

Supplementary material

Garson's algorithm for 2 hidden layers

Algorithm 1: Garson weights algorithm - 2 hidden layers

Input: connection weight matrices W_1, W_2, W_3 for input-hidden1, hidden1-hidden2, hidden2-output layers of dimensions $(\alpha \times \alpha_1), (\alpha_1 \times \alpha_2), (\alpha_2 \times 1)$ respectively, where α is the number of the input nodes, α_1 is the number of the nodes in hidden layer 1 and α_2 the number of nodes in hidden layer 2

Output: relative importance R_j

- 1 $W = (W_1 W_2 W_3)^T$ of dimensions $(1 \times \alpha)$
 - 2 $W^* = |W|$
 - 3 $R_j = \frac{W_{1j}^*}{\sum_{j=1}^p W_{1j}^*}, \forall j \in (1, 2, \dots, \alpha)$
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Relative importance for each time interval

Neural network 1h	Rel-Imp.	Neural network 2h	Rel-Imp.
Interval 1	0.125	Interval 1	0.128
Interval 4	0.025	Interval 4	0.029
Interval 5	0.022	Interval 3	0.027
Interval 3	0.020	Interval 5	0.025
Interval 6	0.017	Interval 6	0.018
Interval 7	0.011	Interval 7	0.014
Interval 2	0.004	Interval 2	0.010
Interval 8	0.004	Interval 9	0.006
Interval 9	0.003	Interval 8	0.005
Interval 10	0.003	Interval 10	0.003

Table 1: Relative importance for each of the 10 time intervals for the neural networks (training set).

Criteria for variable pre-selection

The data provided by UNOS included 62294 patients who underwent liver transplant surgery between 2005 and 2015. Standard analysis files contained 657 variables regarding donors and patients (candidates and recipients). These regarded:

- **identification variables** like *unique encrypted person id*, *unique encrypted donor id*, *candidate listing center*, *OPO serving transplant center*.
- **important dates** such as *transplant date*, *graft failure date*, *cohort censoring date*, *death date*, *graft follow-up date*.
- **status variables**: *death status* (in 1, 3, 5 years and later), *graft failure-free status* (in 1, 3, 5 years and later).
- **demographic variables** such as *age*, *gender*, *race*, *ethnicity*, *socioeconomic status* and *education level*.
- **behavioral variables** e.g. *smoking history*, *alcohol consumption*, *physical activity level*, *cocaine or other drug history*.
- **physiological variables** for example *blood type*, *etiology* (cause of disease), *laboratory measurements* for arginine, serum creatinine, serum sodium, total bilirubin etc.

From those, 97 risk factors (52 donor, 45 patient characteristics) were pre-selected. Our variable pre-selection was based on the following **clinical** and **statistical** grounds:

1. Clinical importance of particular prognostic factors in bibliography regarding LT.
2. Experts in LT from Leiden University Medical Centre (LUMC).
3. Variables available after performing LT were discarded.
4. Variables with more than 40% missing values were excluded. To explain this, it would be infeasible to reconstruct variables with more than 40% missingness with plausible values based on the distribution of the observed data, as they would most likely be noisy factors.
5. Categorical variables with very unbalanced classes (less than 1% sample size for a level) were dropped as they could pose a serious threat to the modelling procedure.
6. Redundant variables were discarded (e.g. *age of the donor* in years and in months, or a numerical variable with one value, or a categorical variables with a single level).

For patients, there were several variables referring to both candidates and recipients as for instance *last encephalopathy*, *diabetes* or *hypertension status*. From those, we pre-selected the ones corresponding to the recipients as they were more relevant for this project. Keeping the variables for the candidates would be more relevant if the focus was on the waiting list mortality.

Individual characteristics

Variable	Value	Variable	Value
Donor age	42	On life support	'No'
Donor type	'Donor Brain Dead'	Pre-treatment status	'Not hospitalised'
Diabetes	'No'	Race	'White'
HCV serology status	'No'	Recipient age	56
log(Total cold ischemic time)	1.99	Re-transplantation	'No'

Table 2: Values for 10 potentially prognostic variables of the reference patient according to our models sorted in alphabetical order. The patient was constructed using the median values for the continuous and the mode values for categorical variables. Patient characteristics were obtained from the test data.

Variable	Value	Variable	Value
Donor age	39	On life support	'Yes'
Donor type	'Donor Brain Dead'	Pre-treatment status	'Intense Care Unit'
Diabetes	'No'	Race	'White'
HCV serology status	'Yes'	Recipient age	44
log(Total cold ischemic time)	2.09	Re-transplantation	'No'

Table 3: Values for 10 potentially prognostic variables of a patient censored at 1.12 years according to our models sorted in alphabetical order. Patient characteristics were obtained from the test data.

Variable	Value	Variable	Value
Donor age	68	On life support	'No'
Donor type	'Donor Brain Dead'	Pre-treatment status	'Not hospitalised'
Diabetes	'Yes'	Race	'White'
HCV serology status	'No'	Recipient age	61
log(Total cold ischemic time)	2.08	Re-transplantation	'No'

Table 4: Values for 10 potentially prognostic variables of a patient censored at 6.86 years according to our models sorted in alphabetical order. Patient characteristics were obtained from the test data.

Variable	Value	Variable	Value
Donor age	54	On life support	'No'
Donor type	'Donor Brain Dead'	Pre-treatment status	'Not hospitalised'
Diabetes	'No'	Race	'White'
HCV serology status	'Yes'	Recipient age	60
log(Total cold ischemic time)	2.08	Re-transplantation	'No'

Table 5: Values for 10 potentially prognostic variables of a patient who died at 0.12 years according to our models sorted in alphabetical order. Patient characteristics were obtained from the test data.

Survival and censoring distributions

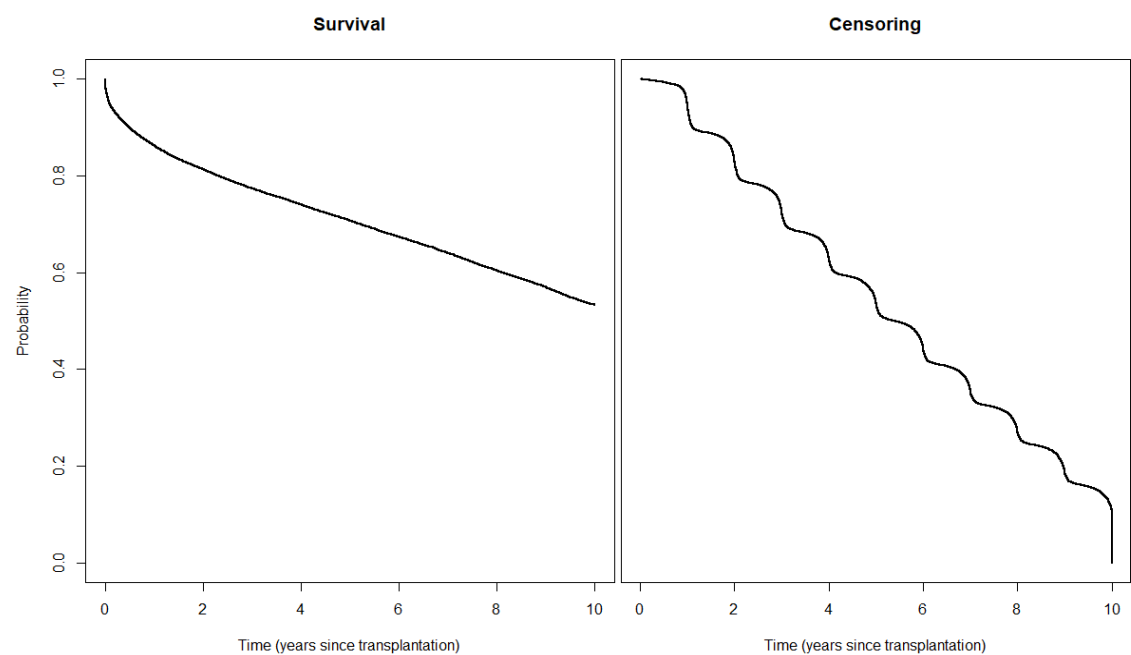


Figure 1: Survival and censoring distribution for the 41530 patients of the training data (overall graft-survival).