Predicting Survival in Patients from In-hospital Resuscitation: Machine Learning VS Logistic Regression

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In-Hospital Cardiac Arrest (IHCA)

Background: IHCA

- Survival rates were poor in patients following in-Hospital Cardiac Arrest (IHCA) (7-24%, Taiwan 18%)
- The classification patterns of recovery can help health care providers and other decision makers (patients and their families), select treatment strategies that take into account costs and potential benefits.
- Need for investigation of prognostic factors from IHCA: Utstein Style definitions for reporting templates and guidelines.

George AL, et al. Am J Med 1989; 87:28-34.
Shih CL & Lu TC. Resuscitation 2007;72:394-403.

Utstein Abbey

- Utstein is synonymous with reporting guidelines for resuscitation.
- The first conference held at Utstein Abbey in 1990, and resulted in guidelines for uniform reporting data from out-of-hospital cardiac arrest (OHCA).
- The first In-Hospital "Utstein Style" were published in 1997 and updated in 2004.

Resuscitation 2005;64:5–6

Background of WRSIR

台大醫院 NTUH 急診醫學部

- Since 2003, National Taiwan University Hospital (NTUH) and the other hospitals around the country, has promoted a pilot study of **Web-Based Registry System on In-hospital Resuscitation** (WRSIR).
- A prospective, web-based, multi-site, and Utstein-based reporting system sponsored by the Department of Health Taiwan.
- Allowing each participating hospital to report each event and outcome of IHCA
- An in-hospital resuscitation task force committee was established and tracks each event to ensure the completeness of registry data every week.

Resuscitation (2007) 72, 394—403

RESUSCITATION

www.elsevier.com/locate/resuscitation

CLINICAL PAPER

A web-based Utstein style registry system of in-hospital cardiopulmonary resuscitation in Taiwan☆

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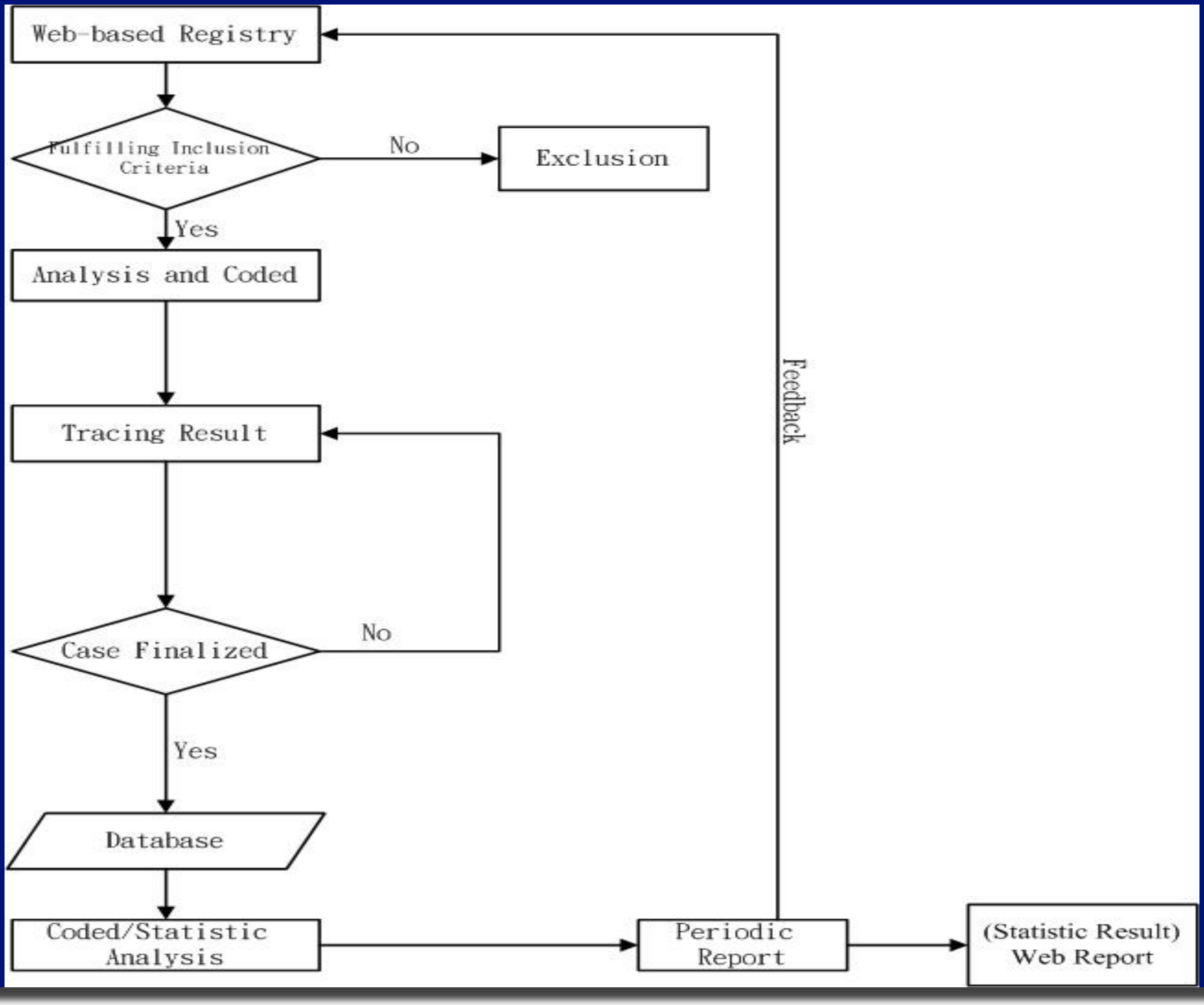
Dataflow of Web-Based Registry System On In-Hospital Resuscitation (WRSIR)



Implementation of the Web-Based Registry

Study Purpose

- To compare performances of machine learning and logistic regression in survival prediction from in-hospital resuscitation
- To assess prognostic determinants selected from different strategies.

Study Methods
-Hospital Setting

- NTUH is a 2,400-bed university-affiliated tertiary medical center serving approximately 2,000 inpatients, 7,000 outpatients, and 300 emergency visits daily. The center has a 227-bed intensive care unit (ICU) and approximately 40 emergency department (ED) observatory units.
- The cardiac arrest team (CAT) consists of a senior medical resident (the team leader), several junior residents, a respiratory therapist, a head nurse, and several registered nurses from the ICU.

Study Methods
-Data collection

- A specially trained staff of the task force logged on the website and entered information into the database. The information was gathered from a standardized data sheet recorded by the leader of CAT.
- Five major defined categories of variables are (1) facility data, (2) patient demographic data, (3) event data, (4) intervention data, and (5) outcome data.

Study Methods
-Case inclusion and exclusion criteria

- A prospective observational study from 1 Jan 2005 to 31 Dec 2007.
- All adult ($\geqq$ 18 years of age) patients, visitors, employees, and staff within NTUH (including areas of out-patients clinic and emergency department) who experienced a resuscitation effort after cardiac arrest were eligible for inclusion.
- Patients who presented as out of hospital cardiac arrest (OHCA) or those who not resuscitated were excluded from the study.
- Those experienced two or more CPR during each admission were considered as one CPR events.

Study Methods
-Statistical and Machine learning approaches

- Logistic Regression
- Machine learning methods
  - -Decision Tree
  - -k Nearest Neighbors (kNN)
  - -Artificial Neural Networks (ANN)

Preliminary Results
-Patient Characteristics and Outcome measures

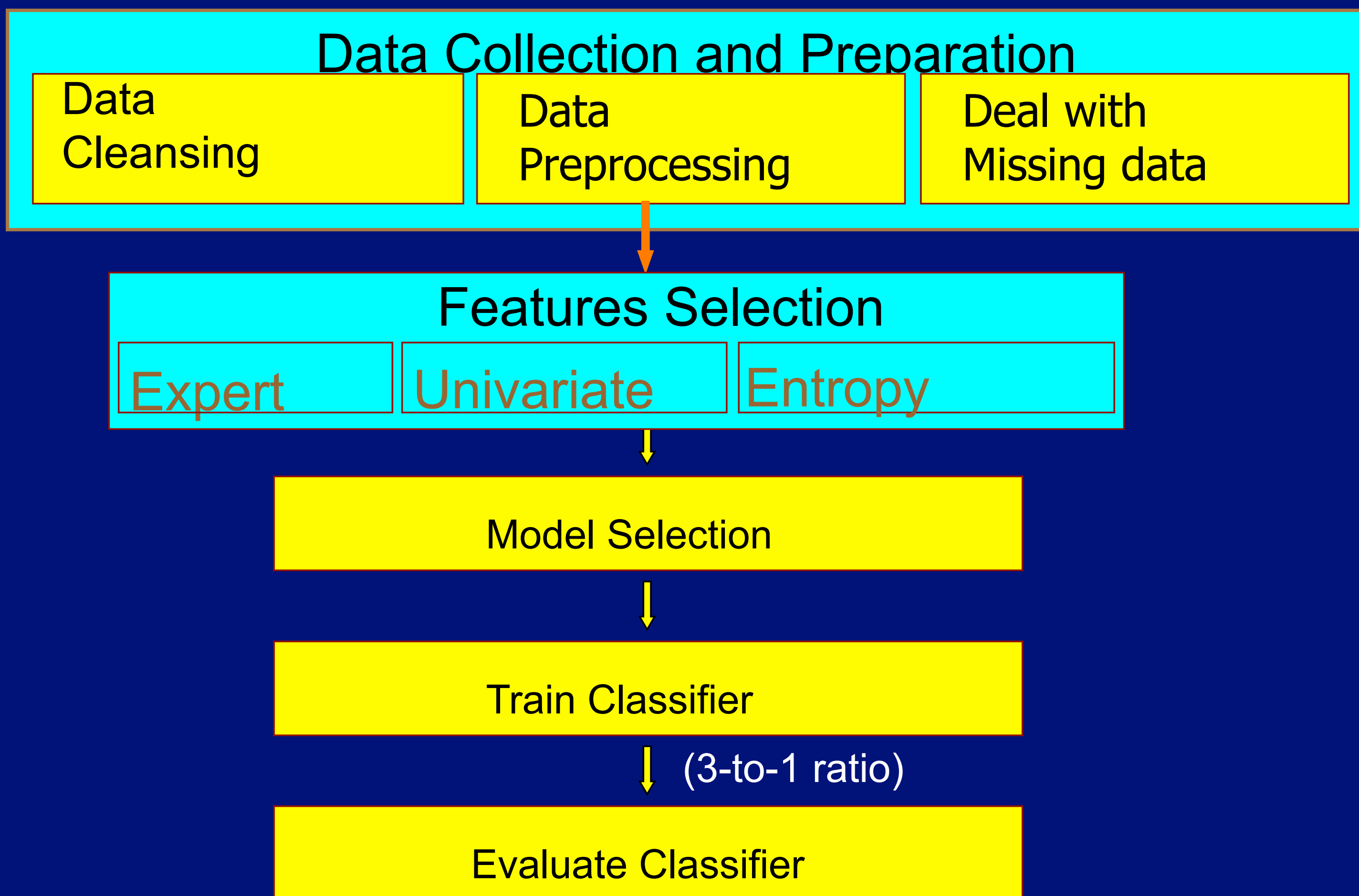
- 1048 adults included. (age 65.5 ± 16.5 years)
  - -797 arrests (76.0%) in hospitalized patients (ward or ICU).
  - -243 (23%) in emergency department.
  - -7 arrest from the out-patient clinic, one from visitor
- **Immediate Outcome**
  - - Returned of spontaneous circulation (ROSC): 688 pts (65.6%)
- **Final Outcome**
  - - Survival to hospital discharge: 174 pts (16.6%)

Time Interval Statistics

Table 5. Time interval characteristics and comparison statistics between cases with ROSC and survival to hospital discharge

	ROSC (N=1048)		P-value	Survival to discharge (N=1048)		P-value
	YES (n=688)	No (n=360)		YES (N=174)	No (N=874)	
Time interval CPR team arrival (minutes) (N=147)						
	(n=100)	(n=47)		(n=29)	(n=118)	
mean (SD)	4 (2)	6(9)	-	4(7)	5(7)	-
median (IQR)	2(1-5)	3(1-7)	0.177	2(1-4)	2(1-5)	0.197
Time interval CPR initiate (minutes)						
mean (SD)	0.51(5)	0.45(4)	-	0.24(1)	0.54(5)	-
median (IQR)	0(0-0)	0(0-0)	0.463	0(0-0)	0(0-0)	0.571
Time interval monitored arrest (minutes)						
mean (SD)	0.57(5)	0.49(4)	-	0.31(1)	0.59(5)	-
median (IQR)	0(0-0)	0(0-0)	0.563	0(0-0)	0(0-0)	0.714
Time interval defibrillation attempt (minutes) (N=341)						
	(n=235)	(n=106)		(n=77)	(n=264)	
mean (SD)	8.10(18)	12.07(17)	-	2.77(6)	11.25(19)	-
median (IQR)	2(0-9)	6(0-19)	0.008	0(0-3)	4(0-14)	<0.001*
Time interval when CPR stopped/death (CPR duration) (minutes)						
mean (SD)	20.09(22)	45.29(29)	-	12.18(14)	32.20(28)	-
median (IQR)	10(4-26)	37(26-59)	<0.001*	6(2-14)	25(10-44)	<0.001*
Time interval when ROSC (minutes) (N=683)[#]						
	(n=683)			(n=165)	(n=518)	
mean (SD)	20(43)	-	-	15(58)	21(38)	-
median (IQR)	10(5-25)	-	-	6(3-15)	13(6-28)	<0.001*

The Design Cycle in Machine Learning (& Logistic regression)



Features Selection

- Expert Opinions: Utstein style variables
- Univariate method:

  -Two outcome measures: ROSC and survival to discharge

  -Supervised feature selection based on comparisons of mean and variances (SPSS V.15)

  -Student's t test for numeric data

  -Mann-Whitney U-test for time variables

  -Chi-square or Fisher's exact test for categorical data
- Entropy measures for ranking feature:

  -Supervised feature selection based on information gain theory (Weka 3.4)

Univariate Selection

Table 10. Significant level (P value) in features selected from univariate analysis

	Outcome	
	ROSC	Survival
Patient characteristics		
Age	0.022*	0.684
Patient type	0.032*	0.379
Comorbidity-Diabetes	0.004*	0.069
Comorbidity-Cancer	0.170	0.001*
Comorbidity-Hepatic	0.02*	0.143
Comorbidity-Renal	0.006*	
Comorbidity-Cardiac	0.088	
Event characteristics		
Arrest location	0.035*	
Discovery status	<0.001	
Immediate cause-Arrhythmia	0.019*	
Immediate cause-Hypotension	<0.001	
Immediate cause-Respiratory failure	0.048*	
First monitored rhythm	0.002*	
Anticipated event-Doctor	0.076	
Anticipated event-Family	0.009*	
Causes of arrest-Cardiac	0.643	
Causes of arrest-Cancer	0.094	
Causes of arrest-Sepsis	0.878	
Estimated preventable rate	0.014*	
Treatment characteristics		
Airway management before intubation	0.011*	0.001*
Ambu-bagging before intubation	0.894	0.017*
Defibrillation attempt	0.223	0.002*
Intubation attempt	<0.001*	<0.001*
Drugs given	0.039*	0.005*
Massage attempt	0.002*	<0.001*
Other treatments-ECMO	0.012*	0.612
Any ROSC	-	<0.001*
Time interval characteristics		
CPR duration	<0.001*	<0.001*

Abbreviations: ROSC, return of spontaneous circulation; CPR, cardiopulmonary resuscitation; ECMO, Extra-Corporeal Membrane Oxygenation.

* P value <0.05

Features Selection & Performances Evaluation in two models

- Logistic regression (LR): SPSS V.15

  -28 selected features were the union of significant features with respect to ROSC (19 features) or survival (another 19 features) from univariate methods

  -Feed 28 features to training set by backward stepwise methods to construct the model (11 independent predictors were therefore selected)

  -Feed those 11 independent prognostic factors to testing set by all possible regression method

- Machine Learning: Statistica V.7

  -Feed all (28) selected features (from univariate) to both training and testing set, and removing features one by one from those with less entropy measures.

  -Select those models with highest AUC performances on the testing set.

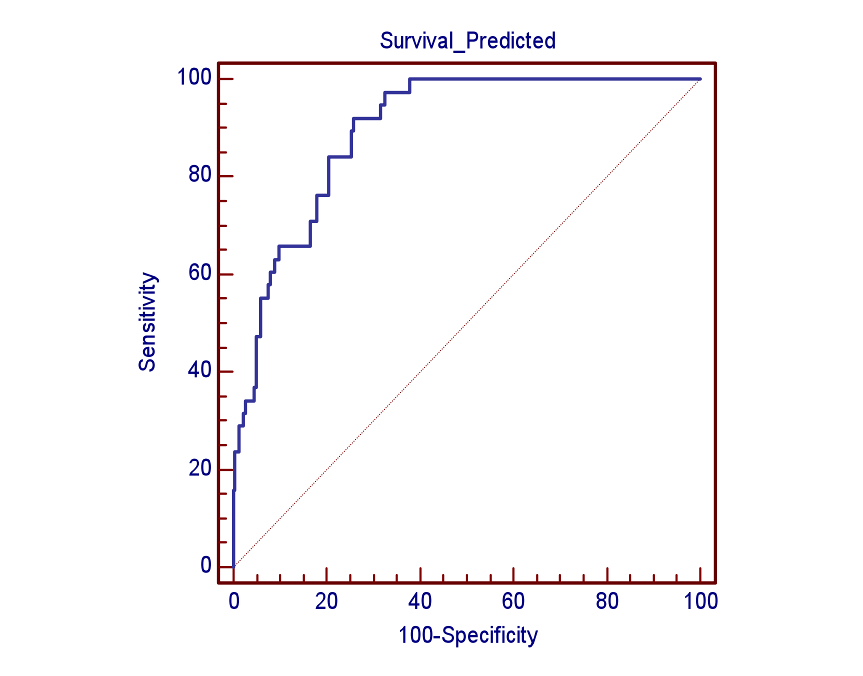
Logistic Regression (LR)

Backward Stepwise:
Variables selection from Training Set

Table 12. Factors associated with survival to hospital discharge by logistic regression following in-hospital resuscitation.

Features	P value	Odds ratio	95.0% C.I.
Age	0.010	0.98	0.967-0.995
Comorbidity -cancer	0.014	2.13	1.166-3.891
Comorbidit-cardiac	0.023	0.57	0.345-0.924
Immediate cause arrhythmia	0.000	0.30	0.185-0.492
Anticipated event doctor	0.001	2.25	1.393-3.636
Ambu-bagging before intubation	0.022	3.61	1.201-10.877
Cause of arrest sepsis	0.006	2.56	1.311-4.997
Other treatment ECMO	0.042	0.42	0.184-0.967
Intubation attempt	<0.000	0.31	0.172-0.569
CPR duration	<0.000	0.96	0.943-0.975
Any ROSC	<0.000	0.18	0.076-0.445

LR Result (Survival Prediction)
Testing dataset



Classification Table(a)

Observed			Predicted		
			Discharge_alive		Percentage Correct
			0	1	0
Step 1	Discharge_alive	0	217	7	96.9
		1	25	13	34.2
	Overall Percentage				87.8

a The cut value is .500

Area under the ROC curve (AUC)	0.896
Standard error	0.0346
95% Confidence interval	0.853 to 0.930
z statistic	11.438
Significance level P (Area=0.5)	0.0001

Machine Learning Methods

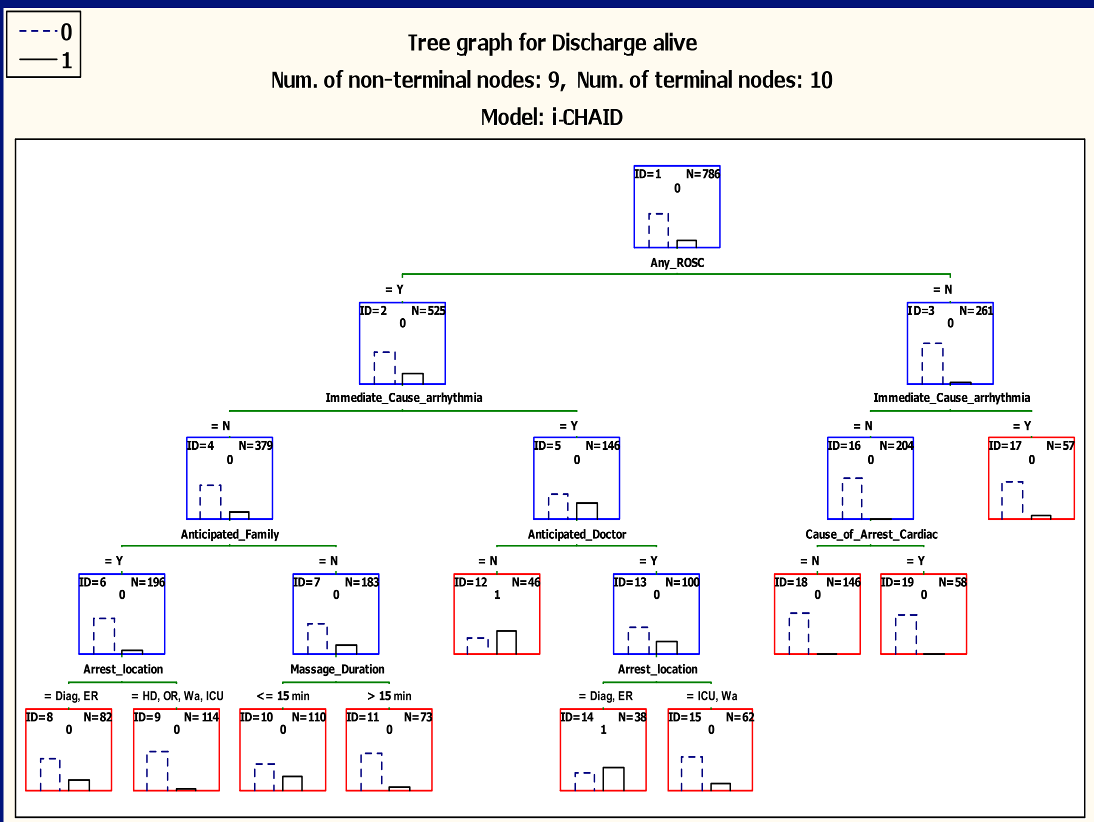
Prediction of Survival to discharge

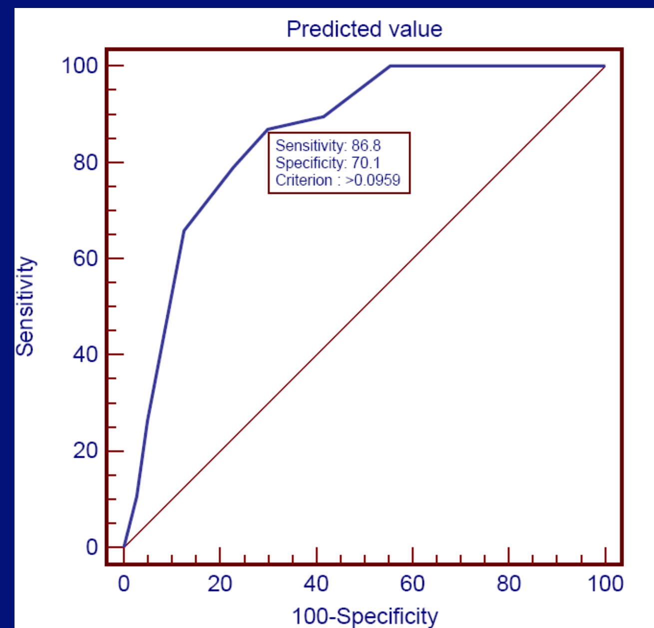
- Decision Trees (CHAID Model)
- k-NN (ten fold cross validation for selection of k)
- ANN

Decision Tree

(CHAID Model)

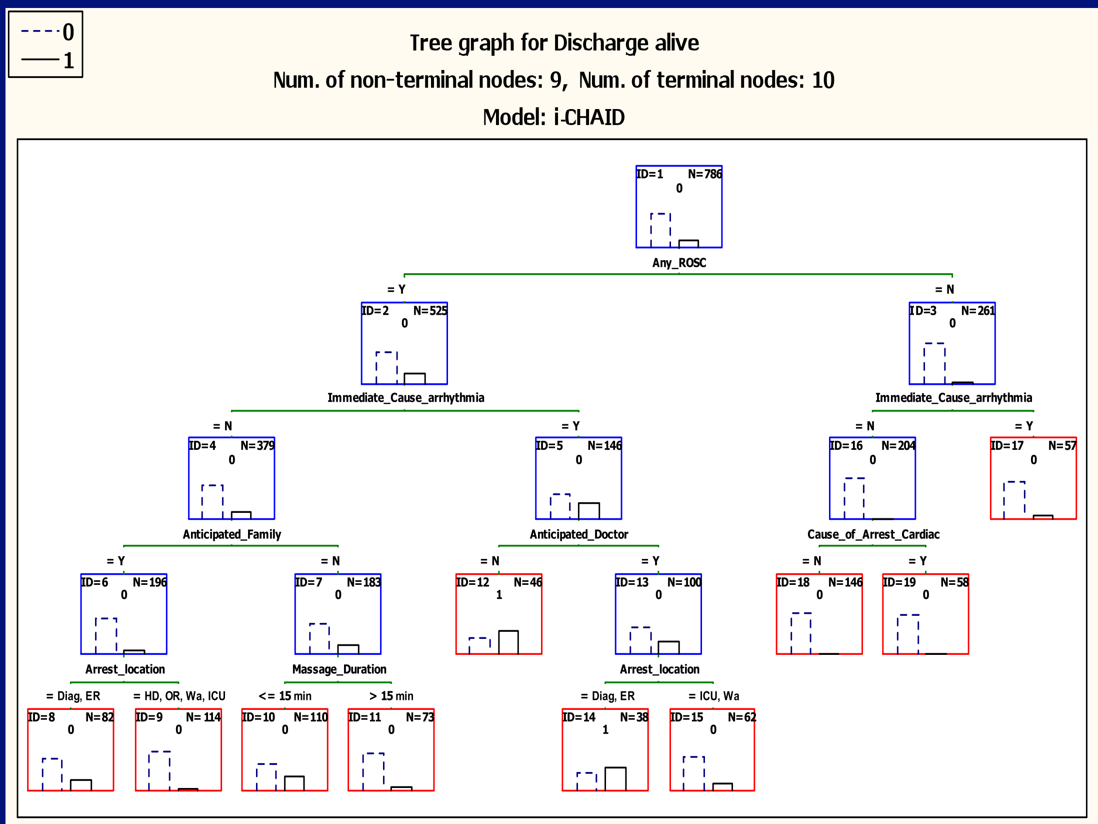
Decision Tree (28 variables)

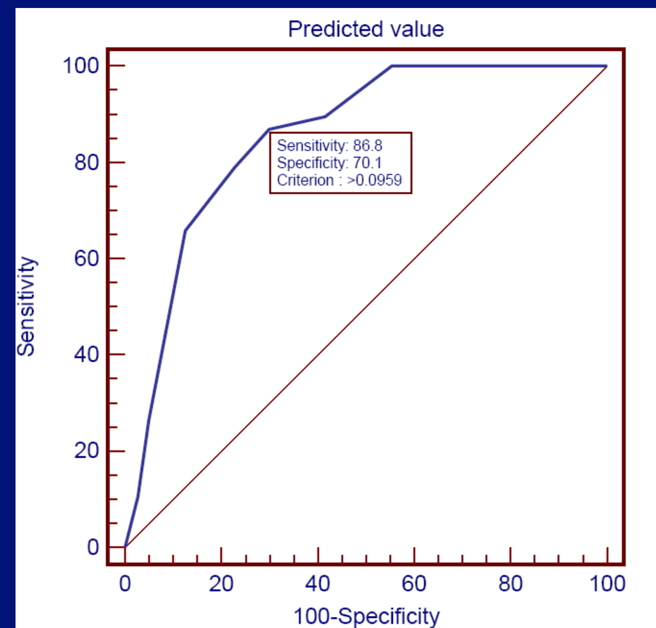




Area under the ROC curve (AUC)	0.854
Standard error	0.0399
95% Confidence interval	0.805 to 0.894
z statistic	8.875
Significance level P (Area=0.5)	0.0001

Decision Tree (7 variables)



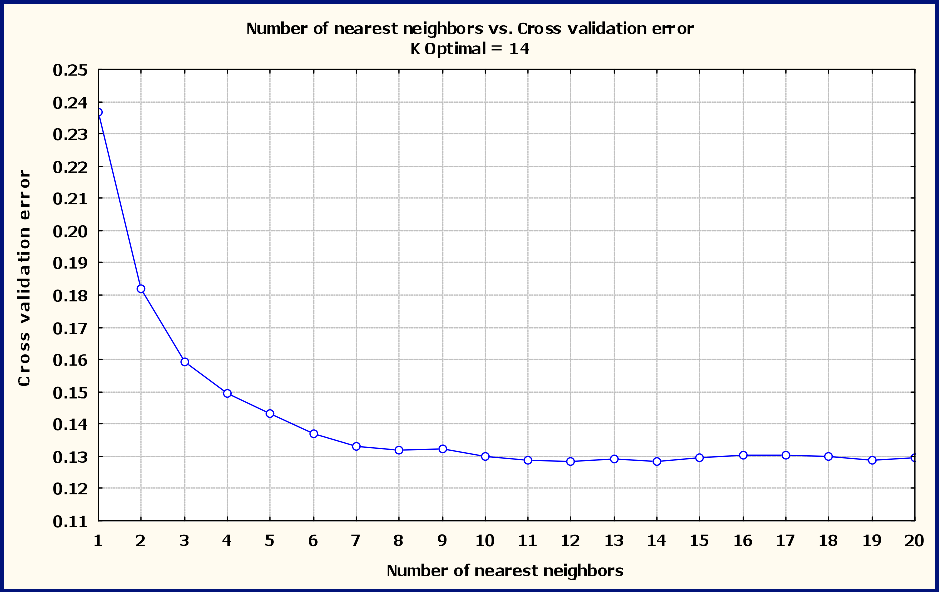


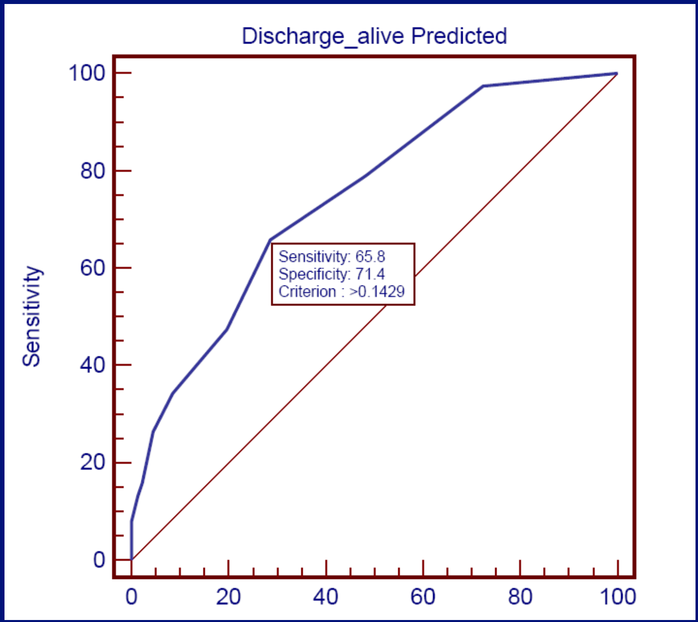
Area under the ROC curve (AUC)	0.854
Standard error	0.0399
95% Confidence interval	0.805 to 0.894
z statistic	8.875
Significance level P (Area=0.5)	0.0001

K Nearest Neighbors

(k-NN)

k-NN (28 variables)

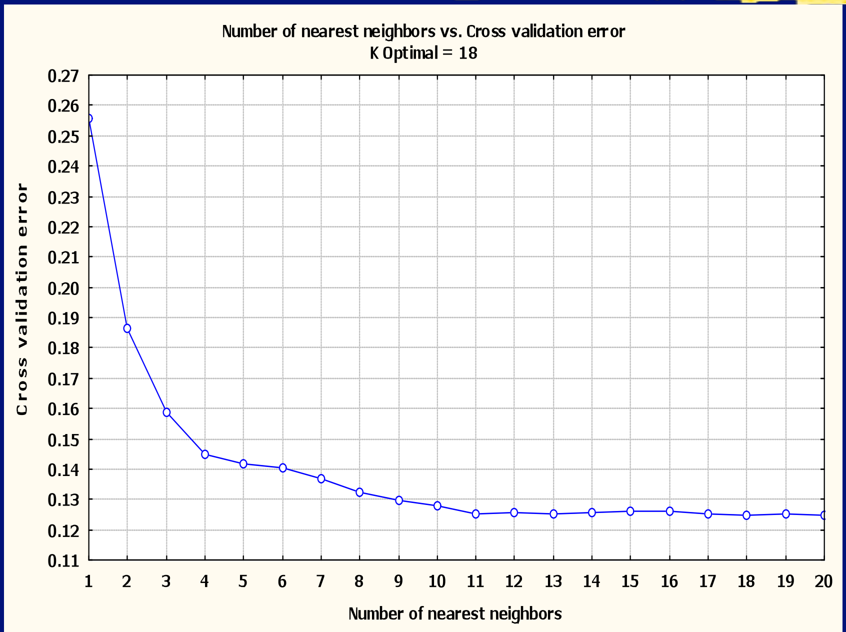


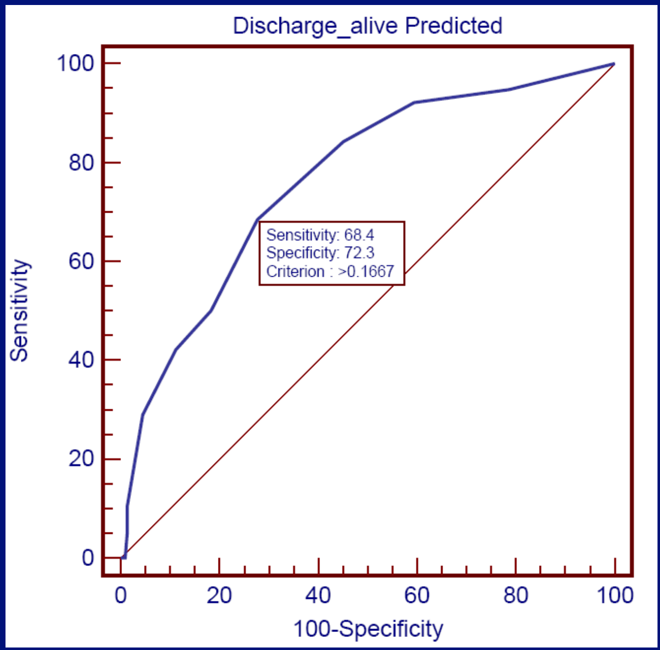


	Value
Number of independents	28
Number of dependent variables	1
Number of nearest neighbors	14
Input standardization	on
Averaging	uniform

Area under the ROC curve (AUC)	0.743
Standard error	0.0482
95% Confidence interval	0.686 to 0.795
z statistic	5.051
Significance level P (Area=0.5)	0.0001

k-NN (19 variables)

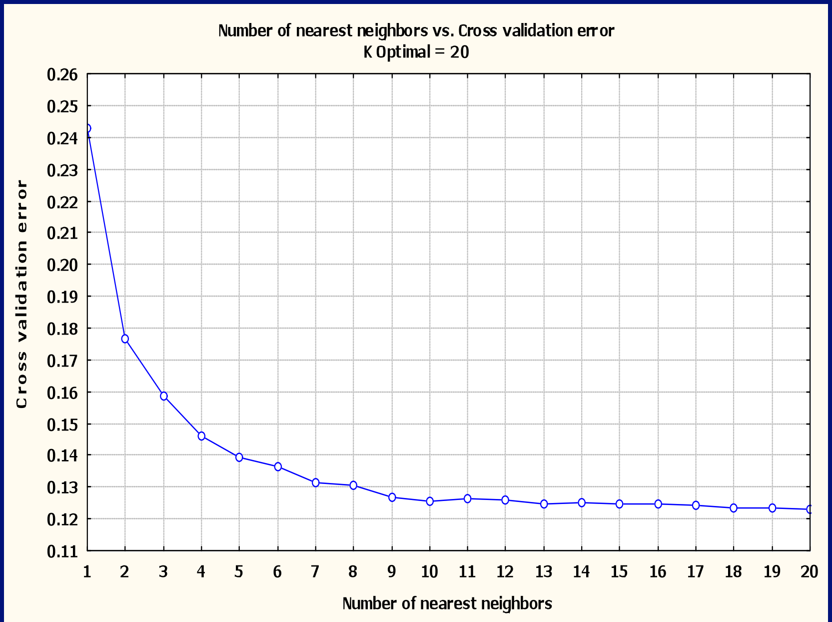


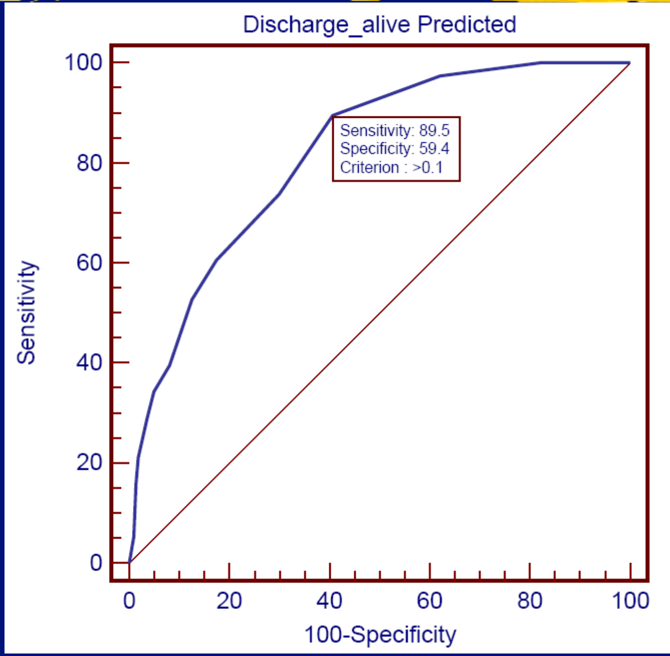


	Value
Number of independents	19
Number of dependent variables	1
Number of nearest neighbors	18
Input standardization	on
Averaging	uniform

Area under the ROC curve (AUC)	0.765
Standard error	0.047
95% Confidence interval	0.709 to 0.815
z statistic	5.643
Significance level P (Area=0.5)	0.0001

k-NN (13 variables)

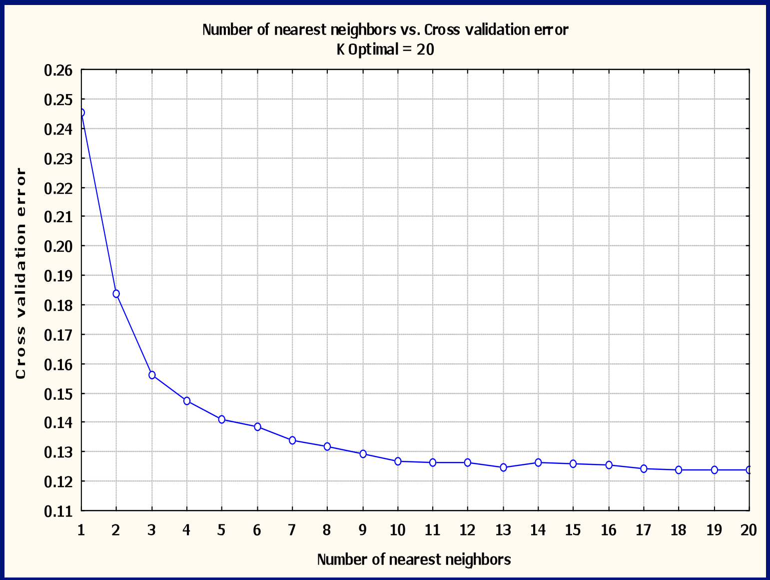


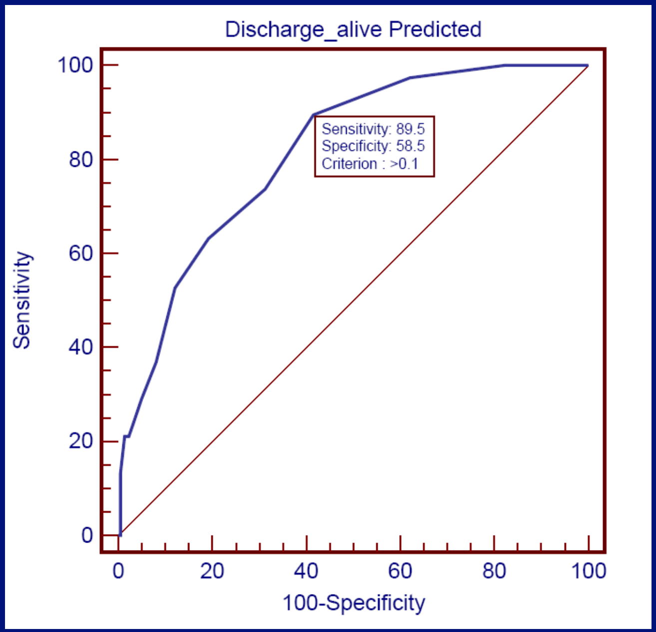


	Value
Number of independents	13
Number of dependent variables	1
Number of nearest neighbors	20
Input standardization	on
Averaging	uniform

Area under the ROC curve (AUC)	0.818
Standard error	0.0432
95% Confidence interval	0.766 to 0.863
z statistic	7.364
Significance level P (Area=0.5)	0.0001

k-NN (12 variables)



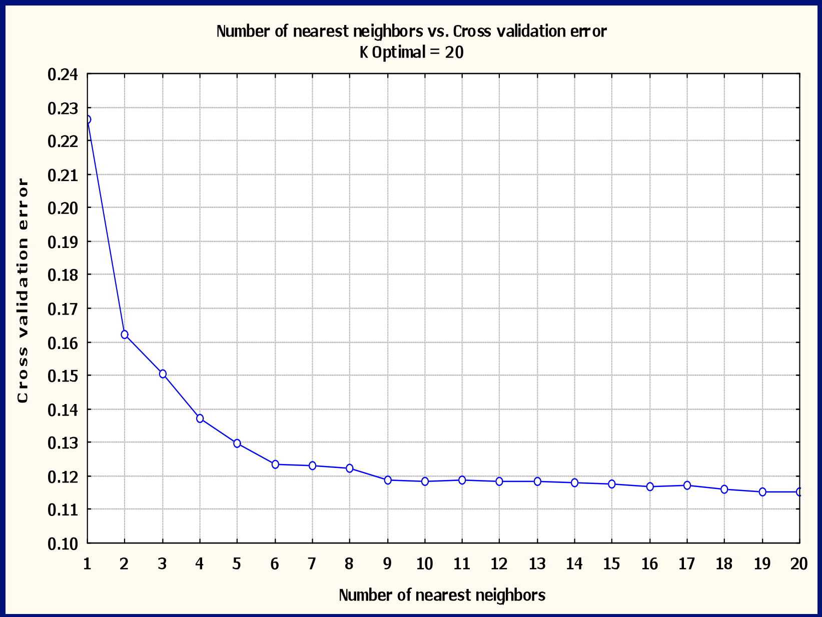


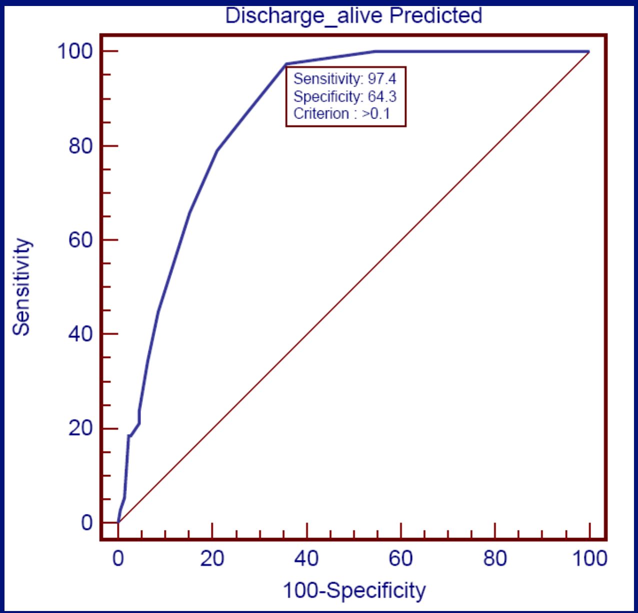
	Value
Number of independents	12
Number of dependent variables	1
Number of nearest neighbors	20
Input standardization	on
Averaging	uniform

Area under the ROC curve (AUC)	0.815
Standard error	0.0435
95% Confidence interval	0.762 to 0.860
z statistic	7.224
Significance level P (Area=0.5)	0.0001

k-NN (13 variables)

with CPR duration Dichotomized



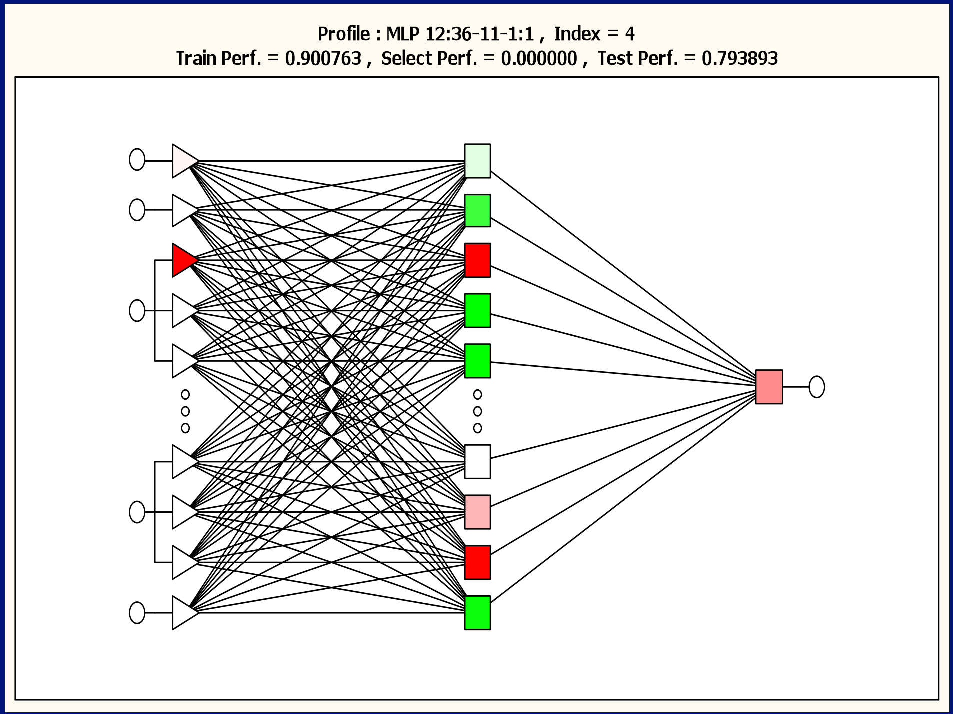


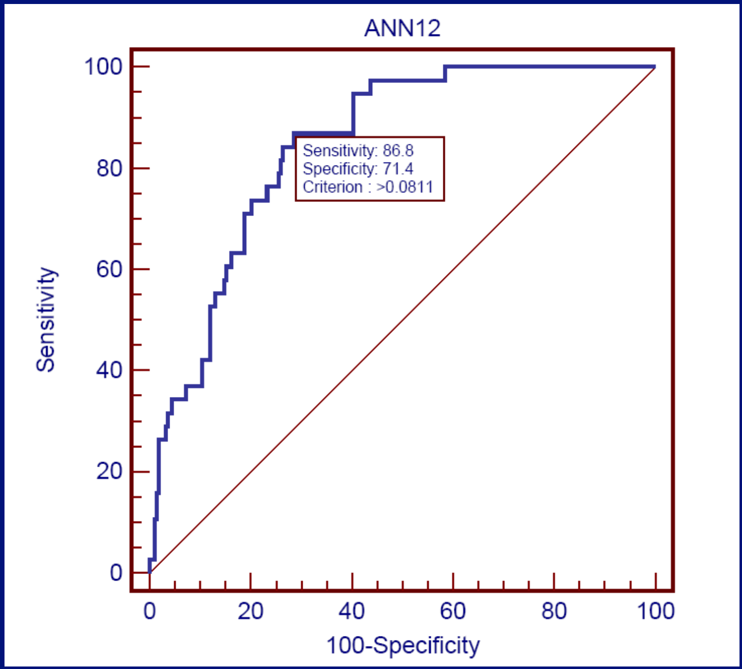
	Value
Number of independents	13
Number of dependent variables	1
Number of nearest neighbors	20
Input standardization	off
Averaging	uniform

Area under the ROC curve (AUC)	0.869
Standard error	0.0382
95% Confidence interval	0.822 to 0.907
z statistic	9.673
Significance level P (Area=0.5)	0.0001

Artificial Neural Networks (ANN)

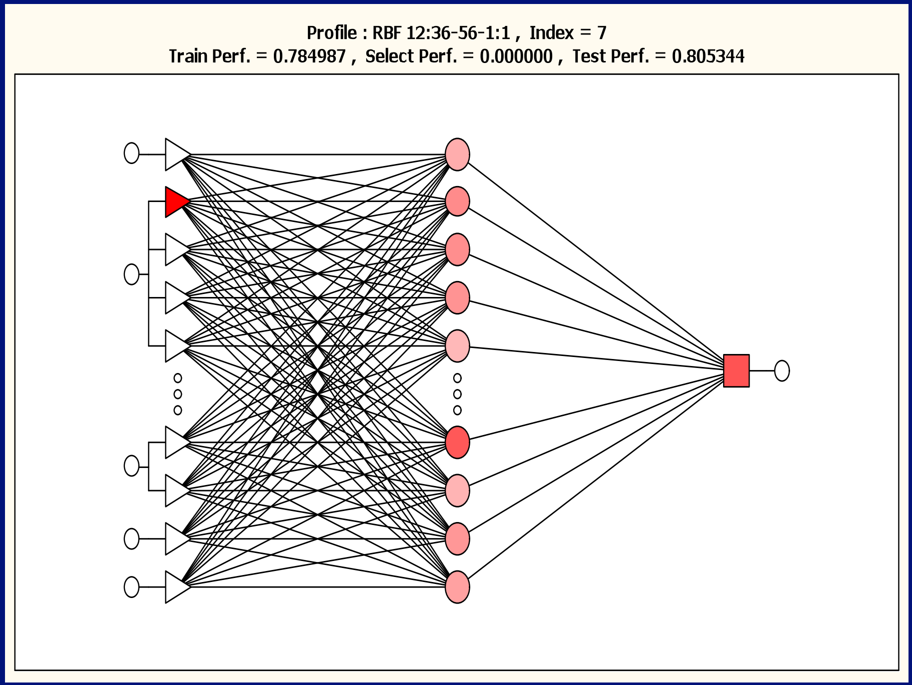
ANN (12 Variables)

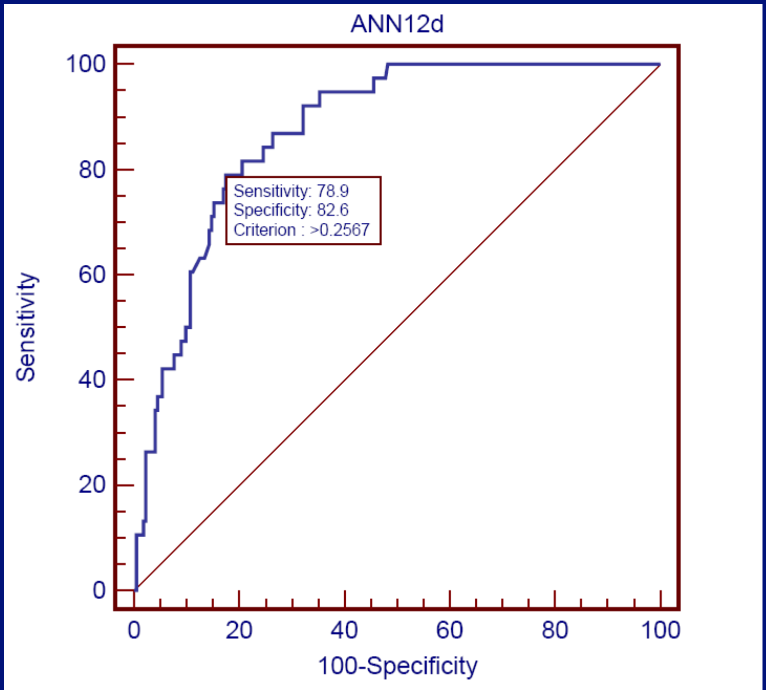




Area under the ROC curve (AUC)	0.846
Standard error	0.0407
95% Confidence interval	0.796 to 0.887
z statistic	8.483
Significance level P (Area=0.5)	0.0001

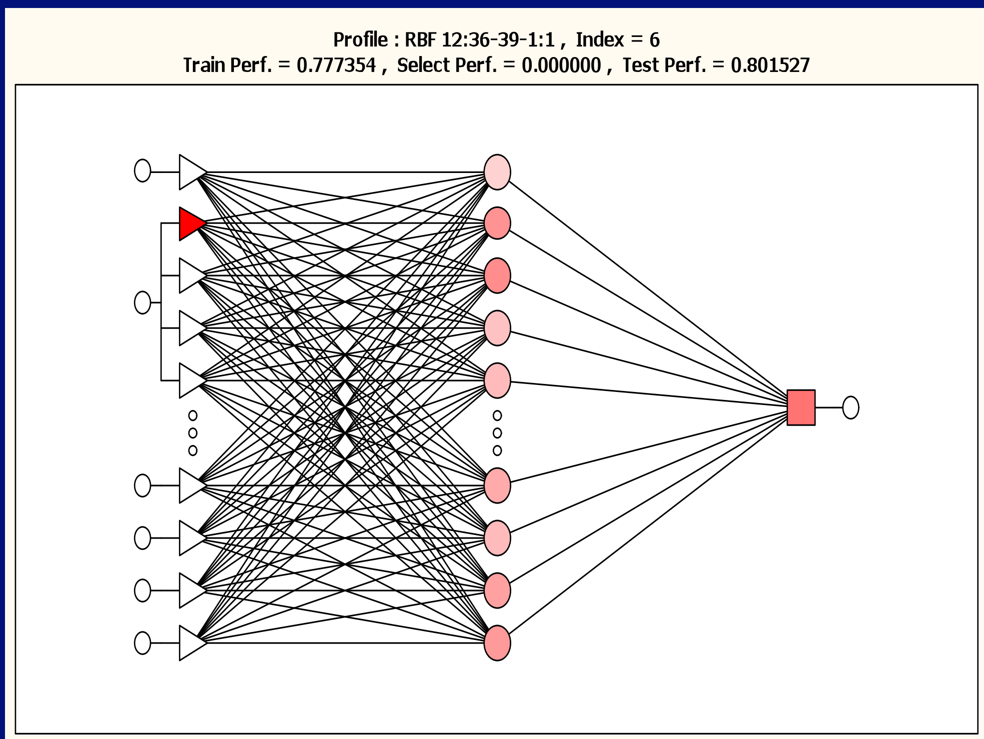
ANN (12 variables)
with CPR duration Dichotomized

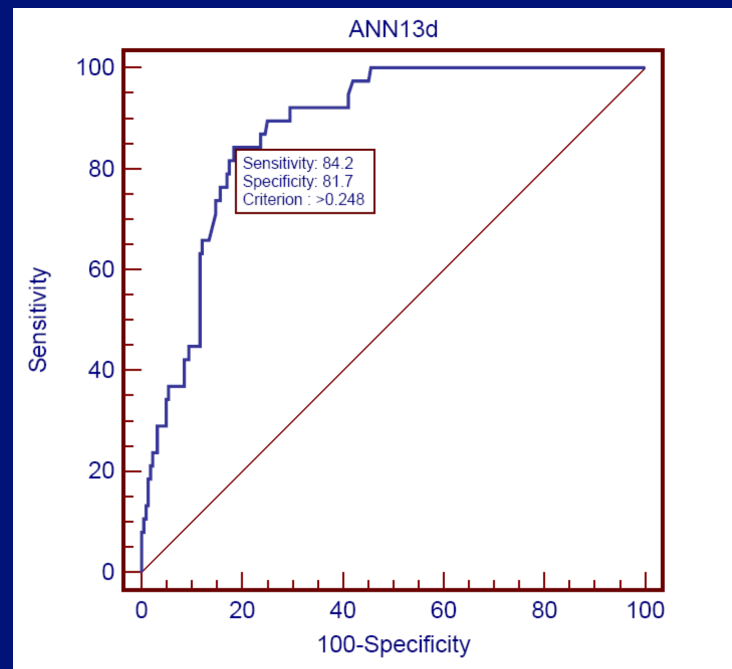




Area under the ROC curve (AUC)	0.874
Standard error	0.0376
95% Confidence interval	0.827 to 0.911
z statistic	9.936
Significance level P (Area=0.5)	0.0001

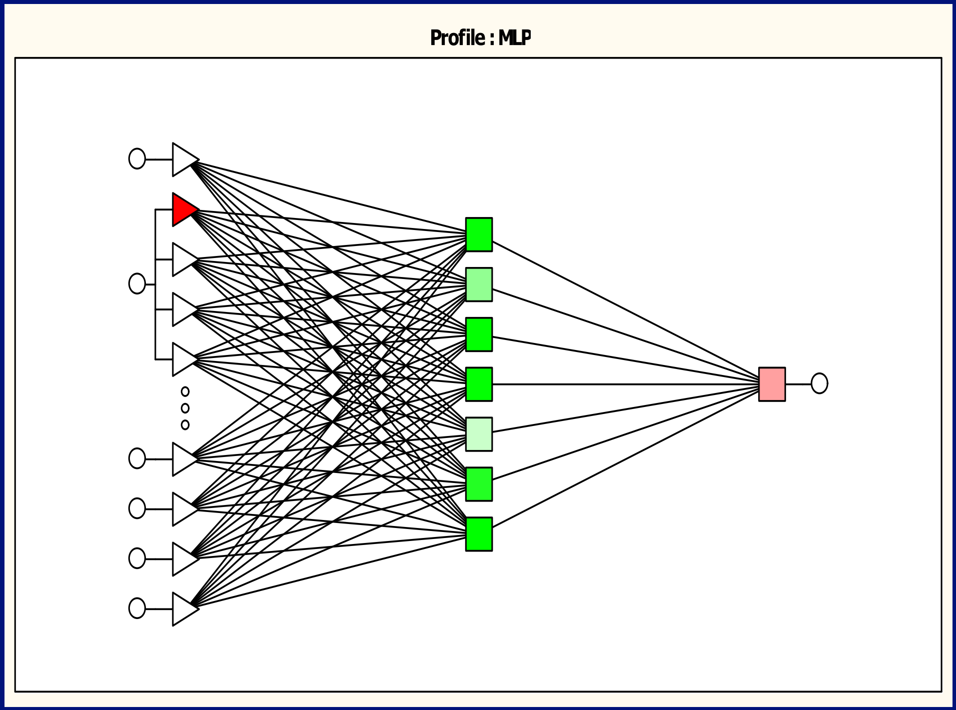
ANN (13 variables)
with CPR duration Dichotomized

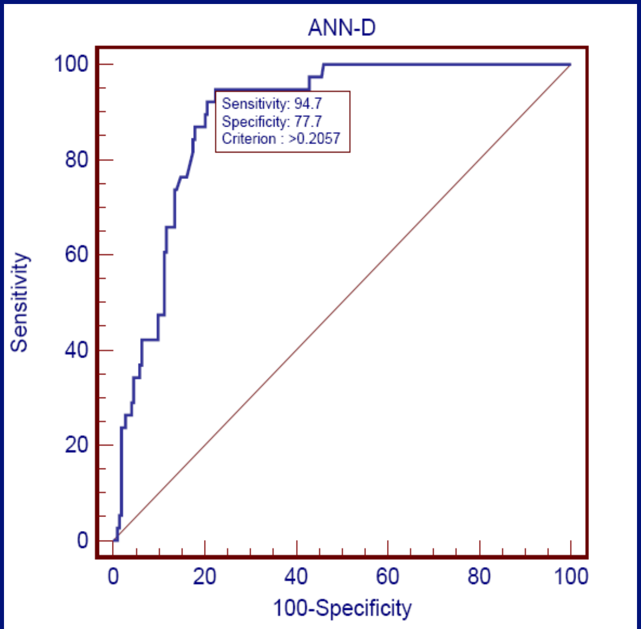




Area under the ROC curve (AUC)	0.877
Standard error	0.0372
95% Confidence interval	0.831 to 0.914
z statistic	10.153
Significance level P (Area=0.5)	0.0001

ANN (14 variables)
with CPR duration Dichotomized





Area under the ROC curve (AUC)	0.889
Standard error	0.0357
95% Confidence interval	0.844 to 0.924
z statistic	10.905
Significance level P (Area=0.5)	0.0001

Performance Evaluation

ROC curves Comparison

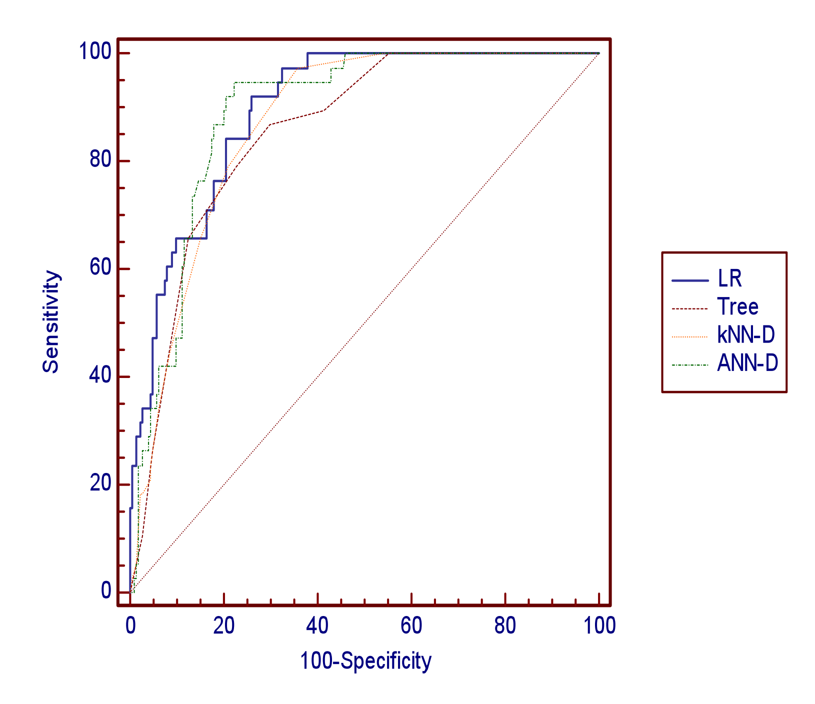


Table 14. Performance of the various methods on the testset of 262 cases.

Methods	AUC	SE	95% CI
Logistic regression	0.896	0.0346	0.853 to 0.930
Decision Tree	0.854	0.0399	0.805 to 0.894
kNN-D	0.869	0.0382	0.822 to 0.907
ANN-D	0.889	0.0357	0.844 to 0.924

Comparison of Selected Features

- Logistic regression: age, cancer cormobidity, immediate cause by arrhythmias, anticipated by doctor, ambu-bagging before intubation, cause of arrest by sepsis, ECMO, intubation attempt, CPR duration, and any ROSC.
- Machine learning identified eight more factors: arrest location, immediate cause arrhythmias, first monitored rhythm, causes of arrest cardiac diseases, airway before intubation, immediate cause hypotension, massage attempt, and anticipated by family
- AUCs improve when CPR duration is dichotomized by time point of 15 minutes

CPR duration dichotomization

Table 13. Survival to discharge status v.s. CPR duration Crosstabulation

			CPR duration		Total
			≦15 mins	>15 mins	
Discharge	alive	Count	135	39	174
		% within CPR duration	28.8%	6.7%	16.6%
	death	Count	333	541	874
		% within CPR duration	71.2%	93.3%	83.4%
Total		Count	468	580	1048
		% within CPR duration	100.0%	100.0%	100.0%
Chi-Square Test			P<0.001		

CPR Duration and Outcome
From Previous Report

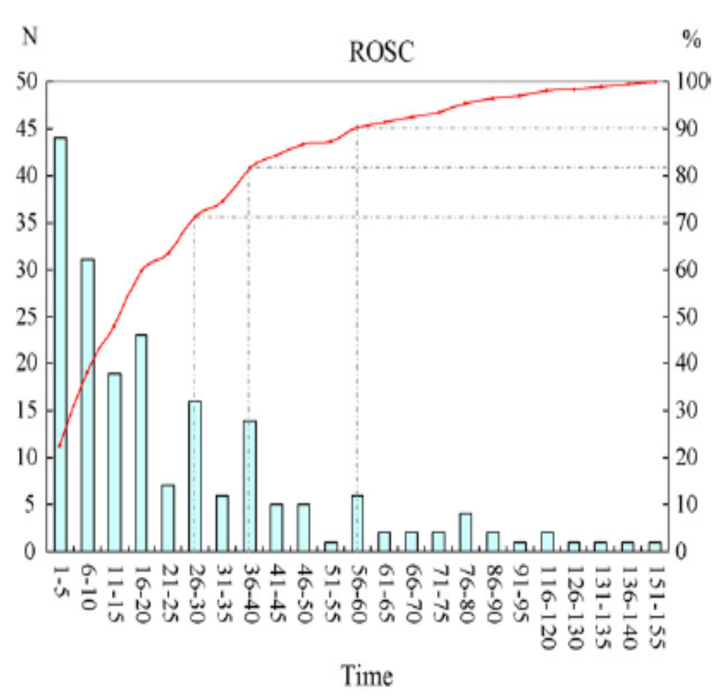


Figure 2 Cumulated number and proportion of ROSC as functions of the duration of resuscitation.

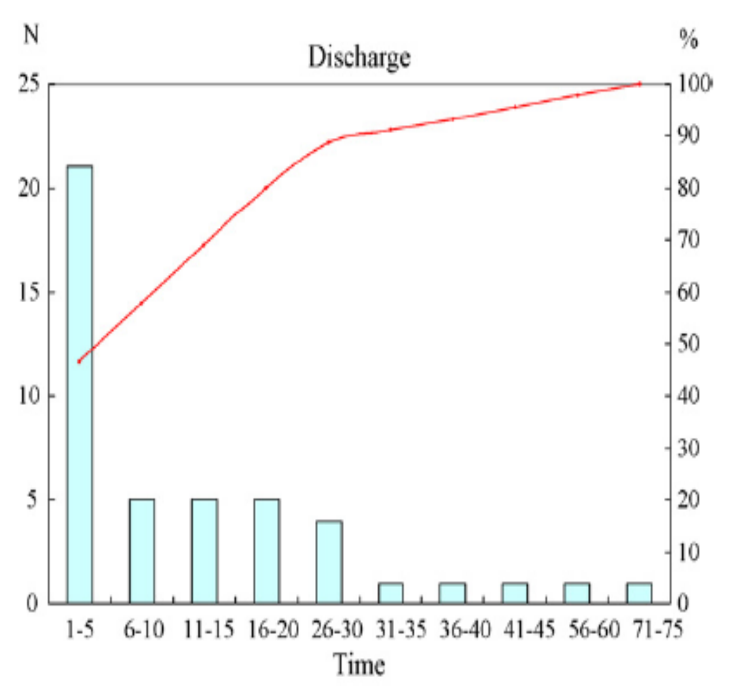


Figure 3 Cumulated number and proportion of survival to discharge as functions of duration of resuscitation.

Shih CL & Lu TC. Resuscitation 2007;72:394-403.

Disposition and Neurologic Outcome in Survivors

Disposition

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Home	127	73.0	73.0	73.0
	Nursing_home	4	2.3	2.3	75.3
	Other_hospital	6	3.4	3.4	78.7
	RCW	23	13.2	13.2	92.0
	Unknown	14	8.0	8.0	100.0
	Total	174	100.0	100.0	

Neurologic_Outcome

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	1	2	1.1	1.1	1.1
	2	128	73.6	73.6	74.7
	3	2	1.1	1.1	75.9
	4	2	1.1	1.1	77.0
	Unknown	40	23.0	23.0	100.0
	Total	174	100.0	100.0	

Length of stay (day)	Overall	Survived	Expired	P value
Mean (SD)	16 (33)	35 (39)	10 (28)	-
Median (IQR)	4 (0-20)	24 (13-40)	1 (0-10)	<0.001*

Cerebral Performance Categories Scale

CPC Scale

Note: If patient is anesthetized, paralyzed, or intubated, use "as is" clinical condition to calculate scores.

CPC 1. Good cerebral performance: conscious, alert, able to work, might have mild neurologic or psychologic deficit.

CPC 2. Moderate cerebral disability: conscious, sufficient cerebral function for independent activities of daily life. Able to work in sheltered environment.

CPC 3. Severe cerebral disability: conscious, dependent on others for daily support because of impaired brain function. Ranges from ambulatory state to severe dementia or paralysis.

CPC 4. Coma or vegetative state: any degree of coma without the presence of all brain death criteria. Unawareness, even if appears awake (vegetative state) without interaction with environment; may have spontaneous eye opening and sleep/awake cycles. Cerebral unresponsiveness.

CPC 5. Brain death: apnea, areflexia, EEG silence, etc.

Safar P. Resuscitation after Brain Ischemia, in Grenvik A and Safar P Eds: Brain Failure and Resuscitation, Churchill Livingstone, New York, 1981; 155-184.

Conclusions

- Machine learning methods can provide comparable performance as LR in predicting who can survive to hospital discharge following in-hospital resuscitation.
- More predictive determinants can be found from different approaches
- The optimal CPR duration with cut-off point of 15 minutes can be used as poor prognostic factor to help end-of-life decision making.

Limitations

- Selection bias exists in that we examined only the dataset at one tertiary teaching hospital.
- Feature selection: drawbacks exist both on univariate and entropy methods, especially when correlated and irrelevant features exist.
- we deselected those variables that are not present in all samples. There may be solution to this problem if robust missing data handling strategies are to be applied.


Thanks
Questions and Comments?