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## **Simplifying the use of prognostic information in patients with traumatic brain injury.**

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## Neurosurgical Forum LETTERS TO THE EDITOR

### Simplifying the use of prognostic information in patients with traumatic brain injury

TO THE EDITOR: We read with great interest the articles recently published by Brennan et al.<sup>2</sup> and Murray et al.<sup>4</sup> concerning the Glasgow Coma Scale-Pupils (GCS-P) score, and we commend the authors on the efforts undertaken to improve traumatic brain injury (TBI) prognostication (Brennan PM, Murray GD, Teasdale GM: Simplifying the use of prognostic information in traumatic brain injury. Part 1: The GCS-Pupils score: an extended index of clinical severity. *J Neurosurg* 128:1612–1620, June 2018; Murray GD, Brennan PM, Teasdale GM: Simplifying the use of prognostic information in traumatic brain injury. Part 2: Graphical presentation of probabilities. *J Neurosurg* 128:1621–1634, June 2018). In this regard, we would like to raise some issues that could contribute to the refinement of the new proposed tool.

The basic assessment of a prognostic score should comprise at least its 1) calibration (the agreement between observed outcomes and predictions); 2) discrimination (ability to distinguish between those with or without the outcome); and 3) overall performance (global accuracy). The GCS-P models were adequately calibrated, as depicted on the graphics; however, no discrimination statistics were reported. It would be interesting to report the area under the receiver operating characteristic curve (AUC-ROC) for the GCS-P model and the GCS-P plus Age & CT models. This is the most widely used discriminatory capacity measure in the medical literature and its interpretation is broadly understood, which facilitates comparisons between models.<sup>1</sup>

The Nagelkerke  $R^2$  (similarly to all pseudo  $R^2$  statistics) is an overall performance measure. Although valid, it lacks intuitive understanding and its direct interpretation as “the proportion of variability in outcome that is explained by the logistic regression model” is highly vulnerable to criticism and statistical reasoning (most pseudo  $R^2$  statistics do not have 1.0 as the maximum value, and even the adjusted Nagelkerke  $R^2$  is not adequately scaled).<sup>3</sup>

The Nagelkerke  $R^2$  differences between the GCS-P and GCS (for modeling death: 18.4 vs 15.5, difference 2.9; for favorable outcome: 22.2 vs 19.8, difference 2.4) are similar to those between the Corticosteroid Randomisation

After Significant Head Injury (CRASH) CT model and the GCS-P/Age/CT chart (death: 41.9 vs 39.7, difference 2.2; favorable outcome: 42.1 vs 39.7, difference 2.4). Thus, some may find it difficult to understand why the GCS-P was considered superior to the GCS but the GCS-P/Age/CT chart was considered sufficiently non-inferior to the CRASH-CT model. The AUC-ROC analysis could further elucidate this question.

Considering that the incidence of pupil alteration is higher in patients with severe TBI, we could be losing valuable prognostic information for mild and moderate TBI if the GCS-P model were to be routinely recommended over the CRASH model. On the general pooled sample reported in the paper, the CRASH model was at least marginally superior to the new proposed tool. Could we hypothesize that this superiority would be higher for nonsevere TBI? It would be enlightening to see a stratified analysis by TBI severity.

Nowadays medical apps are widely used for instant prognostic score calculations, and the CRASH/International Mission for Prognosis and Clinical Trials in Traumatic Brain Injury (IMPACT) models can be assessed as fast as any chart.<sup>5</sup> Many prognostic scores and decision rules are already routinely used in the emergency department and intensive care unit by other specialties.

In conclusion, although it may be too early to endorse the GCS-P/Age/CT model over the CRASH/IMPACT CT models for regular TBI management, it is indeed an interesting alternative approach and could be a step forward to advance prognostic reasoning and more rational decision making.

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## Disclosures

The authors report no conflict of interest.

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## Response

We thank Dr. Solla and colleagues for their interest in our papers. We agree that there are many different measures available to assess performance of a prognostic model, each with its own strengths and limitations. Many papers report detailed technical evaluations of prognostic models in TBI, and we have ourselves contributed to many such studies. We nonetheless very deliberately avoided the temptation of writing our two papers as statistical treatises, but instead aimed to focus on practical relevance, and we presented our results in terms of a simple overall measure of performance.

The fundamental thrust of our papers was to point out that utility and acceptability are at least as important as the “technical” performance of a prognostic model. A well-calibrated and powerfully discriminatory model is futile if its complexity deters its use in practice. In spite of the authors’ assertions to the contrary, our perception echoes previous views referred to in our papers<sup>1–4</sup> and is supported by an informal survey of UK neurosurgical units, which found that statistical models are not widely used in TBI. Our suggestion is that a simple chart might make the breakthrough that leads to prognostic models for TBI becoming incorporated widely in clinical practice.

Moreover, we do not consider the performance of our charts to be “sufficiently non-inferior” to the CRASH models. What we do present a quantification of the inevitable tradeoff in performance between complexity on the one hand and ease of use and interpretation on the other. It will be for clinicians caring for a patient to decide if the simpler, less-powerful approach is to be preferred on the grounds of utility.

We present in Table 1 the relevant data for the “area under the curve” for the receiver operating characteristic, or the c-statistic as it is also known. As might be expected, these closely mirror the results expressed in terms of Nagelkerke’s  $R^2$ . In particular, with both the IMPACT and CRASH models, the performance of the Age/GCS-P/CT chart lies between that of the simpler and more complex models, and is generally closer to that of the more complex models than to that of the simpler models.

We have severe reservations as to the wisdom of using measures of model performance within subsets stratified by severity, for if one wished to optimize the performance of a model within a subset of patients defined by severity then one would develop a model restricted to those pa-

**TABLE 1. Predictive yield for a range of models including GCS**

Model	c-Statistic	
	Modeling Death	Modeling Favorable Outcome
GCS score as linear variable	0.717	0.731
GCS-P as linear variable	0.731	0.741
GCS-P as linear variable & age as linear variable	0.778	0.787
GCS-P as linear variable & age as linear variable & CT findings in 3 groups	0.806	0.803
IMPACT patient group		
IMPACT core model	0.734	0.749
IMPACT extended model	0.775	0.788
Age/GCS-P/CT chart	0.765	0.774
CRASH patient group		
CRASH basic model	0.820	0.817
CRASH CT model	0.849	0.834
Age/GCS-P/CT chart	0.840	0.825

**TABLE 2. Predictive yield for a range of models based on a stratified analysis of the CRASH data set**

Model	c-Statistic	
	Modeling Death	Modeling Favorable Outcome
CRASH patient group w/ GCS score $\leq 8$		
CRASH basic model	0.742	0.746
CRASH CT model	0.790	0.780
Age/GCS-P/CT chart	0.772	0.767
CRASH patient group w/ GCS score $> 8$		
CRASH basic model	0.778	0.759
CRASH CT model	0.824	0.783
Age/GCS-P/CT chart	0.815	0.767

tients. Nevertheless, in the interests of transparency, we present in Table 2 such an analysis with the CRASH data, stratifying patients as GCS  $\leq 8$  (a widely used definition of “severe” TBI) versus GCS  $> 8$ . This shows that the GCS-P/Age/CT chart still performs well relative to the CRASH models for the patients with a better prognosis.

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