

## **BIOMARKERS OF TBI ARE USEFUL ADJUNCTS IN CLINICAL PRACTICE – NO**

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The literature related to the outcome prediction after severe TBI is rapidly growing, but there are still limitations that hinder the ability of biomarkers to move into the clinical activity.

We agree that an important role of biomarkers could be of help in selecting the TBI patients who will benefit more from rehabilitation services and to support a clinician's opinion that a given patient would benefit from rehabilitation. Unfortunately, the literature at this time does not include any study linking biomarkers to the rehabilitative outcome.

Almost all studies are focused on generic outcome end points such as 'good or bad' or "dead or alive"; these are not specific end points that limit the possibility to assess a more detailed clinical usefulness of the biomarkers. It would be necessary to use measures of functional outcome or of quality-of-life.

Another important point is that the patients in all studies had severe TBI, whereas other demographic characteristics, including age, sex, and race, were not homogenous.

Moreover the studies had very different inclusion and exclusion criteria that could become critical when pathologies, that may affect serum biomarker concentrations, are not excluded. It is the case of acute nontraumatic neurologic symptoms such as posttraumatic seizures or hypoxemia, chronic nontraumatic neurologic pathologies such as previous strokes, and acute noncranial injuries such as fractures, that can all accompany acute TBI and can all affect serum biomarkers as well as outcome.

Furthermore there aren't studies in the current literature in which clinical, radiologic, and demographic variables are combined to determine predictive ability. It is likely that a combination of predictors will provide a higher specificity and a positive value for predicting outcome and response to rehabilitation procedures.