracy	91.3% ± 0.3%	89.4% ± 0.5%	89.7% ± 0.7%	42.88	<0.01
Precision	65.2% ± 3.9%	47.6% ± 2.2%	49.3% ± 3.2%	105.82	<0.01
Sensitivity	28.5% ± 2.0%	51.5% ± 2.0%	53.3% ± 4.1%	222.95	<0.01
Specificity	98.3% ± 0.2%	93.7% ± 0.5%	93.8% ± 1.0%	166.78	<0.01
PPV	65.2% ± 3.9%	47.6% ± 2.2%	49.3% ± 3.2%	105.82	<0.01
NPV	92.5% ± 0.2%	94.5% ± 0.2%	94.7% ± 0.4%	183.00	<0.01

Table 4
Results of central line classifier performance presented as mean with standard deviation. AUC = area under the curve, PPV = positive predictive value, NPV = negative predictive value.

	Logistic regression	Gradient boosted trees	Deep learning	F	p
AUC	0.811 ± 0.005	0.811 ± 0.008	0.816 ± 0.006	1.89	0.17
Accuracy	74.1% ± 0.5%	71.5% ± 0.7%	73.3% ± 1.1%	50.17	<0.01
Precision	69.8% ± 0.9%	59.9% ± 0.7%	62.6% ± 1.8%	321.85	<0.01
Sensitivity	57.4% ± 0.7%	78.1% ± 1.4%	76.2% ± 2.7%	350.65	<0.01
Specificity	84.5% ± 0.6%	67.4% ± 0.7%	71.5% ± 3.1%	392.40	<0.01
PPV	69.8% ± 0.9%	59.9% ± 0.7%	62.6% ± 1.8%	321.85	<0.01
NPV	76.1% ± 0.3%	83.1% ± 0.9%	82.8% ± 1.2%	177.51	<0.01

4. Discussion

Incidence of CLABSI has proven difficult to predict and has been associated with increased mortality and poor ICU working environments [17,18]. This study represents a novel use of the MIMIC III database with machine learning to predict the outcome of CLABSI. This database is ideal for this study because the rate of mortality with CLABSI from this database (18%) is identical to the attributable CLABSI mortality rate used by the Agency for Healthcare Research and Quality in their "Tools for Reducing Central Line-Associated Bloodstream Infections" [19]. These tools provide comprehensive checklists and metrics which hospitals can use to reduce CLABSI. This study demonstrates that additional tools can be developed using machine learning to identify patients at risk for CLABSI.

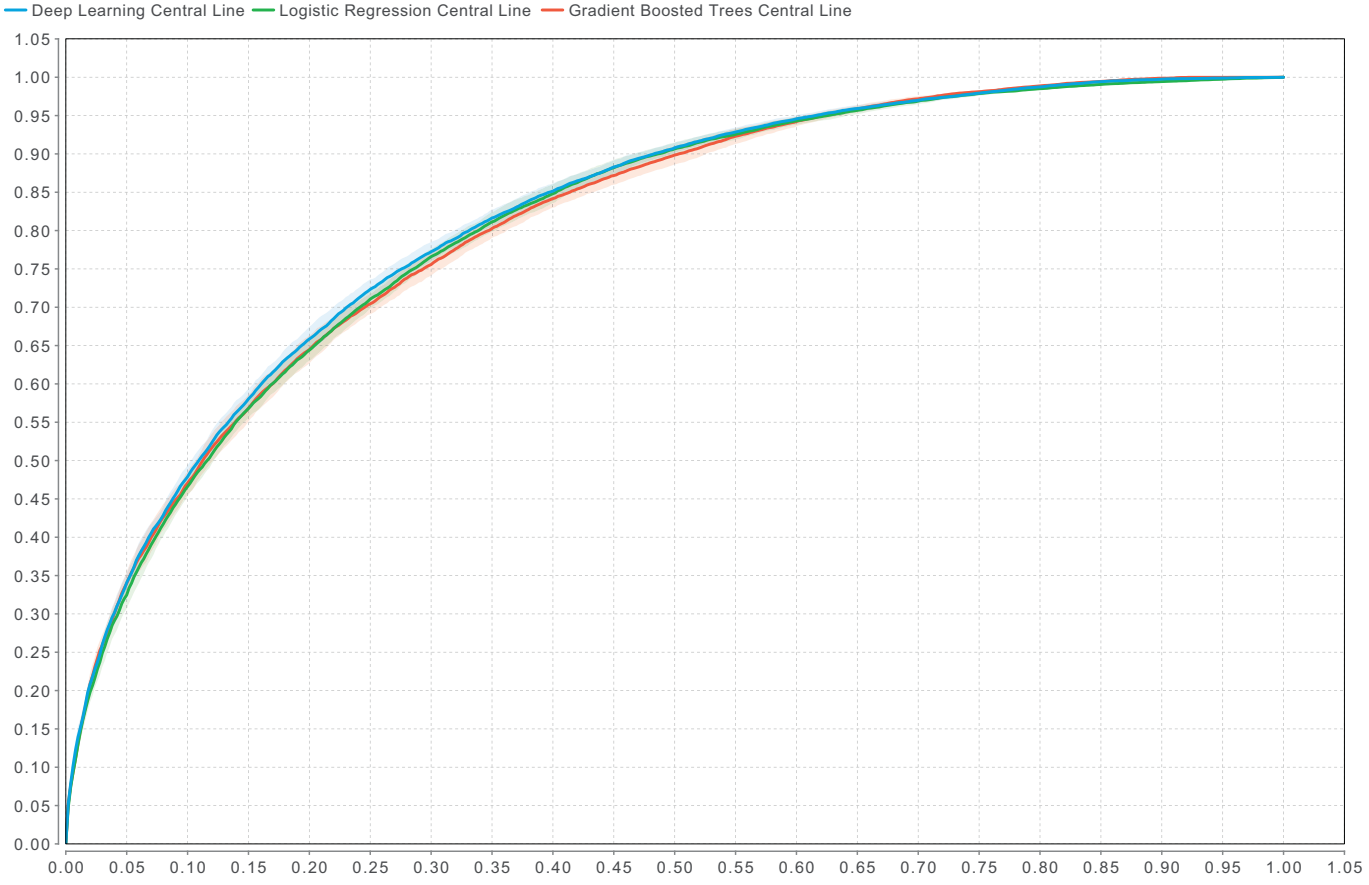

Fig. 2. Central line classifier performance receiver operating characteristic curve of 10 fold cross validation. Shaded portion represents the range while solid line represents the mean. The x-axis is the false positive rate and the y-axis is the true positive rate.

Table 5
Results of central-line associated bloodstream infection classifier performance presented as mean with standard deviation. AUC = area under the curve, PPV = positive predictive value, NPV = negative predictive value.

	Logistic regression	Gradient boosted trees	Deep learning	F	p
AUC	0.722 ± 0.048	0.710 ± 0.040	0.642 ± 0.049	8.13	<0.01
Accuracy	98.6% ± 0.0%	97.6% ± 0.3%	97.3% ± 0.7%	43.83	<0.01
Precision	0.0% ± 0.0%	7.1% ± 4.9%	4.3% ± 4.0%	–	–
Sensitivity	0.0% ± 0.0%	5.3% ± 4.9%	4.0% ± 3.7%	7.86	<0.01
Specificity	100.0% ± 0.0%	98.9% ± 0.4%	98.7% ± 0.7%	48.40	<0.01
PPV	0.0% ± 0.0%	7.1% ± 4.9%	4.3% ± 4.0%	–	–
NPV	98.6% ± 0.0%	98.6% ± 0.1%	98.6% ± 0.1%	4.99	0.01

In the late 1990s, Dybowski et al. published a report of using artificial intelligence with ICU data to predict mortality with an AUC of 0.86 [20]. This performance is similar to the best reported mortality predictor of 0.88 that used a "Super Learner" method of parameter optimization [21]. No parameter optimization was performed in this study in order to demonstrate the simplicity of applying machine learning techniques in the ICU. Despite this, deep learning outperformed logistic regression for predicting mortality (AUC 0.885 versus 0.878, $p < 0.01$, Table 3) and line placement (AUC 0.818 versus 0.811, $p < 0.01$, Table 4). This study adds to the previous reports of using machine learning in the ICU by demonstrating strong predictive performance for CLABSI by the gradient boosted trees algorithm with an AUC of 0.710 with a higher sensitivity and positive predictive value than logistic regression ($p < 0.01$, Table 5). The low values for sensitivity and specificity for the logistic regression classifier suggests that parameter optimization could improve this classifiers performance. Kim et al. showed that a decision trees algorithm outperformed (AUC 0.89) other data mining techniques and APACHE III (AUC 0.87) for predicting mortality in the ICU [22]. An advantage of using a decision trees based algorithms is that the variable importance can be determined and potentially applied clinically [23].

The SAPS II score was by far the most important variable for predicting mortality (46.7%) with the gradient boosted trees algorithm. The original validation sample of SAPS II reported in the early 1990s had a lower AUC (0.86) than was obtained by the best performing classifier in this study (0.885, Table 3) [24]. The APS III score was also an important variable for predicting mortality in this study (10.3%). This scoring system was first developed in the 1980s but the version used in the MIMIC III database was recently recalibrated for mortality using the MIMIC II database [25]. The APS III respiratory rate was the most important variable for predicting CLABSI (6.2%). The overall mean APS III respiratory rate score was 5.36 ± 3.70 while patients with a CLABSI had a higher mean score of 6.33 ± 3.52 ($p < 0.01$, Table 2). Similarly, the overall OASIS respiratory rate score 2.42 ± 2.64 was lower than in patients with CLABSI 3.10 ± 2.87 ($p = 0.01$, Table 2). Respiratory rate was the only sepsis criteria that appeared among the top importance for the gradient boosted trees classifier. This could be reflective of the fact that respiratory infections are the most common overall source of sepsis and these patients are at higher risk for developing respiratory organ dysfunction and subsequent ICU admission [26]. Limitations of this study include using ICD-9 codes to identify patients with CLABSI. This introduces the possible confounder of coding error. Other limitations of this study include those of using a retrospectively collected database such information bias due to measurement error and misclassification.

Despite these limitations, this study demonstrates the ability of using machine learning to easily design a predictive model for CLABSI using readily available patient variables. Incorporating such predictive models in ICU protocols has the potential to further reduce hospital acquired infections by early identification of patients at risk for these preventable complications. Areas of further research includes creating an

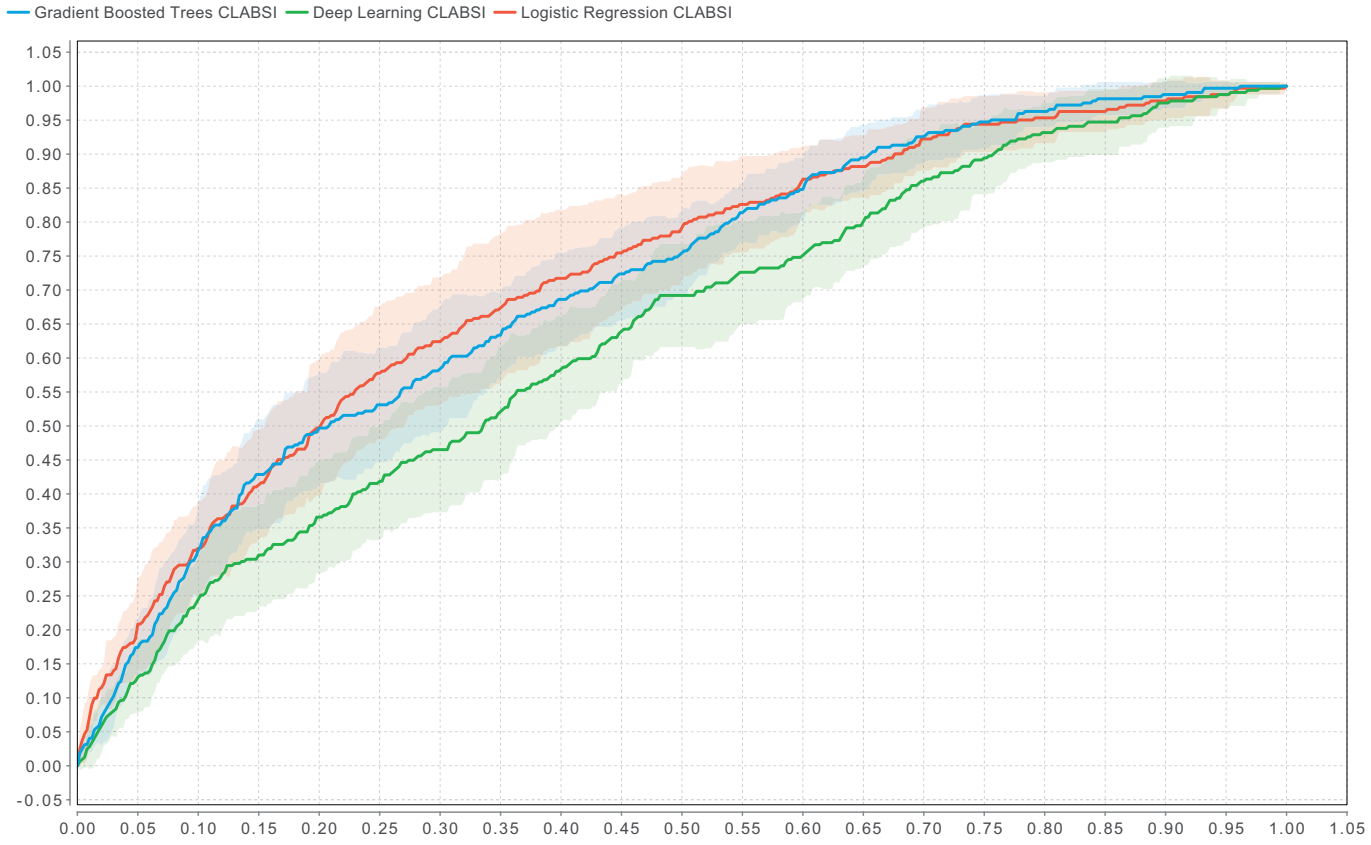

Fig. 3. Central-line associated bloodstream infection classifier performance receiver operating characteristic curve of 10 fold cross validation. Shaded portion represents the range while solid line represents the mean. The x-axis is the false positive rate and the y-axis is the true positive rate.

adaptive algorithm that can be applied to patients as they progress through the ICU stay. Such a model should be able to more precisely predict a CLABSI event before it occurs.

5. Conclusions

This study demonstrates the utility of supervised artificial intelligence to accurately predict central line placement, CLABSI, and mortality in patients admitted to the ICU. Comparing different machine learning algorithms across a range of related outcomes demonstrates advantages of certain algorithms over others. Specifically, gradient boosted trees allows for identifying the most important variables and can help guide further efforts to prevent infections. Utilizing the predictive models in this study has implications for outcome, quality, and cost improvements.

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