The Age Factor Influencing Long Term Physical Functionality in Stroke Patients Undergoing Intra-arterial Thrombectomy Treatment

Henry Horng-Shing Lu (hslu@stat.nctu.edu.tw)
National Chiao Tung University https://orcid.org/0000-0002-4392-3361
Chi-Ling Kao
National Chiao Tung University
Chih-Ming Lin
Changhua Christian Medical Foundation Changhua Christian Hospital
Shu-Wei Chang
Dayeh University
Chi-Kuang Liu
Changhua Christian Medical Foundation Changhua Christian Hospital
Yang-Hao Ou
Changhua Christian Medical Foundation Changhua Christian Hospital

---

Research article

Keywords: Age threshold, Intravenous thrombolysis, intra-arterial thrombectomy, acute ischemic stroke, functional outcome, NIHSS score, mRS score, Barthel index

Posted Date: March 5th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-16209/v1

Abstract

Background The treatment of acute ischemic stroke is heavily time-dependent, and even though, with the most efficient treatment, the long-term functional outcome is still highly variable. In this current study, the authors selected acute ischemic stroke patients who were qualified for intravenous thrombolysis with recombinant tissue plasminogen activator and followed by intra-arterial thrombectomy. With primary outcome defined by the functional level in a one-year follow-up, we hypothesize that patients with older age are at a disadvantage in post-stroke recovery. However, an age-threshold should be determined to help clinicians in selection of patients to undergo such therapy.

Methods This is a retrospective chart review study that include 92 stroke patients in Changhua Christian hospital with a total of 68 evaluation indexes recorded. The current study utilized the forward stepwise regression model whose Adj-R2 and p-value in search of important variables for outcome prediction. The chngpt package in R indicated the threshold point of the age factor directing the better future functionality of the stroke patients.

Results Datasets revealed the threshold of the age set at 79 the most appropriate. Admission Barthel Index, Age, Ipsi ICA RI, Ipsi VA PI, Contra MCA stenosis, Contra ECA RI, and in-hospital pneumonia are the significant predicting variables. The higher the age, in-hospital pneumonia, Contra MCA stenosis, Ipsi ICA RI and Ipsi VA PI, the less likely patient to recover from functional deficits as the result of acute ischemic stroke; the higher the value of Contra ECA RI and Admission Barthel Index, the better chance to recover at one-year follow up.

Conclusions Parameters of pre-intervention datasets could provide important information to aid first-line clinicians in decision making. Especially, in patients whose age is above seventy-nine receives diminish return in the benefit to undergo such intervention and should be considered seriously by both the patients and the physicians.

Introduction

The treatment of acute ischemic stroke is heavily time-dependent, and even though, with the most efficient treatment, the long-term functional outcome is still highly variable. In general, there are three clusters of parameters that influence the treatment outcome; these are the pre-intervention baseline characteristics, such as age, sex, body weight, co-morbidities, nature of the stroke, etc.; second, interventional methods; and lastly, post-interventional care, including method of secondary prevention, rehabilitation program and much more.

In this current study, the authors selected acute ischemic stroke patients who were qualified for intravenous thrombolysis with recombinant tissue plasminogen activator and followed by intra-arterial thrombectomy, following the 2018 American Heart and Stroke Association's guidelines[1]. Additionally, all of the patients who underwent intra-arterial thrombectomy in Changhua Christian Hospital also received carotid Doppler examination as part of the protocol. This offers additional data for evaluation in this study.

The primary goal of this study was to investigate whether pre-thrombectomy treatment parameters and baseline characteristics can offer valuable information in predicting patients' long-term functional outcomes in acute ischemic stroke patients who underwent intravenous thrombolysis followed by intra-arterial thrombectomy. Therefore, allow clinicians to better select the appropriate candidate for such treatment.

Material And Methods

In this current study, all patients were selected from Changhua Christian Hospital with a retrospective chart review conducted by the Department of Neurology. Participants were selected based on the confirmed diagnosis of first acute ischemic stroke and underwent intravenous thrombolysis therapy with recombinant tissue plasminogen activator (rtPA), followed by intra-arterial thrombectomy. Patients were selected based on the current indication for intravenous thrombolysis of presenting within 4.5 hours of the onset of symptoms[1] and did not have any contraindications to receive rtPA. CT angiography perfusion scan was followed in these patients to screen for candidates to receive intra-arterial thrombectomy.

Additional inclusion criteria are neuroimage confirmed anterior circulation obstruction, above eighteen of age, and were followed for at least one year. Patients with intracerebral hemorrhage, aneurysm rupture, cerebral arteriovenous malformation, and recurrent stroke were excluded. A total of 92 patients was selected fulfilling the above criteria between 2015 and 2017.

Pre-intervention data include baseline patient demographics such as age, body mass index, systolic and diastolic blood pressure, total cholesterol, HbA1c, and other comorbidities were documented. Additionally, in-hospital complication such as pneumonia was also recorded.

As part of the protocol, all patients underwent carotid doppler examination for evaluation of the status of blood flow in large vessels including the common carotid artery (CCA), internal carotid artery (ICA), external carotid artery (ECA), and vertebral artery (VA), and the presence of artherosclerotic plaque. Multiple parameters were extrapolated, including peak systolic velocity (PSV), end-diastolic velocity (EDV), resistance index (RI), and pulsatility index (PI).

Primary outcome in this study was to identify any significant change in the functionality of patients who underwent treatment, which is done by assessment of NIHSS score[2], mRS score[3], and Barthel index[4] both upon admission to the hospital and at 1-year follow up. Additionally, using statistical methods, described in the following section, to determine whether any of the pre-intervention variables have a significant impact on the functional outcome.

Statistical analysis

Data was collected from 92 stroke patients with a total of 68 independent pre-interventional indexes and 4 outcome variable (Appendix 1) were recorded. Authors use principal component analysis (PCA) to integrate the prognostic variables into an aggregative index, *prognosis*, which is an index that takes into account all four outcome variables and their contribution to the overall outcome. Then using the forward stepwise regression model to determine which, if any, of the sixty-eight independent variables had a significant effect on the *prognosis*. Authors end up with only eleven variables and only seven of which had statistically significance.

Classify the Variables

To facilitate the analysis, the data is first divided into pre-interventional and outcome variable, which are classified into categories, orders, and continuations. The outcome variables include the following: Follow up CT cerebral bleeding, MBD NIHSS, MBD mRS, MBD Barthel Index, and the remaining 68 variables are classified as pre-interventional independent variables.

Use Principal Component Analysis on the prognostic variables

The authors use principal component analysis (PCA) to integrate the outcome variables into an aggregative index, *prognosis*. According to equation (1), each principal component recombines the original variables into a new set of several independent variables. The coefficient of X_i in the linear combination is its eigenvector which is obtained by maximizing the explanatory variation of the corresponding principal component[5]. Therefore, authors can determine the relationship between the principal component and the original variable.

$$PCA = \phi_1 X_1 + \phi_2 X_2 + \ldots + \phi_n X_n \qquad (1)$$

In the current study, prognosis is an outcome variable that is influenced by the need of follow up head CT in case of suspected intracranial bleed, the NIHSS score, mRS score, and Barthel index. The relationship is shown in the below equation (2):

Prognosis = 0.218 Follow.up.CT + 0.566 NIHSS + 0.528mRS - 0.595B.I (2)

Exploratory Data Analysis

The exploratory data analysis section was performed with the ggplot2 package in R. Authors describe the statistics of variables in order to understand the simple information of the data.

Model Architecture

(1) Multiple Regression Model

Multiple regression is to explore the correlation between the independent variable and the dependent variable and to build a regression model[6]. The equation (3) shown below.

$y = b_0 + b_1x_1 + b_2x_2 + ... + b_nx_n$ ($b_0 ... b_n$: Regression coefficients)   (3)

In our research , authors regarded all variables in pre-intervention as independent variables, and *prognosis* as a dependent variable, and built a multiple regression model. Authors find that only a few variables are significant, however, with Adj-R^2 being only 0.3106, the model has a relatively low explanatory power. In order to improve the model, forward stepwise regression model is then used.

(2) Forward Stepwise Regression Model

The forward stepwise regression begins with an empty regression, adding variables one by one to select the best performing model according to the Akaike information criterion (AIC). AIC is a standard for assessing the complexity of statistical models and measuring the superiority of statistical model fit the data. The model with the lowest AIC value should be given priority when selecting the model. This is done by adding the independent variables one by one until the additional contribution of any one of the variables does not provide any statistical significance. Finally, the authors identified eleven variables with only seven of them are significant (table 3). This method improved the Adj-R^2 of our model from 0.3106 to 0.4588, with p-value less than 0.05, and therefore, the model setup by using forward stepwise regression provides more explanatory power.

(3) Segmented linear regression

Segmented linear regression is a method when the independent variables clustered into different groups[7]. That is, there are different relationships between the variables in these regions. The following equation (4) is a threshold equation model:

$\eta = \alpha_1 + \alpha_2^T z + \beta_1 (x - e)_+ + yx$ (4)

In this equation 'e' is the threshold parameter, and 'x' is the predictor with threshold effect, 'z' denotes additional predictors.

Authors estimate a segmented linear regression model to determine if there is a threshold for independent variable age, that would mark as a boundary for poor prognosis with statistical significance. The package authors utilized is chngpt package in R and uses the formula built in forward stepwise regression.

Results

<u>Exploratory Data Analysis</u>

Table 1 shows the significantly pre-interventional predictive variables in acute ischemic stroke patients who underwent intravenous thrombolysis followed by intra-arterial thrombectomy.

The patients' Barthel Index on admission is averaged to a value of 13.42 (range 0 to 80, lower the score means higher disability). This suggested that patients who presented with acute ischemic stroke were already disabled upon admission. The patients' average age is 65, the youngest patient is 25, and the oldest patient is 88. It showed the majority of patients who suffered from stroke are elderly patients. The average value of Ipsi ICA RI is 0.7259, with a minimum value of 0.5100, and a maximum value of 1.7700. The average value of Ipsi VA RI is 0.7815, with a minimum value of 0.5300, and a maximum value of 1.0000. The average value of Contra ECA RI is 0.9466, with a minimum value of 0.7400, and a maximum value of 2.3100. This indicates that stroke was more likely to occur in a person with high arterial stagnation. The average value of Contralateral MCA stenosis CTA is 0.3216, with a minimum value of 0.0000, and a maximum value of 1.0000. The average value of Inhospital pneumonia is 8.413, with a minimum value of 5.0000, and a maximum value of 10.0000.

Furthermore, admission Barthel Index, age, Ipsi ICA RI, Ipsi VA PI, Contra ECA RI, Contra MCA stenosis on CTA, and Inhospital pneumonia are the most significant variables based on the dataset analysis. (Table 1).

Multiple Linear Regression and Forward Stepwise Regression

Table 2 showed the difference between the original model and forward stepwise regression model. The Adj-R^2 of original model is 0.3106 and the p-value of original model is 0.07819. The Adj-R^2 of forward stepwise model is 0.4588 and the p-value of forward stepwise model is 3.137e-09. The result showed that the forward stepwise model is superior to the original model.

In Table 3, it showed that Admission Barthel Index (p-value = 0.00212), Age (p-value = 0.03030), Ipsi ICA RI (p-value = 0.00155), Ipsi VA PI (p-value = 0.01274), Contra MCA stenosis CTA (p-value = 0.03008), Contra ECA RI (p-value = 0.02184) and In-hospital pneumonia (p-value = 0.02126) are the significant variables.

Using the aforementioned equations (2) and (3), shown once again below. If the age is increased by one year, the *prognosis* value will increase by 0.017807, from equation (3). Then setting equation (2) is equal to equation (3), authors inferred that patients with older age were more likely to receive a follow up CT of the head due to intracranial bleed, a higher NIHSS and mRS scores, and lower Barthel Index score upon discharge. Using the same logic, the authors arrive at the same conclusion with other variables such as Ipsi ICA RI, Ipsi VA PI, Contra MCA stenosis CTA, and Inhospital pneumonia.

Prognosis = 0.218(Follow.up.CT) + 0.566(NIHSS) + 0.528(mRS) - 0.595(B.I forward) (2)

Prognosis = -0.026867(Admission Barthel Index) + 0.017807(Age) + 2.493430(Ipsi ICA RI) + 0.214155(Ipsi VA PI) + 0.546799(Contralateral MCA stenosis CTA) - 1.148134(Contra ECA RI) - 0.437726(Stroke right left) + 0.561732(Inhospital pneumonia) - 0.449998(MRA ipsilateral Collateral flow) + 0.006712(CTP mismatch) + 0.140513(Admission CT ASPECTS) (3)

On the other hand, if the value of Contra ECA RI rises by value of one, the prognosis will decrease by 1.148134. That is to say, the higher the value of Contra ECA RI, the less chance to have follow up CT cerebral bleeding, and the better chance to recover. Other variables like Admission Barthel Index and MRA ipsilateral collateral flow showed similar trends.

Segmented Linear Regression

Figure 1 showed the three plots of the threshold of this data. The first plot shows the scatter plot between Age and Prognosis, and it represents that the samples scattered around 60 to 80 years old. The second plot shows the threshold of the Age variables is 79. The third plot shows the threshold which is estimated by bootstrap in order to know the frequency. As we find that the frequency around 80 is the highest, thus we can presume the threshold for the variable 'age' is 79.

According to the result of the segmented linear regression, the authors made the Age beyond 79 as 1, and below 79 as 0, and conducted a simple linear regression to determine if there is a statistical difference between the two samples. The result is shown in Table 4, and it confirmed our presumption in the early paragraph that patients with age greater than 79 indeed have a worse prognosis than those who are younger than the age of 79 (p-value = 0.008757).

Discussion

The current study demonstrated the higher the age, the less likely a stroke patient might recover from receiving treatment with intravenous thrombolysis followed by intra-arterial thrombectomy. This is especially resourceful for first-line clinicians in selecting whom to receive such treatment and as a tool to weigh out the benefit and risk. We believe this is the first paper that pinpointed the age threshold as an important indicator of functional outcome in acute ischemic stroke patients underwent such treatment.

As far as pre-intervention carotid doppler parameters, the higher the Ipsi VA RI, which indicates compromised blood flow starting at the inlet of posterior circulation, therefore in the event of acute ischemic stroke of the anterior circulation, there are less available blood flow to rescue the ischemic brain cells and leading to higher risk of functional disability[7] in such patients.

Interestingly, the current study showed that the higher the value of Contra ECA RI leads to a better functional outcome in ischemic stroke patients. We hypothesize that impaired contralateral blood flow re-directs blood flow toward the opposite side, which is the ischemic hemisphere, that is sufficient to prevent the progression of the disease and is meaningful in predicting the long-term functional outcome in patients.

The authors used different statistical analysis methods to identify specific variables and whether each had a significant impact on the overall prognosis. However, the Adj-R^2 of the forward stepwise regression is only 0.4588, and the Adj-R^2 of the simple linear regression is only 0.06361, which both can be attributed to the relatively small sample size(N = 92), therefore, the model had low explanatory power. It would increase our confidence in our observation if future studies with larger sample size and still showed similar trends.

The statistical analysis method we used was all supposed that there were linear relation between outcome variables and pre-interventional variables, therefore authors use multiple linear regression and segmented regression as study models. However, it might be nonlinear relationship between two variables, and this should be considered in future studies to tailor consistency between the model and the real-world situation.

A major strength of this study is low heterogeneity among participants, given that most patients came from the surrounding local communities and shared the same ethnic group. Other strengths were technical consistency, as the same technician performed all of the carotid duplex scans, and the ability to compare each patient's functional scores one year after the treatment allowed adequate time to also observe functional improvement. However, this could also potentially introduce confounding factors, such as different types of rehabilitation programs that participants may have attended within the year. The major shortcoming of the current study is of relatively small sample size (N = 92) as well as the fact there was no placebo group for comparison. Besides, the homogeneity in the ethnic group might not be able to represent other ethnic groups and therefore the general application can be limited in such regard.

Conclusion

The higher the age, in-hospital pneumonia, Contra MCA stenosis on CTA, Ipsi ICA RI and Ipsi VA PI, are correlated with higher risk of functional disability, whereas higher the value of Contra ECA RI and Barthel Index on admission showed relative better likelihood in improving functional outcome in the long-term in acute ischemic stroke patients who underwent ITT and IAT.

Pre-intervention parameters can serve as important indicators to aid first-line clinicians in decision making. The higher the age, in-hospital pneumonia, Contra MCA stenosis on CTA, Ipsi ICA RI and Ipsi VA PI, are correlated with higher risk of functional disability, whereas higher the value of Contra ECA RI and Barthel Index on admission showed relative better likelihood in improving functional outcome in the long-term in acute ischemic stroke patients who underwent ITT and IAT. Especially, in patients whose age is above 79 receives diminish return in the benefit to undergo such intervention and should be considered seriously by both the patients and the physicians.

Declarations

Ethics approval and consent to participate

The study procedures were approved by the Institutional Review Board of the Changhua Christian Hospital in Changhua, Taiwan (CCH IRB number: 180409). Informed consent was obtained in the usual way as the procedures were the usual standard of care. As the study is retrospective in nature, the informed consent was waived and approved by the committee.

Consent to publish

Not applicable.

Availability of data and materials

The patient datasets are stored after the study is done and sent to the committee for security reasons. It is our hospital policy to guarantee no breach of personal information.

Funding

This project received no support or funding from any organization.

Acknowledgements

Not applicable.

Authors' contributions:

Conceptualization and study design by Chih Ming Lin, Shu-Wei Chang, and Henry Horng-Shing Lu; Methodology by Chih Ming Lin, and Henry Horng-Shing Lu; Data curation by Chih Ming Lin, Yang-Hao Ou, and Chi-Kuang Liu; Formal analysis by Chi-Ling Kao, and Henry Horng-Shing Lu; Writing - Original draft preparation by Yang-Hao Ou, Chi-Ling Kao, and Chih Ming Lin. Writing - Review & Editing by Yang-Hao Ou, and Chih Ming Lin.

Conflicts of Interest

The authors have no competing interests to declare

References

1. de los Ríos la Rosa, Felipe, et al. "Eligibility for intravenous recombinant tissue-type plasminogen activator within a population: the effect of the European Cooperative Acute Stroke Study (ECASS) III Trial." *Stroke*6 (2012): 1591-1595.
2. Wu, Zimu, et al. "Time-dependence of NIHSS in predicting functional outcome of patients with acute ischemic stroke treated with intravenous thrombolysis." *Postgraduate medical journal*1122 (2019): 181-186.
3. Prabhakaran, Shyam, Ilana Ruff, and Richard A. Bernstein. "Acute stroke intervention: a systematic review." *Jama*14 (2015): 1451-1462.
4. Quinn, Terence J., Peter Langhorne, and David J. Stott. "Barthel index for stroke trials: development, properties, and application." *Stroke*4 (2011): 1146-1151.
5. Shlens, Jonathon. "A tutorial on principal component analysis." arXiv preprint arXiv:1404.1100 (2014).
6. Rencher, Alvin C. Multivariate statistical inference and applications. New York: Wiley, 1998.

7. Fong, Youyi, et al. "chngpt: threshold regression model estimation and inference." *BMC bioinformatics*1 (2017): 454.

Tables

Table1. Pre-interventional independent variables with statistical significance

Admission. Barthel.Index	Age	Ipsi.ICA.RI	Ipsi.VA.RI
Min. : 0.00	Min. :25.00	Min. :0.5100	Min. :0.5300
1st Qu.: 5.00	1st Qu.:55.75	1st Qu.:0.6400	1st Qu.:0.7000
Median :10.00	Median :68.00	Median :0.7000	Median :0.7850
Mean :13.42	Mean :65.01	Mean :0.7259	Mean :0.7815
3rd Qu.:20.00	3rd Qu.:77.00	3rd Qu.:0.7625	3rd Qu.:0.8500
Max. :80.00	Max. :88.00	Max. :1.7700	Max. :1.0000
Contra. MCA stenosis CTA	**Contra.ECA.RI**	**Inhospital pneumonia**	
Min. :0.0000	Min. :0.7400	Min. : 5.000	
1st Qu. :0.0000	1st Qu. :0.8175	1st Qu. : 8.000	
Median :0.0000	Median :0.9100	Median : 9.000	
Mean :0.3261	Mean :0.9466	Mean : 8.413	
3rd Qu.:1.0000	3rd Qu.:1.0000	3rd Qu. : 9.000	
Max. :1.0000	Max. :2.3100	Max. :10.000	

These variables were identified using the forward stepwise regression model. Indicating that these seven out of the total of sixty-eight pre-interventional variables showed significant influence on the overall prognosis. Additionally, showing the minimum, maximum, median and quartile values of each variable.

Table 2. Model Architecture

	Original Model	Forward Stepwise Regression
Formula	Prognosis ~ all variables	Prognosis ~ Admission Barthel Index + Age + Ipsi ICA RI +Ipsi VA PI + Contra MCA stenosis CTA + Contra ECA RI +Stroke right left + Inhospital pneumonia + MRA ipsilateral Collateral flow +CTP mismatch + Admission CT ASPECTS
Residual standard error	1.189	1.054
Multiple R-squared	0.7954	0.5243
Adjusted R-squared	0.3106	0.4588
F-statistic	1.641	8.015
p-value	0.07819	3.137e-09 ***

This table showed the difference between the original model using multiple regression and forward stepwise regression model. The Adj-R^2 of original model is 0.3106 and the p-value of original model is 0.07819. The Adj-R^2 of forward stepwise model is 0.4588 and the p-value of forward stepwise model is 3.137e-09.

Table3. Pre-interventional variables in the forward stepwise regression analyses

Categories	Coefficients	P-value
Admission Barthel Index	-0.026867	0.00212 **
Age	0.017807	0.03030 *
Ipsi ICA RI	2.493430	0.00155 **
Ipsi VA PI	0.214155	0.01274 *
Contralateral MCA stenosis CTA	0.546799	0.03008 *
Contra ECA RI	-1.148134	0.02184 *
Stroke right left	-0.437726	0.06663 .
Inhospital pneumonia	0.561732	0.02126 *
MRA ipsilateral Collateral flow	-0.449998	0.06348 .
CTP mismatch	0.006712	0.11008
Admission CT ASPECTS	0.140513	0.14005

(Significant Value: ***: p-value < 0.001; **: p-value < 0.01; *: p-value < 0.05;

. : p-value < 0.01)

This table showed total of 11 variables identified using forward stepwise regression model, and 7 of the variables showed statistical significance. Admission Barthel Index (p-value = 0.00212), Age (p-value = 0.03030), Ipsi ICA RI (p-value = 0.00155), Ipsi VA PI (p-value = 0.01274), Contra MCA stenosis CTA (p-value = 0.03008), Contra ECA RI (p-value = 0.02184) and In-hospital pneumonia (p-value = 0.02126) are the significant variables.

Table 4. The linear regression for age threshold

	Model
Formula	Prognosis ~ Age
Residual standard error	1.386
Multiple R-squared	0.0739
Adjusted R-squared	0.06361
F-statistic	7.182
p-value	0.008757

To verify the presumption derived from the scatter plot that age of 79 may be a threshold for poor prognosis, the authors divided age variables into two groups; the first group with age greater than 79, and the second group with age below 79, conducted a simple linear regression. The result is shown in this table and confirmed that there was a significant difference in the prognosis between these two age groups.

Appendix

Appendix 1. List of all 68 pre-interventional variables and 4 outcome variables

1. Preoperative variables

Stroke right/left	Intra posterior stenosis CTA	Ipisilateral MCA stenosis CTA
Contralateral MCA stenosis CTA	Stroke location MRI	MRA ipsilateral Collateral flow
It belongs to 2a/2b	Occlusion site endovas	Gender
DM	HTN	mixed hyperlipidemia
Smoking	Drinking	Previous stroke
Af history	Gout	CAD
CHF	CKD	Inhospital pneumonia
Inhospital UTI	IMT ipsilateral	Duplecx plaque type
Endovascular mTICI grading	Admission mRS	Admission CT ASPECTS
CTP ischemic core	CTP mismatch	CTP perfusion Tmax
Age	Admission NIHSS	Admission Barthel Index
SBP	DBP	BMI
Admission LDL	Admission HDL	Triglyceride
Total Cholesterol,hSCRP	BUN	Cr
Uric acid	HbA1c	Ac Sugar
Ipsi CCA RI	Contra CCA RI	Ipsi ICA RI
Contra ICA RI	Ipsi ECA RI	Contra ECA RI,
Ipsi VA RI	Contra VA RI	Plaque index ipsi

Plaque index contra	Ipsi CCA PI	Contra CCA PI
Ipsi ICA PI	Contra ICA PI	Ipsi ECA PI
Contra ECA PI	Ipsi VA PI	Contra VA PI
IMT ipsilateral		

2. Prognosis variables

Follow up CT cerebral bleeding	MBD mRS
MBD Barthel Index	MBD NIHSS

Figures

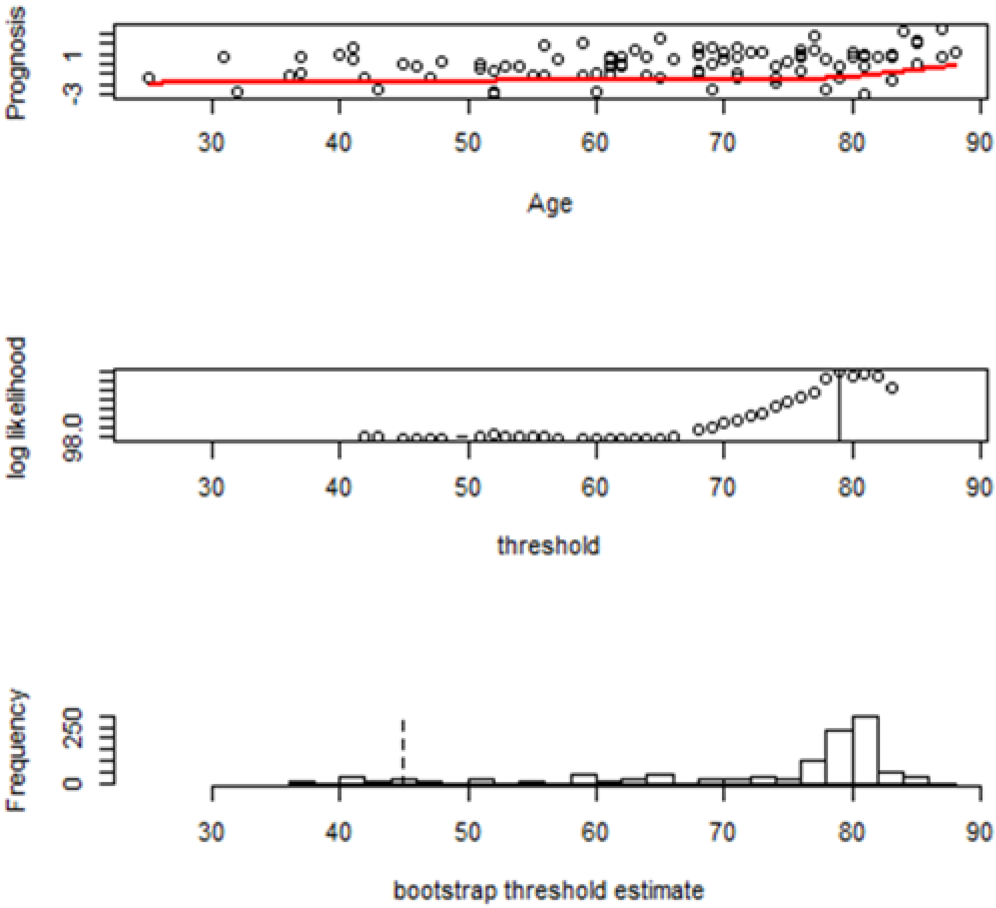

Figure 1

Threshold of the Age