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REVOLUTIONISING MEDICINE - THE NEW FRONTIER

Machine Learning Survival Models Predict Timing of Onset of Nonalcoholic Fatty Liver Disease Onset in a Non-obese Population

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The Problem: No current risk models predict timing of NAFLD onset

Clinical Significance of Lean NAFLD

- NAFLD is common, worldwide prevalence 25%
- Associated with obesity, but can also occur in 'lean' (i.e. non-obese) individuals
- May progress to liver cirrhosis and hepatocellular carcinoma.
- Lean NAFLD comprises up to 40% of all NAFLD patients.
- Clinicians may have a lower index of suspicion for NAFLD in lean individuals compared to those who are obese

Time of onset is a clinically important prediction endpoint

- Current risk models use cross-sectional or case-control methods to predict NAFLD at a specific time point or within a specific period
- Do not predict actual timing of NAFLD onset
- Clinician alerted to possible NAFLD developing in lean individuals
- What is clinically useful
  > Time-to-event analysis (i.e. survival analysis) of NAFLD onset
  > In non-obese individuals (i.e. lean NAFLD)
  > To guide clinical decision making (e.g. timing of imaging).

The Solution: Machine Learning Survival Models for NAFLD onset prediction

Clinical Significance of Machine Learning

- Identify complex relationships between predictive parameters
- Combine these in a non-linear fashion
- No current studies have applied machine learning in survival modelling of time to NAFLD onset.

Study Aims

- Develop machine learning survival models to predict time of NAFLD onset in a non-obese population.
- Compare machine learning models (DeepSurv, multitask logistic regression, survival forest) with a classical model (Cox proportional hazards)

Study Methods

- Open dataset
- Single center in China comprising 16 173 non-obese individuals
- Random 80:20 split into training and test sets
- Inputs: Routine anthropometric and laboratory parameters
- Output: Time to NAFLD diagnosis in months
- Evaluation metrics: concordance index (c-index), Brier score

Results

- Total of 543 874 person-months of follow up
- Overall incidence of NAFLD 14.4% (2322 individuals)
- Median time to NAFLD onset 24.1 months (IQR 12.9-36.5)

Model	Concordance Index	Integrated Brier Score
Cox Proportional Hazards	0.86	0.08
DeepSurv	0.88	0.07
Neural MultiTask Logistic Regression	0.87	0.06
Random Survival Forest	0.86	0.07
Conditional Survival Forest	0.86	0.07
Extra Survival Trees	0.84	0.08
Linear MultiTask Logistic Regression	0.71	0.35

Table 1. Evaluation Metrics for Cox and ML models

- Cox model performed well (c-index 0.86, Brier score 0.08)
- Outperformed by machine learning models, especially deep neural network based models
  - DeepSurv (c-index 0.88, Brier score 0.07)
  - Neural MultiTask Logistic Regression (c-index 0.87, Brier score 0.06).

- Better prediction of survival by machine learning models at times further from the baseline

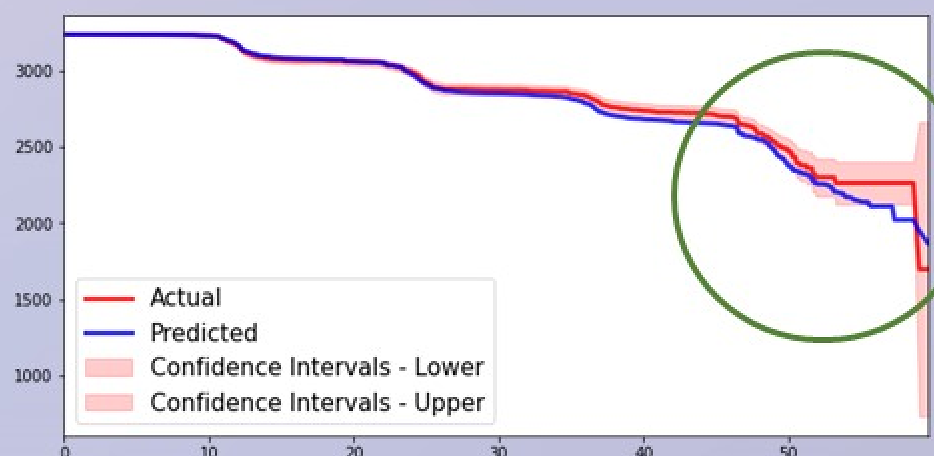

Fig 1A. Comparison of survival curve predicted by Cox model against actual survival curve

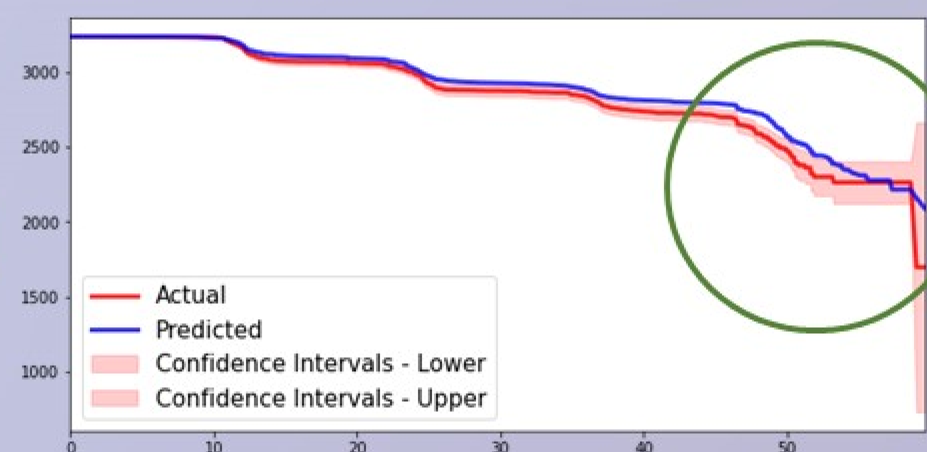

Fig 1B. Comparison of survival curve predicted by DeepSurv model against actual survival curve

Conclusion

In a large, single center cohort of non-obese individuals with no NAFLD at baseline, machine learning survival models accurately predicted time to NAFLD diagnosis from routine demographic, anthropometric, and laboratory test data. Deep neural network based models in particular had superior performance when compared to the classical Cox model.

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