Analysis of the TBI Data 6
Joint modeling of ICP and ICULOS (new)

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1 Background

Here we are interested in the relationship between IUCLOS (outcome) and ICP values (adjusted by other factors). Taking ICULOS as the outcome, we're really interested in the relationship between time to ICU discharge and other factors, including ICP. Meanwhile, since ICP measurements is a repeated measure over-time (as well as some other factors), we can not simply take the mean of ICP as the covariate, instead, a better way is to use joint modeling in which we use survival model to model ICULOS and use model the ICP values using longitudinal modeling method.

Specifically,

$$\begin{cases} h_i(t|\mathbf{w}_i, m_i(t)) = h_0(t)\exp[\boldsymbol{\gamma}^t\mathbf{w}_i + \alpha m_i(t)] \\ y_i(t) = m_i(t) + \varepsilon_i(t) = \mathbf{x}_i^t(t)\boldsymbol{\beta} + \mathbf{z}_i^t(t)\mathbf{b} + \varepsilon_i(t), \quad \varepsilon_i(t) \sim N(0, \sigma^2) \end{cases} \tag{1}$$

where t is the time to event (ICU discharge), i.e. ICULOS; $m_i(t)$ is the ICP measurements for subject i at time t; $\mathbf{w}_i$ are the time independent variables for subject i; $\mathbf{x}_i$ are the fixed effect covariates and $\mathbf{z}_i$ are the random effects covariates.

In terms of survival model, patients who died during the ICU stay are defined as censored (event=0) and patients who survived during the ICU stay are cases (event=1).

Note

Since there is no direct indicator variable for ICU discharge status (death or alive), I create a variable for it and **assigned it as 0 (means death at ICU discharge) if** $ICULOS >= HospLOS$**,** otherwise 1 (means alive at ICU discharge). Thus with this method, patients who have either ICULOS or HospLOS missing can not be defined as case or censoring and therefore will not be included in the analysis.

2 Some results

	Event Process				Longitudinal Process		
	Value	Std.Err	p-value		Value	Std.Err	p-value
Age	-0.01	0.01	0.2218	(Intercept)	20.39	2.09	< 0.0001
Gendermale	-0.03	0.31	0.9115	Age	-0.16	0.03	< 0.0001
eyereactivity1	-0.53	0.45	0.2472	Gendermale	3.46	1.52	0.0227
eyereactivity2	0.01	0.23	0.9792	eyereactivity1	2.82	1.43	0.0489
newCTD2	-0.64	0.33	0.0539	eyereactivity2	-0.78	0.84	0.3535
newCTM	-0.89	0.26	0.0006	newCTD2	4.42	1.23	0.0003
Assoct	-0.02	0.02	0.4104	newCTM	4.03	1.03	0.0001
$\log(\xi_1)$	-7.39	0.73		HAI	0.00	0.00	0.1607
$\log(\xi_2)$	-5.63	0.64		GCS.sum	-0.32	0.11	0.0054
$\log(\xi_3)$	-5.48	0.64		$\log(\sigma)$	2.05	0.02	
$\log(\xi_4)$	-4.81	0.65					
$\log(\xi_5)$	-5.04	0.67		D_{11}	37.82	11.19	
$\log(\xi_6)$	-4.72	0.69					
$\log(\xi_7)$	-4.15	0.73					

Table 1: Parameter estimates, standard errors and p-values under the joint modeling analysis. D_{ij} denote the ij-element of the covariance matrix for the random effects.

	Event Process				Longitudinal Process		
	Value	Std.Err	p-value		Value	Std.Err	p-value
Age	-0.01	0.01	0.2155	(Intercept)	19.46	2.52	< 0.0001
Gendermale	-0.03	0.31	0.9176	Age	-0.16	0.03	< 0.0001
eyereactivity1	-0.53	0.45	0.2478	Gendermale	3.40	1.52	0.0251
eyereactivity2	0.01	0.23	0.9742	eyereactivity1	2.74	1.44	0.0563
newCTD2	-0.63	0.33	0.0565	eyereactivity2	-0.81	0.86	0.3429
newCTM	-0.88	0.26	0.0006	newCTD2	4.48	1.24	0.0003
Assoct	-0.02	0.02	0.3854	newCTM	4.11	1.06	0.0001
$\log(\xi_1)$	-7.37	0.73		HAI	0.00	0.00	0.2137
$\log(\xi_2)$	-5.61	0.63		GCS.sum	-0.33	0.12	0.0047
$\log(\xi_3)$	-5.46	0.64		PCO2	0.03	0.05	0.4988
$\log(\xi_4)$	-4.80	0.65		$\log(\sigma)$	2.05	0.02	
$\log(\xi_5)$	-5.02	0.67					
$\log(\xi_6)$	-4.71	0.68		D_{11}	38.11	11.29	
$\log(\xi_7)$	-4.13	0.72					

Table 2: Parameter estimates, standard errors and p-values under the joint modeling analysis. D_{ij} denote the ij-element of the covariance matrix for the random effects.

Interpretation & Clarification

1. In *Event Process* (left part of the table), the value corresponds to "Assoct" is the estimate for parameter α in Equation (1). Negative value means that increased ICP values leads to longer time to event (smaller hazard rate), i.e. ICU discharge.

2. The right side of the tables above are the *Longitudinal Process*, where the ICP is the outcome variable. I fitted two models here which are the only two I can get the results. I tried include MAP, SjvO2 or other variables, but the models failed to converge.