Category :**Hematology: bleeding\transfusion**

A275 - ***Phenogrouping of hemorrhagic trauma patients using latent variable machine learning***

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Introduction:

The CRASH2 trial [1] was previously conducted to estimate the effect of early administration (<8 hours from injury) of tranexamic acid (TXA) on outcomes such as mortality in a cohort of n=20,21 bleeding trauma patients. 10,096 were treated with TXA (1g over 10min then infusion of 1g over 8hrs).

Methods:

We applied Deep Cox Mixtures latent variable model [2] to recover phenogroups that demonstrate different survival rates in the CRASH2 population conditioned on baseline covariates (Age, Sex, Trauma type (blunt/penetrating), Systolic BP, Respiratory Rate, Heart Rate, Glasgow Coma Score). The recovered phenogroups were compared using Kaplan-Meier estimators and SHAP [3] values were used to explain the phenogroups in terms of the baseline patient variables. Multivariate Cox regression was performed to identify phenogroup-specific predictors of survival.

Results:

Deep Cox Mixtures recovered 3 phenogroups from the CRASH2 study demonstrating differential mortality rates: High (Group A, n=3,074, 13.68-15.00 days), Low (Group B, n=12,277, 27.70-28.06 days) and Medium Risk (Group C, n=4757, 24.30-25.00 days) (Times are 95% CIs of 30 Day Restricted Mean Survival). Hours since Injury and Age of Patient were predictive of survival in high risk patients. Nature of Trauma was not found to be predictive for the Medium Risk patients.

Conclusion:

Latent Variable machine learning models can recover diverse patient phenogroups and have potential for supporting precise decisions, contextualized to specific subjects treated for trauma care with hemorrhage.

References:

[1] Crash-2 Collaborators. "The importance of early treatment with tranexamic acid in bleeding trauma patients: an exploratory analysis of the CRASH-2 randomised controlled trial." Lancet, 2011.

[2] Nagpal, C. et al. "Deep Cox Mixtures for Survival Regression". 6th Machine Learning for Health Conference, PMLR 2021

[3] Lundberg, Scott M. et. al. "A unified approach to interpreting model predictions." NeurIPS, 2017.

Image :

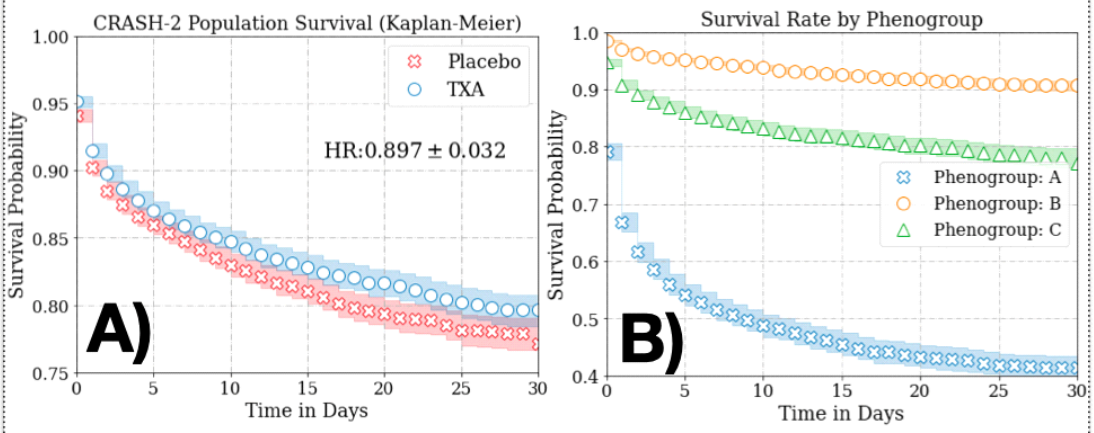

Fig 1 (A): Population Level Kaplan-Meier Estimate of the Mortality in CRASH2 for the TXA Arm vs. Placebo (Hazard Ratio: 0.897±0.032) (Bootstrapped CI). (B) Kaplan-Meier survival rates within phenotypes (*K*=3) recovered with Deep Cox Mixtures methodology. Phenogroup A (n=3074) was identified as 'High-Risk' while Phenogroup B (n=12,277) was 'Medium Risk' and Phenogroup C (n=4757) was 'Low Risk'.

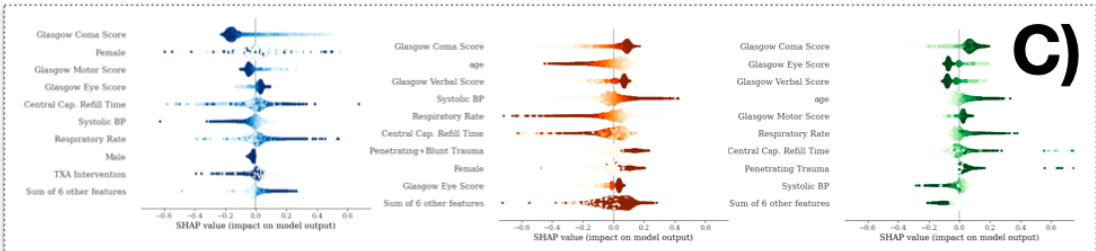

Fig 1 (C): SHAP explanations of the recovered phenotypes in terms of features. Darker color represents feature is responsible for assignment to phenotype.

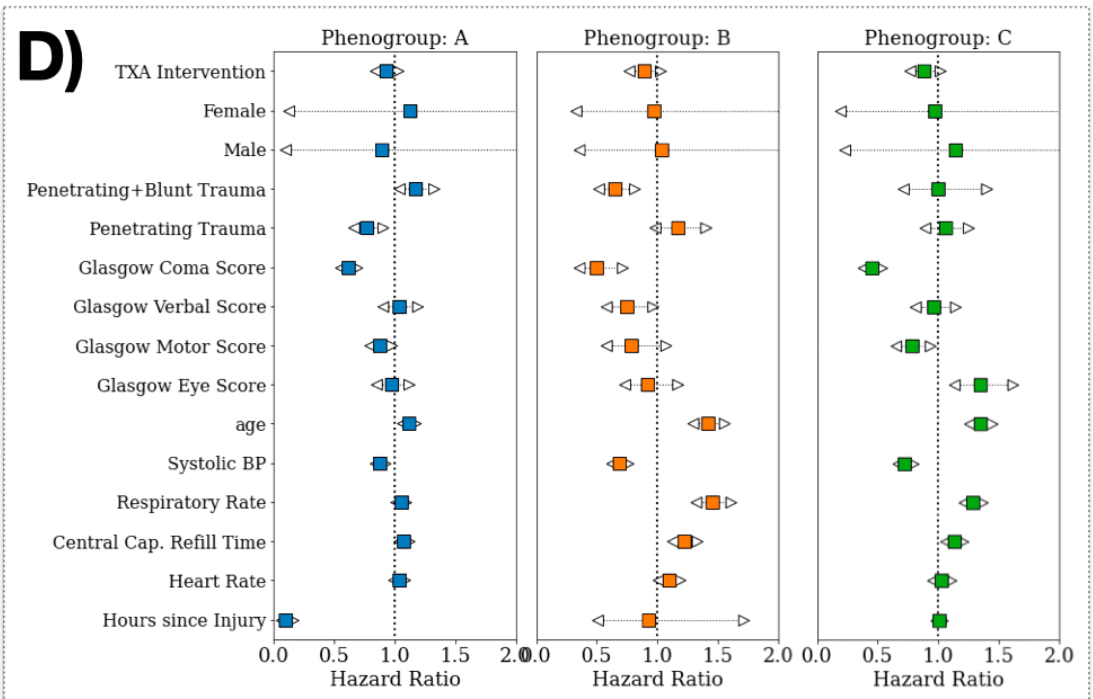

Fig 1 (D): Predictors of phenotype specific survival estimated using a multivariate Cox Model. For the High Risk, Phenogroup A, *Hours since Injury* and *Age of Patient* are predictive of the survival. As opposed to High and Low risk phenotypes, the *Nature of Trauma (Blunt vs. Penetrating)* was not found to be predictive of the survival rate within the Medium Risk, Phenotype C.

Survival Rates and Hazard Ratios stratified by Discovered Phenogroups