Withdrawal of Life-Sustaining Therapies in Stroke

An Insight from Florida Stroke Registry

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Disclosures

- **NIH/NINDS** K23NS126577 “MUSICA –MUsic and Speech Induced Cerebral Activation”.

- **KL2 CTSI** Career Development Award CTSI-KL2-FY2020-02, the CTSI grant award number (UL1TR002736) “Electrophysiologic Biomarkers of Consciousness Recovery: the EBC study”

- **NIH/NINDS** R01NS106014-01A1 “Recovery of Consciousness Following Intracerebral Hemorrhage (RECONFIG study)”

What do we know so far?

- Stroke is a common cause of death and disability worldwide.
- After severe acute brain injury, over a third of patients can reach independence at 6 to 12 months follow-up.
- Early DNR is associated with doubling the hazard of death independent of basic demographics, location, intraventricular hemorrhage, and ICH volume

Withdrawal of Life-Sustaining Therapies in Stroke

What?
When?
Who?
Where?
How?

Self-fulfilling Prophecy

An error that could lead to death in patients who may have chance of recovery

Table 1 Feedback received when positive test results motivate withdrawal of treatment

POSITIVE TEST RESULTS Outcome predicted: poor	
FALSE POSITIVE	**TRUE POSITIVE**
Patient dies after life-sustaining treatment is withdrawn, based on the poor prognosis	Patient dies after life-sustaining treatment is withdrawn, based on the poor prognosis
However, patient would have a good outcome (given continued life-sustaining treatment)	Regardless, patient would have a poor outcome (given continued life-sustaining treatment)
Prognosis changes outcome --> **Transformative self-fulfilling prophecy**	Prognosis does *not* change outcome --> **Operative self-fulfilling prophecy**
Outcomes observed: POOR (death of the patient) **--> Unreliable feedback**	

Table 2 Feedback received when negative test results motivate continuation of treatment

NEGATIVE TEST RESULTS Outcome predicted: good	
FALSE NEGATIVE	**TRUE NEGATIVE**
Life-sustaining treatment is continued based on good prognosis	Life-sustaining treatment is continued based on good prognosis
However, patient has poor outcome after continuation of treatment, based on the good prognosis (which is an error signal)	Indeed, patient has good outcome after continuation of treatment, based on the good prognosis (yielding no error signal)
Prognosis does *not* change outcome --> **No self-fulfilling prophecy**	Prognosis does *not* change outcome --> **No self-fulfilling prophecy**
Outcome observed: POOR **--> Reliable feedback**	**Outcome observed: GOOD** **--> Reliable feedback**

Mertens M, et al. J Med Ethics

Dr. J. Claude Hemphill on ICH Score

"Ironically, in the first draft of the manuscript, I did not even include these numbers, just an overall graph. But one of the reviewers demanded they be put in and, as a young investigator wanting to get published, I complied. It has been extremely disappointing when I hear that physicians have chosen to not treat a patient aggressively or transfer to a higher level of care hospital because of a high ICH Score.

I actually recall a conversation at the International Stroke Conference around 2003, when an ED physician in a community hospital thanked me for developing the ICH Score, because now he had a reason to avoid accepting transfers from smaller community hospitals for patients with ICH Scores of 4 or higher because they would always do poorly. This saddened me."

Key Questions

1. What are the factors associated with the decision to withhold or withdraw life-sustaining therapy in hospitalized acute ischemic stroke, intracerebral hemorrhage, and subarachnoid hemorrhage patients?

1. What is the relation between impaired level of consciousness and the decision to withhold or withdraw life-sustaining therapy after acute ischemic and hemorrhagic strokes?

Key Questions

1. What are the factors associated with the decision to withhold or withdraw life-sustaining therapy in hospitalized acute ischemic stroke, intracerebral hemorrhage, and subarachnoid hemorrhage patients?

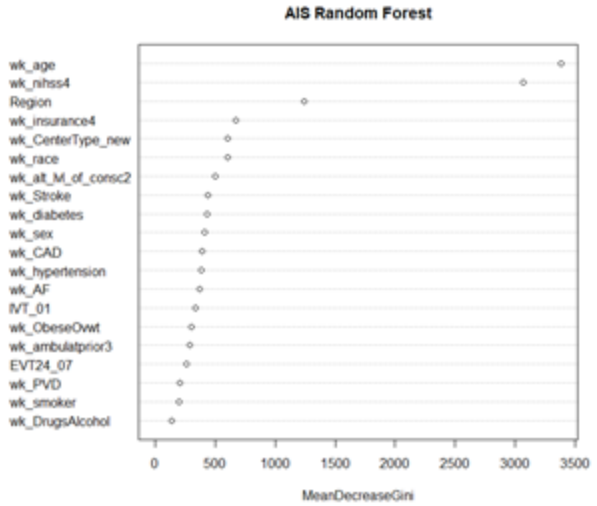
Determinants of WLST in ICH, SAH, AIS

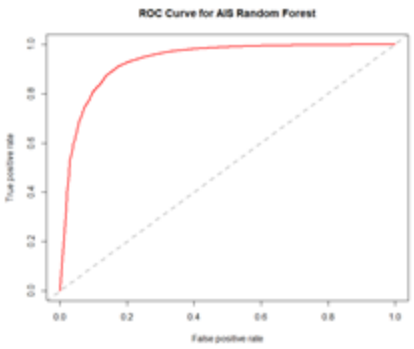
AIS: 309,393 **ICH:** 47,485 **SAH**: 16,694

1. We generated importance plot using Random Forest

1. After reviewing the plots, we selected the most predictive variables that contribute to WLST

3. Then we performed ROC-AUC using Logistic Regression and and Random Forest (Training/testing/validation 75/15/15)





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Alkhachroum et al., not published

Determinants of WLST in ICH, SAH, AIS

	AIS: 309,393	**ICH:** 47,485	**SAH**: 16,694
WLST	**9%**	**28%**	**19%**

- WLST were older (77 vs. 69 years), more women (57% vs. 49%), White (76% vs. 67%)
- Greater stroke severity on NIHSS ≥ 5 (29% vs.19%)
- More likely to be treated in comprehensive stroke centers (52% vs. 44%)
- More likely to have Medicare insurance (53% vs. 44%), less likely to be uninsured (8% vs. 13%)
- More likely to undergo surgical treatments (1.2% vs 0.3%)
- More likely to have impaired level of consciousness (38% vs. 12%)

Florida Stroke Registry

Alkhachroum et al., not published

Determinants of WLST in ICH, SAH, AIS

AIS: 309,393

Age
Stroke Severity
Region
Insurance Status
Stroke Center Type
Race
Consciousness Status

ICH: 47,485

Age
Consciousness Status
Region
Race
Insurance Status
Stroke Center Type
Ambulation

SAH: 16,694

Age
Consciousness Status
Region
Insurance
Race
Stroke Center Type

Florida Stroke Registry

Alkhachroum et al., not published

Determinants of WLST in ICH, SAH, AIS

AIS: 309,393

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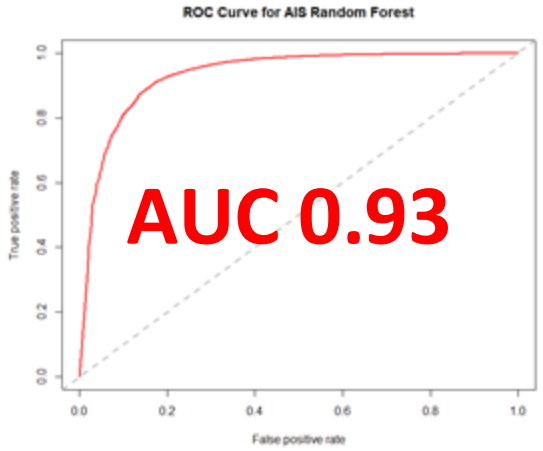

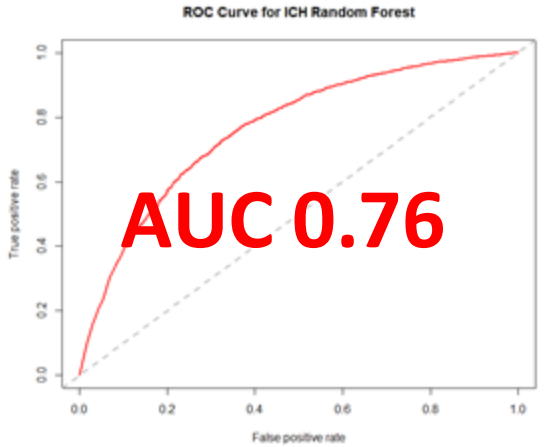

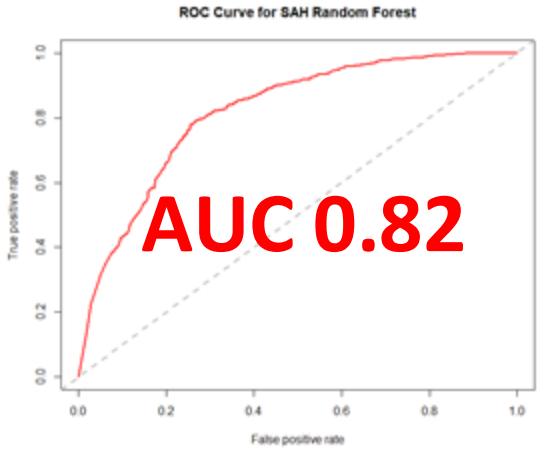

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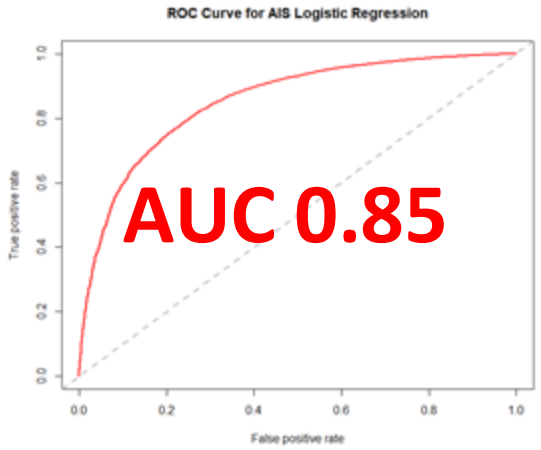
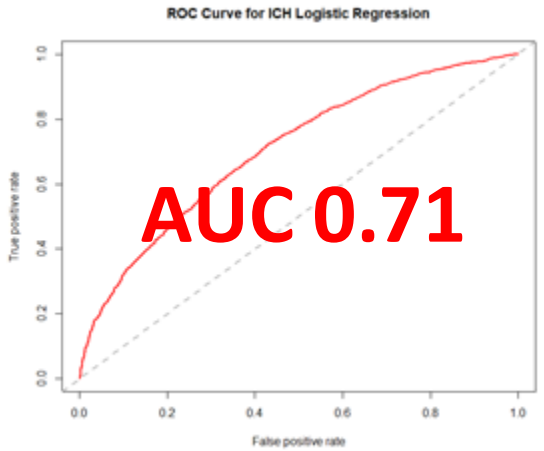
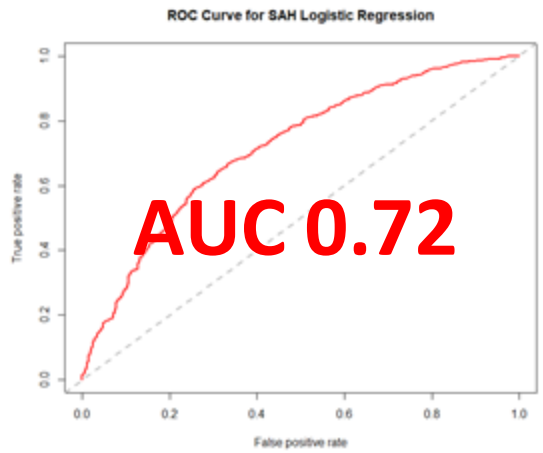






Key Questions

1. What are the factors associated with the decision to withhold or withdraw life-sustaining therapy in hospitalized acute ischemic stroke, intracerebral hemorrhage, and subarachnoid hemorrhage patients?

   - Among acute hospitalized stroke patients; age, level of consciousness, disease severity, state region, race, insurance status, ambulation status at baseline, and stroke center type could contribute to the decision to WLST.

Key Questions

2. What is the relation between impaired level of consciousness and the decision to withhold or withdraw life-sustaining therapy after acute ischemic and hemorrhagic strokes?

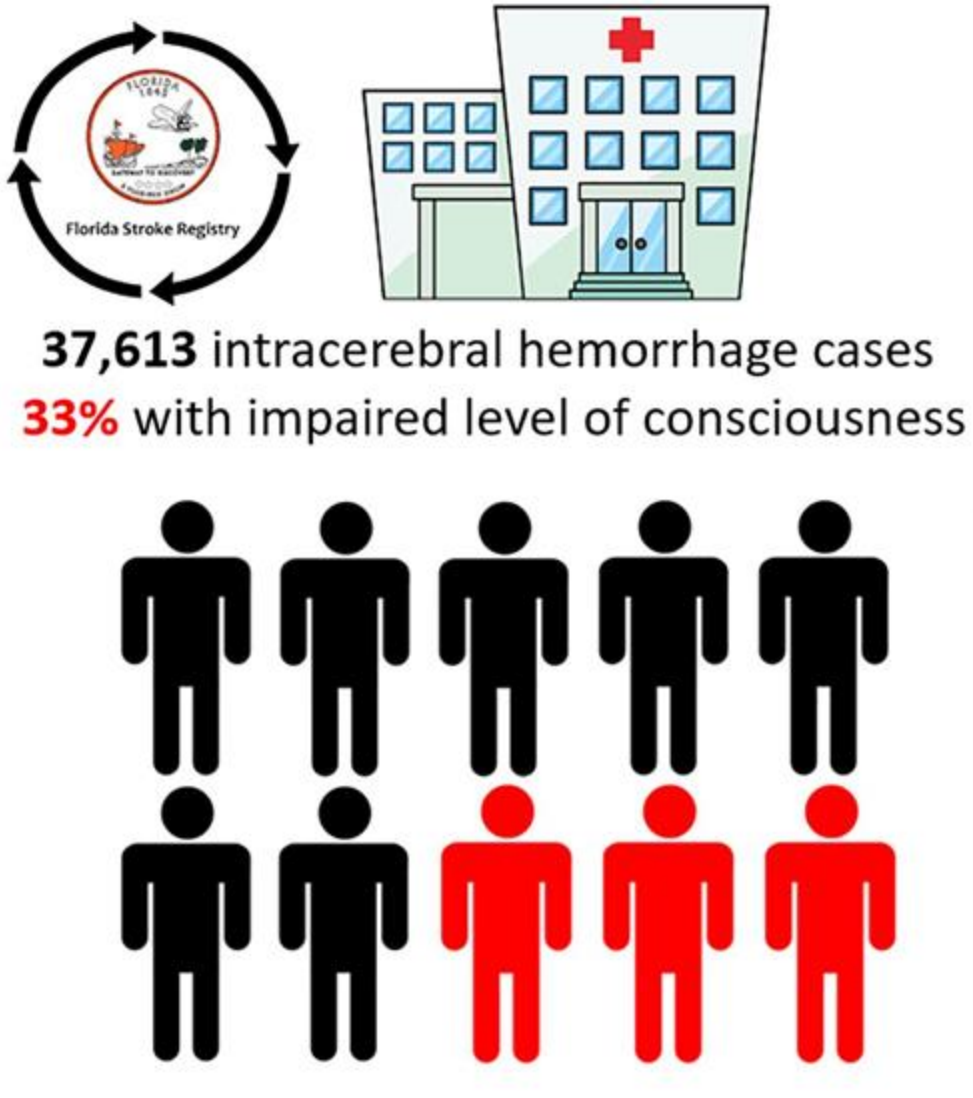
Stroke

CLINICAL AND POPULATION SCIENCES

Withdrawal of Life-Sustaining Treatment Mediates Mortality in Patients With Intracerebral Hemorrhage With Impaired Consciousness

Ayham Alkhachroum, MD; Antonio J. Bustillo, MSPH; Negar Asdaghi, MD, MSc; Erika Marulanda-Londono, MD; Carolina M. Gutierrez, PhD; Daniel Samano, MD, MPH; Evie Sobczak, MS; Dianne Foster, BSN, MBA; Mohan Kottapally, MD; Amedeo Merenda, MD; Sebastian Koch, MD; Jose G. Romano, MD; Kristine O'Phelan, MD; Jan Claassen, MD, PhD; Ralph L. Sacco, MD, MS; Tatjana Rundek, MD, PhD

Stroke. 2021;52:3891–3898. DOI: 10.1161/STROKEAHA.121.035233



Accounting for basic demographics, comorbidities, hospital size and teaching status

Alkhachroum et al, Stroke, 2021

Future Shock: Does Pessimism Contribute to Poor Outcome After Intracerebral Hemorrhage?

H.E. Hinson

Originally published 29 Sep 2021 | https://doi.org/10.1161/STROKEAHA.121.036761 | Stroke. 2021;52:3899–3900

"If unearned pessimism is indeed contributing to poor outcomes as this work suggests, it may be prudent to delay prognostication by several days, if not longer, in comatose patients in all but the clearest cases (loss of all brain stem reflexes, for example).

To move forward, clinicians need more sensitive and specific methods of determining prognosis in coma after intracerebral hemorrhage, likely combining the modalities of physical exam plus biomarkers (advanced imaging, electrophysiological, fluid based) as has been done effectively in cardiac arrest.

Developing these tools will require clinicians to suspend prognostic judgment for proper study in clinical trials.

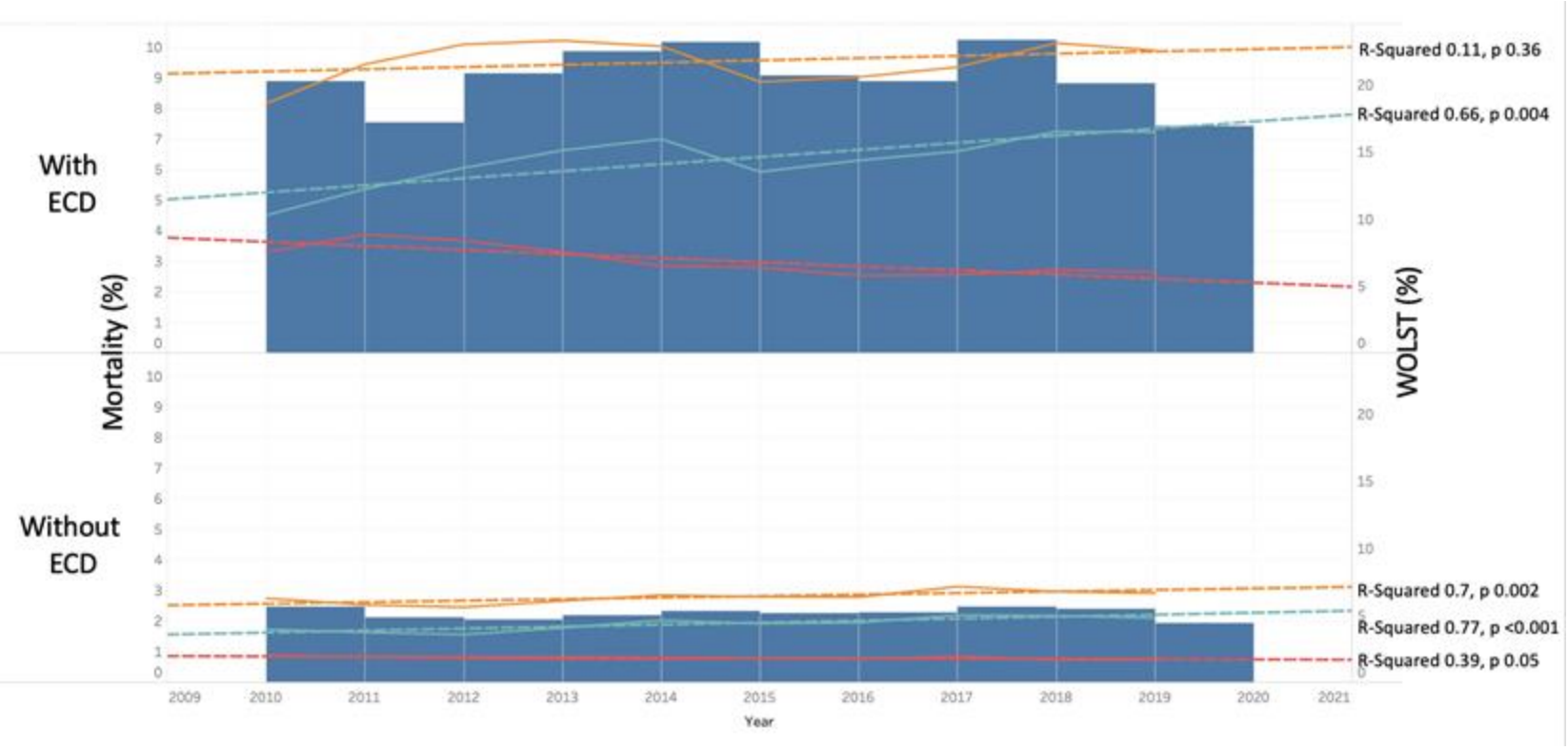
If we hope to cure coma, as the Neurocritical Care Society aims to do, early surrender may no longer be an option."

SHARE April 05, 2022; 98 (14) RESEARCH ARTICLE

Association of Acute Alteration of Consciousness in Patients With Acute Ischemic Stroke With Outcomes and Early Withdrawal of Care

Ayham Alkhachroum, Antonio J. Bustillo, Negar Asdaghi, Hao Ying, Erika Marulanda-Londono, Carolina M. Gutierrez, Daniel Samano, Evie Sobczak, Dianne Foster, Mohan Kottapally, Amedeo Merenda, Sebastian Koch, Jose G. Romano, Kristine O'Phelan, Jan Claassen, Ralph L. Sacco, Tatjana Rundek

First published February 15, 2022, DOI: https://doi.org/10.1212/WNL.0000000000200018



- 238,989 patients – 14% with ECD
- WLST significantly mediated the effect of ECD on mortality (mediation effect 265, 95% CI 217–314).

Even after adjusting for basic demographics (age, sex, race/ethnicity) and NIHSS

Alkhachroum et al, Neurology, 2022

Key Questions

2. What is the relation between impaired level of consciousness and the decision to withhold or withdraw life-sustaining therapy after acute ischemic and hemorrhagic strokes?
   - In acute ischemic and hemorrhagic strokes, impaired level of consciousness is associated with increased mortality, largely influenced by the decision to withdraw life-sustaining therapies.

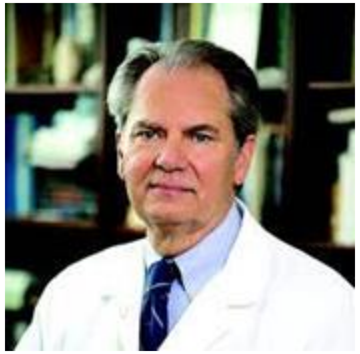
Future Directions

- We need biomarkers to detect and predict recovery of consciousness after acute brain injury – shortly after injury
- To understand better the complex process of recovery – physiologic and non-physiologic factors
- More data on long-term recovery
- Patient-oriented outcomes
- Therapeutics +biomarkers toward a personalized medicine approach

Thank you













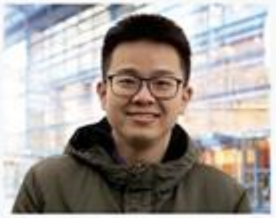








American Heart Association.



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NIH National Institute of Neurological Disorders and Stroke

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The BUONICONTI FUND