Beyond Mild, Moderate, and Severe: Classifying TBI Subgroups with Machine Learning

Abe M [1,8], Merisaari H [2,3], Posti J [4,5], Tenovuo O [4,6], Ngum P [4,6,7,8]

[1] Johns Hopkins University, Whiting School of Engineering, Baltimore, Maryland, USA
[2] Turku Brain and Mind Center, University of Turku, Turku, Finland
[3] Department of Diagnostic Radiology, Turku University Hospital,, Turku, Finland
[4] Turku Brain Injury Center, Turku University Hospital, Turku, Finland
[5] Neurocenter, Department of Neurosurgery, Turku University Hospital, Turku, Finland
[6] Department of Clinical Neurosciences, University of Turku, Turku, Finland
[7] Johns Hopkins University, Carey Business School, Baltimore, Maryland, USA
[8] CerebraNetics, Baltimore, Maryland, USA

Introduction

- **Background:** Traditional TBI classifications into mild, moderate, and severe fail to capture patient heterogeneity.
- **Objective:** We used **unsupervised machine learning** to integrate **clinical** and **biomarker** data, aiming to identify distinct TBI **subgroups.**

Methods

Data Processing and Cluster Identification

1. Dataset Overview:

- **200 TBI** patients from the EU-funded TBIcare project reduced to **181** after excluding those with missing GOSE scores.

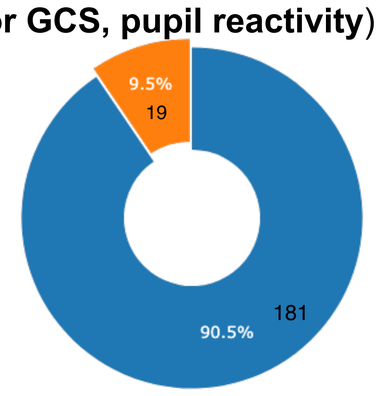
2. Predefined Feature Selection:

- IMPACT core variables[1] (**age, motor GCS, pupil reactivity**) and biomarkers (**GFAP, UCHL1**)

Core Variables
Age
Motor Glasgow Come Scale
Pupil reactivity

+

Admission GFAP and UCHL1 Blood Biomarkers

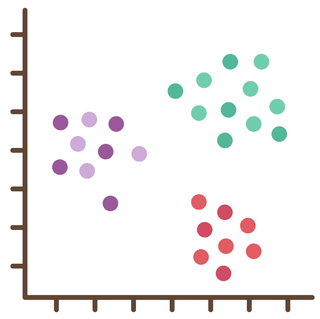


✓ Included – 181 TBI Patients
✓ Excluded -19 (missing GOSE)

3. Preprocessing Approach:

Imputation (Median, Mode)
↓
Scaling (StandardScaler)
↓
Encoding (One-Hot)
↓
Clustering (KMeans)
↓
Evaluation (Silhouette, cluster characteristics)

4. What is KMeans?:



K-Means is an unsupervised machine-learning algorithm that can **group similar objects** together **without predetermined labels**

Silhouette Score (0 to 1) Higher values indicate better cluster separation.

Results

1. Key Findings:

Unsupervised machine learning identified four distinct TBI patient clusters, each characterized by unique combinations of demographics, injury severity, biomarker levels, and recovery outcome.

- ✓ **Cluster 0**: **Younger patients** with mild TBI had the **best outcomes** (**GOSE: 7.00**) and lower biomarker levels (UCHL1: 170.04 pg/mL, GFAP: 6035.76 pg/mL).
- ✓ **Cluster 1**: **Older patients** with severe TBI showed the **worst outcomes** (**GOSE: 3.00**) and highest biomarker levels (UCHL1: 843.13 pg/mL, GFAP: 48972.32 pg/mL).
- ✓ **Cluster 2**: Small sample with very poor outcomes (**GOSE: 1.00**).
- ✓ **Cluster 3**: **Older patients** with **moderate outcomes** (**GOSE: 6.00**) had intermediate biomarker levels (UCHL1: 389.98 pg/mL, GFAP: 22972.62 pg/mL).

Table 1 Summary of Characteristics for 4 Cluster

Cluster	Age (Mean)	Sex (%) M	UCHL1 (Mean)	GFAP (Mean)	ED GCS (Median)	GOSE (Median)
0	30	69	170.04	6035.76	15	7
1	54	83	843.13	48972.3	0	3
2	88	100	16664.6	1763136	9	3
3	65	65	389.98	22972.6	15	6

Kruskal-Wallis test for GOSE across clusters: H-statistic: 45.92, P-value: 5.91e-10

Core + Blood-based Biomarkers

# of Clusters	Silhouette Score	Subjects per Cluster
2	0.631488	[111, 70]
3	0.571195	[60, 59, 62]
4	0.548746	[57, 42, 37, 45]
5	0.531188	[48, 24, 38, 45, 26]
6	0.540199	[24, 38, 31, 35, 44, 9]
7	0.506225	[31, 34, 34, 18, 38, 9, 17]

Table 2: Cluster Summary Metrics

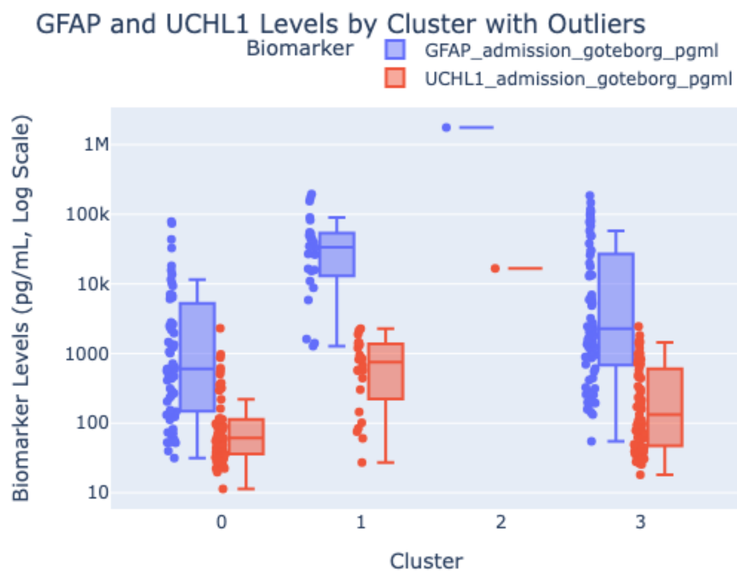


Figure 1: "GFAP and UCHL1 Levels by Cluster." Significant variation in biomarker levels across clusters, with Cluster 2 showing exceptionally elevated values, highlighting potential outlier characteristics.

Conclusion

Unsupervised machine learning provides a **valuable approach to patient stratification** especially in TBI with **no clear ground truth**. Future studies should aim to validate these clusters in larger cohorts and integrate additional data types. Limitations include the small sample size of certain clusters, severe outliers, and potential bias in feature selection.

1. Steyerberg EW, Mushkudiani N, Perel P, et al. Predicting outcome after traumatic brain injury: Development and international validation of prognostic scores based on admission characteristics. *PLoS Med.* 2008;5:e165. discussion e165.