Neurological Prognostication of Post-Cardiac-Arrest Coma Patients Using EEG Data: A Dynamic Survival Analysis Framework with Competing Risks

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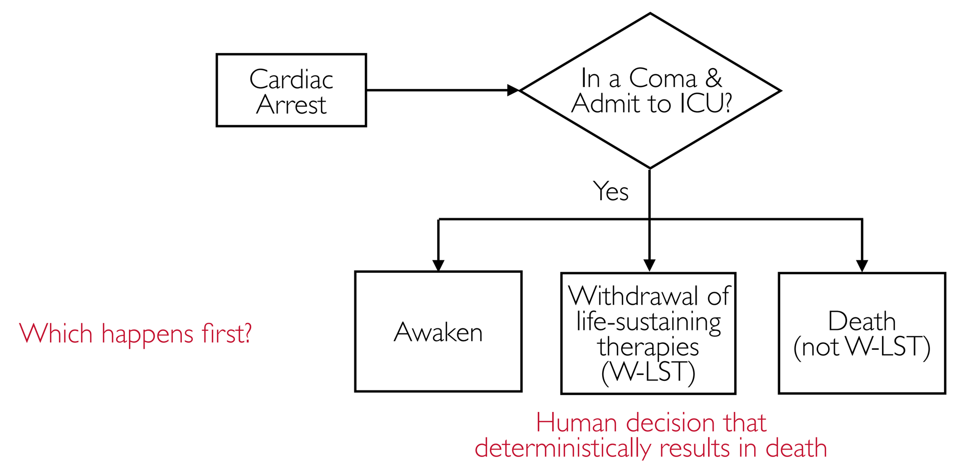
Neurological Prognostication



Importance of *neurological prognostication* (forecast neurological outcome) for cardiac arrest patients in a *coma*

- Withdrawal of life-sustaining therapies (W-LST) → inevitable death
- Some patients who died from W-LST may have recovered if kept on life-sustaining therapies

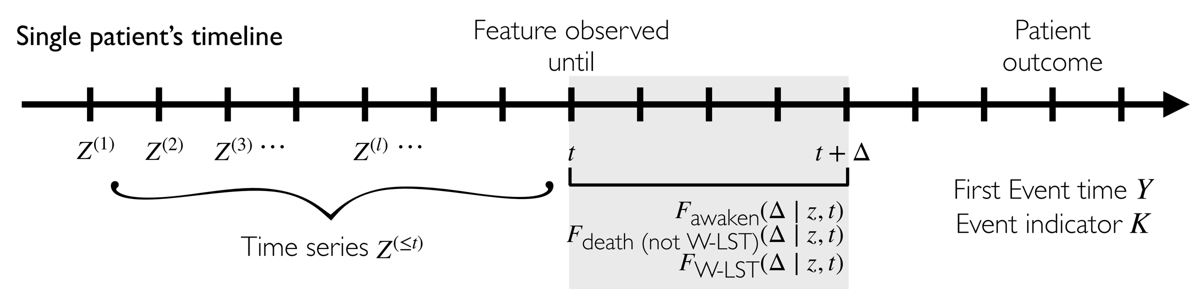
Prior literature:

- Existing methods are not truly dynamic - patients' time series must be the same; make predictions at a single time after cardiac arrest
- Issues with the common classification setup - need to exclude patients who died from W-LST

Main Contributions

- Propose a framework for neurological prognostication of post-cardiac-arrest coma patients:
  - works with any existing *dynamic competing risks* (DCR) model
  - is dynamic and makes predictions for a patient over time as more time-series data becomes available
  - model three competing risks simultaneously as to what happens first to a patient
- Derive a classifier from DCR model to aid decision-making
- Develop a patient-specific heat map visualization for the classifier

Dynamic Competing Risks (DCR) Model



Training data, patient i

- Feature vector with corresponding time stamp:
  $Z_i := \big((X_i^{(1)}, X_i^{(2)}, \ldots, X_i^{(L_i)}), (T_i^{(1)}, T_i^{(2)}, \ldots, T_i^{(L_i)})\big)$
- Event indicator (which event happens first):
  $K_i \in \{\text{awaken, death (not W-LST), W-LST, censoring}\}$,
- Time of earliest occurring event: $Y_i \in \mathbb{R}$

when data collection ended, patient was still in a coma so true eventual earliest outcome is unknown

Prediction target - cumulative incidence function (CIF)

The probability of event j happening within time duration $\Delta \ge 0$ starting from time $t \in \mathbb{R}$, given a time series observed up until time t

$$F_j(\Delta \mid z, t) := \mathbb{P}(Y \le t + \Delta, K = j \mid Z^{(\le t)} = z^{(\le t)}, Y > t) \quad \text{for } \Delta \ge 0$$

Examples of DCR models

- Fine and Gray (1996), using only last time step's data
- Dynamic-DeepHit (Lee et al., 2019)
- DDRSA (Venkata and Bhattacharyya, 2022), with modification
- SurvLatent ODE (Moon et al., 2022)

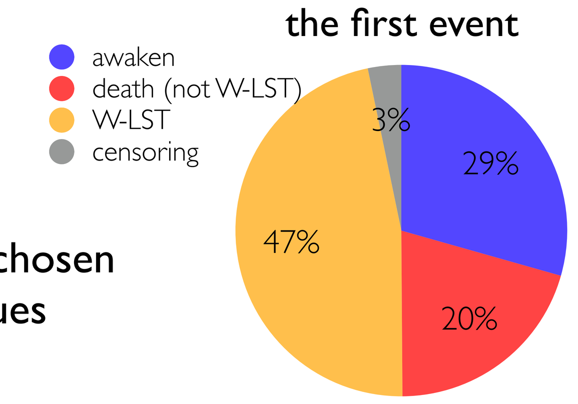
Generalizable Insights for Neurological Prognostication of Post-Cardiac-Arrest Coma Patients:

- The classical Fine and Gray (1999) model is highly competitive
- We recommend using a competing risks setup with the three competing events we model

Real-World Clinical Data Experiment

A real-world dataset of 922 post-cardiac-arrest coma patients, with EEG data recorded over time

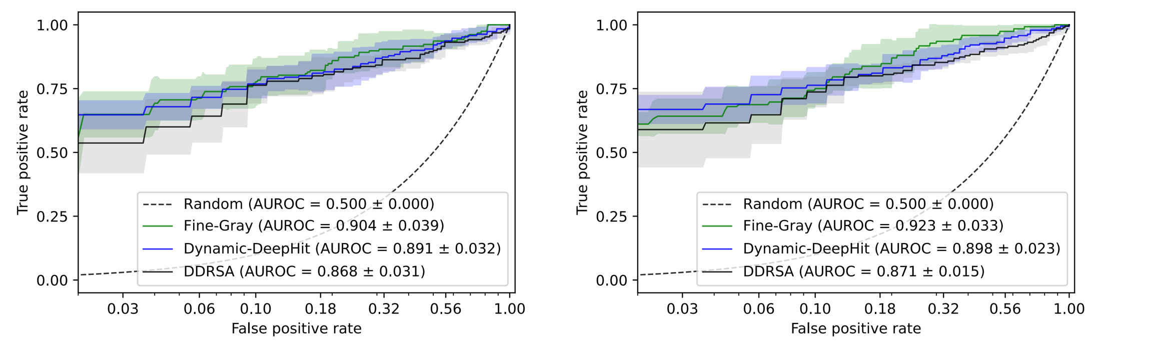
Proportion of the first event



$t = 6,\ 12$ and $\Delta = 24,\ 48,\ 72$ chosen for evaluation; can be other values without model re-training

Table 1: Test set c-indices (average ± standard deviation across five experimental repeats) for three DCR models. The entries with bold values represent the highest average c-index for each (event, t, Δ) combination.

Model	Prediction time	Event	Evaluation time horizon $\Delta = 24$ hrs	$\Delta = 48$ hrs	$\Delta = 72$ hrs
Fine and Gray	$t = 6$	awaken	**0.853 ± 0.017**	**0.874 ± 0.012**	**0.875 ± 0.012**
		death (not W-LST)	0.633 ± 0.171	0.673 ± 0.081	0.684 ± 0.061
		W-LST	0.691 ± 0.063	**0.634 ± 0.050**	**0.652 ± 0.039**
	$t = 12$	awaken	0.831 ± 0.032	0.851 ± 0.023	0.854 ± 0.023
		death (not W-LST)	**0.751 ± 0.110**	**0.709 ± 0.040**	0.713 ± 0.044
		W-LST	0.709 ± 0.082	**0.675 ± 0.035**	**0.681 ± 0.024**
Dynamic-DeepHit	$t = 6$	awaken	0.851±0.018	0.867±0.012	0.864±0.017
		death (not W-LST)	**0.702±0.080**	**0.684±0.096**	**0.697±0.071**
		W-LST	**0.742±0.103**	0.612±0.062	0.621±0.031
	$t = 12$	awaken	**0.847±0.038**	**0.859±0.020**	**0.858±0.024**
		death (not W-LST)	0.701±0.078	0.699±0.042	**0.722±0.044**
		W-LST	**0.739±0.076**	0.640±0.028	0.666±0.017
DDRSA	$t = 6$	awaken	0.821±0.032	0.845±0.028	0.836±0.030
		death (not W-LST)	0.599±0.072	0.615±0.059	0.633±0.075
		W-LST	0.677±0.151	0.626±0.121	0.637±0.100
	$t = 12$	awaken	0.825±0.021	0.818±0.025	0.798±0.027
		death (not W-LST)	0.681±0.095	0.651±0.086	0.651±0.074
		W-LST	0.663±0.126	0.652±0.092	0.670±0.068



$(a)\ t = 6, \Delta = 24$ $(b)\ t = 12, \Delta = 24$

Figure 3: Test set ROC curve (average curve ± standard deviation intervals across five experimental repeats). The x-axis is on a log scale to emphasize the low FPR regime.

Ablation Study with Fewer Events

1. With two competing risks:
   - awaken
   - death (not W-LST)
2. With single event:
   - awaken

↓

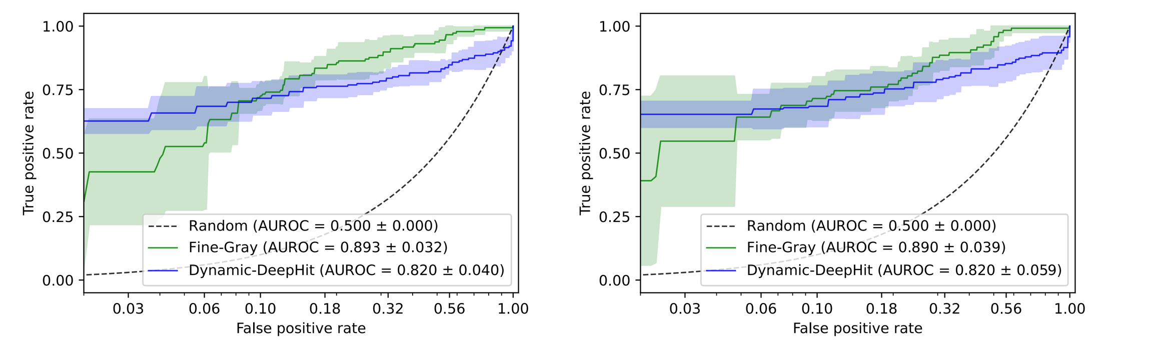
Three competing events setup provided more information without sacrificing accuracy

Table 3: Test set c-indices (average ± standard deviation across five experimental repeats) for the Fine and Gray model and Dynamic-DeepHit with two competing events. The entries with bold values represent the highest average c-index for each (event, t, Δ) combination.

Model	Prediction time	Event	Evaluation time horizon $\Delta = 24$ hrs	$\Delta = 48$ hrs	$\Delta = 72$ hrs
Fine and Gray	$t = 6$	awaken	0.835 ± 0.030	**0.870 ± 0.012**	**0.867 ± 0.008**
		death (not W-LS)	**0.723 ± 0.040**	**0.697 ± 0.075**	**0.707 ± 0.061**
	$t = 12$	awaken	0.822 ± 0.020	0.855 ± 0.014	0.851 ± 0.014
		death (not W-LS)	**0.664 ± 0.272**	**0.678 ± 0.146**	**0.706 ± 0.101**
Dynamic-DeepHit	$t = 6$	awaken	**0.852 ± 0.019**	0.858 ± 0.011	0.855 ± 0.007
		death (not W-LS)	0.638 ± 0.074	0.622 ± 0.073	0.642 ± 0.050
	$t = 12$	awaken	**0.842 ± 0.017**	**0.860 ± 0.007**	**0.857 ± 0.007**
		death (not W-LS)	0.599 ± 0.092	0.639 ± 0.095	0.649 ± 0.078

Table 4: Test set c-indices (average ± standard deviation across five experimental repeats) for the Fine and Gray model and Dynamic-DeepHit with a single event. The entries with bold values represent the highest average c-index for each (event, t, Δ) combination.

Model	Prediction time	Event	Evaluation time horizon $\Delta = 24$ hrs	$\Delta = 48$ hrs	$\Delta = 72$ hrs
Fine and Gray	$t = 6$	awaken	**0.864 ± 0.021**	**0.883 ± 0.013**	**0.877 ± 0.010**
	$t = 12$	awaken	0.843 ± 0.023	**0.866 ± 0.018**	**0.861 ± 0.015**
Dynamic-DeepHit	$t = 6$	awaken	0.850 ± 0.031	0.861 ± 0.019	0.855 ± 0.021
	$t = 12$	awaken	**0.845 ± 0.021**	0.855 ± 0.014	0.855 ± 0.018



$(a)\ t = 6, \Delta = 24$ $(b)\ t = 12, \Delta = 24$

Figure 4: Test set ROC curve in the case of modeling two competing events (average curve ± standard deviation intervals across five experimental repeats). The x-axis is on a log scale to emphasize the low FPR regime.

Framework with DCR Model

A Derived Classifier from DCR Model

Key idea: condition on the event W-LST not happening for test patient

Reason: the classifier is meant to help with deciding on whether to withdraw the test patient from life-sustaining therapies so we assume that it has not happened

probability of death (not W-LST) within time Δ

$$P_{\text{death (not W-LST)}}(\Delta \mid z, t) := \frac{\boxed{F_{\text{death (not W-LST)}}(\Delta \mid z, t)}}{\boxed{F_{\text{awaken}}(\infty \mid z, t) + F_{\text{death (not W-LST)}}(\infty \mid z, t)}}$$

probability of awakening within time Δ

$$P_{\text{awaken}}(\Delta \mid z, t) := \frac{\boxed{F_{\text{awaken}}(\Delta \mid z, t)}}{\boxed{F_{\text{awaken}}(\infty \mid z, t) + F_{\text{death (not W-LST)}}(\infty \mid z, t)}}$$

probability of eventually awakening or eventually dying (not of W-LST)

If $\dfrac{P_{\text{death (not W-LST)}}(\Delta \mid z, t)}{P_{\text{awaken}}(\Delta \mid z, t)} > 1$: predict *positive (bad)*

Otherwise: predict *negative (good)*

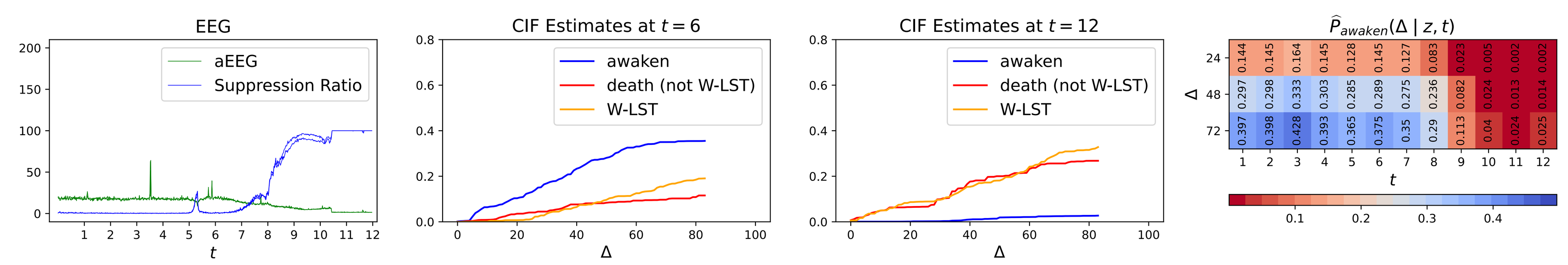
Three competing events, only one happens first:

- awakening
- death (not W-LST)
- W-LST

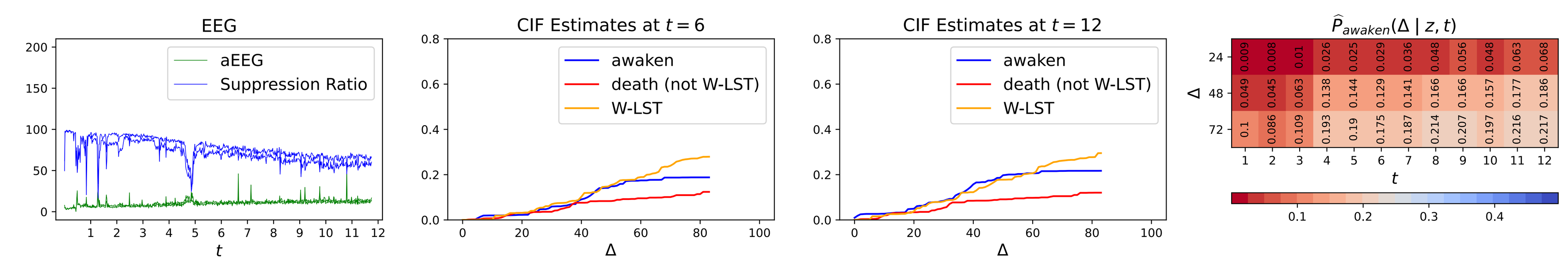
Goal

- Better formulate the neurological prognostication problem
- Help clinicians interpret the information contained in the CIFs

Patient-Specific Visualization



Example Patient 1: died (not from W-LST) at hour 17



Example Patient 2: still in a coma at hour 118

Future Work

- New DCR model that considers events happening recurrently, not only first hitting time
- Better evaluation of the derived binary classifier with censoring data
- A decision support system that is deployment-ready

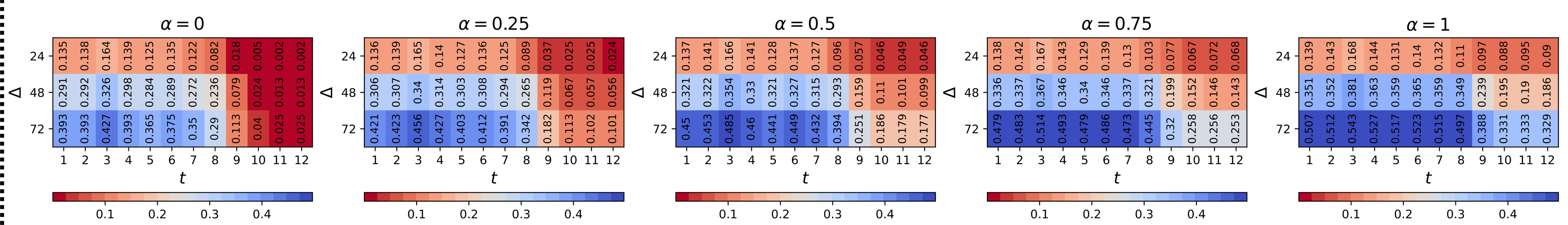
Alternative approach to deriving a binary classifier (worth investigating further)

Instead of conditioning on W-LST not happening, reason about counterfactual outcome of whether patient would have awakened or would have died (not of W-LST) *if W-LST were not an option*

- e.g., assume that among patients who died from W-LST, a fraction $\alpha \in [0,1]$ of them would have awaken instead if W-LST were not an option

$$\widetilde{P}_{\text{awaken}}(\Delta \mid z, t) = F_{\text{awaken}}(\Delta \mid z, t) + F_{\text{W-LST}}(\Delta \mid z, t) \times \alpha$$

Note: α is unknown so we make heat maps of $\widetilde{P}_{\text{awaken}}$ for different values of α



Example Patient 1