Study the Prognostic Value of Computed Tomographic Characteristics in Cases of Traumatic Brain Injury

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ABSTRACT

Introduction: Both Marshall and Rotterdam CT classifications are the most frequently used prognostic methods that incorporates the anatomical nature of the injury in the determination of outcome after acute traumatic brain injury.

Objectives: to compare the utility of the Marshall and Rotterdam CT classifications in predicting outcome in patients with traumatic brain injury.

Methods: GCS score documented on arrival to Emergency Room. Outcomes were in-hospital mortality, unfavourable neurologic outcome [Glasgow Outcome Scale Extended (GOS-E) 1–4] at three months, Poor functional outcome [Disability Rating Scale (DRS) ≥ 7], and ICU length of stay (LOS).

Results: A total of 70 patients were enrolled; Nineteen patients (27.1%) died, thirty six (51.4%) had unfavourable neurologic outcome, thirty six (70.6%) of the survivors had poor functional outcome (DRS $\geq$7). When predicting in-hospital mortality; both the Marshall and Rotterdam CT classifications were independent predictors of mortality (AUC: 0.848 versus 0.850, $p = 0.979$). When predicting unfavourable outcome, both classification systems predicted unfavourable outcome but Rotterdam score showed higher AUC (AUC: 0.712 versus 0.771, $p = 0.196$). When predicting poor functional Outcome (the Rotterdam score showed higher AUC than the Marshall score (0.77 vs. 0.72).

Conclusions: The Rotterdam CT classification and the Marshall CT classification both are good predictors of mortality. However, the Rotterdam CT classification was superior to the Marshall CT classification in predicting neurologic and functional outcome.

Running Title: Rotterdam score and Marshall score as a Predictor of TBI Outcomes

INTRODUCTION

Traumatic brain injury (TBI) is a leading cause of death and disability worldwide. Predictors of outcome would not only facilitate clinical management, but also allow for rational allocation of global health resources.[1] Most studies on outcome prediction in TBI investigated the combination of demographic, clinical, and radiological characteristics.[2, 3] Age, total Glasgow Coma Scale (GCS) score or GCS-motor score, pupil reactivity, major extra cranial injuries and the occurrence of a post-injury hypotensive and/or hypoxic period, proved the most powerful clinical predictors.[1, 4]

Computed tomography (CT) of the brain is the first choice of examination in the acute phase after head injury and provides essential diagnostic information with therapeutic implications for surgical intervention. To predict the outcome of patients with TBI, two scoring systems that use initial CT findings but group them differently have been introduced: Marshall Score in 1991[5] which was followed by Rotterdam score in 2005 [6] in an attempt to improve the performance yield in predicting patients' outcome. Both scoring systems are currently used widely in studies

assessing patients with TBI either to show subject demographics or as independent predictor of patients' outcome.[1]

The aim of the work was to compare the utility of the Marshall and Rotterdam CT classifications in predicting outcome in patients with traumatic brain injury

METHODS

Participants

Consecutive adults with isolated TBI admitted to the Critical Care Medicine Department of Alexandria Main University Hospital were enrolled in the study. The definition of TBI used for this study is *"an alteration in brain function, or other evidence of brain pathology, caused by an external force"*.[7] The study was approved by the Alexandria Faculty of Medicine Ethics Committee, and informed consent was obtained from every patient's next of kin.

Procedure

For every eligible patient; Demographic data including age & sex were collected. GCS was assessed on admission after primary respiratory and hemodynamic stabilization. All patients had CT scanning of the head after initial resuscitation. Only the initial CT-scans of patients admitted to the hospital within 24 h after sustaining the head injury was analysed in this study. Each CT-scan was scored, based on visual inspection, according to the Marshal classification, Rotterdam CT score.

Outcome Measures

Patients were prospectively followed up for primary outcomes of in-hospital or 28-day mortality, Extended Glasgow Outcome Scale (GOSE)[8] at three months and the disability rating score (DRS)[9] at three months. For the final prediction model GOSE was dichotomized as unfavourable (score 1-4) versus favourable (score 5-8) and the DRS dichotomized as good (score < 7) versus bad (score ≥ 7). Secondary outcome was survivors' ICU length of stay (ICU LOS).

Statistical analysis

Data are presented as median with interquartile range (IQR) for continuous variables and as frequencies and percentages for categorical variables. A binary logistic regression analysis was performed to reveal the odds ratios of Marshall CT Classification and Rotterdam CT score in predicting mortality, neurologic outcome, and functional outcome. Analyses for scales considered unadjusted models as well as models which adjusted for age, sex, and Glasgow Coma Score. The relation is significant if the 95% Confidence Interval (CI) for the OR does not include the value 1. Discrimination of the logistic models was assessed by calculating the area under receiver operating characteristic (ROC) curve. ROC curve is a graph plotting the combination of sensitivity (true-positive rate) and 1-specificity (false-positive rate) across a series of cut-off values covering the whole range of values of a given predictor.[10] The area under ROC curve (AUC) varies between 0.5 (No discrimination) and 1.0 (perfect discrimination). Usually, predictors are considered as having moderate discriminative properties when AUC are higher than 0.75 and as excellent more than 0.90. The best cut-off point was chosen as that one which maximizes the Youden index (sensitivity + specificity - 1).[10] The correlation between Marshall CT Classification, Rotterdam CT score and the ICU LOS was determined by calculating Pearson's Correlation Coefficient. Data were analysed by SPSS 21.0 for Windows (SPSS Inc., Chicago, Illinois, USA) and ROC curve analyses were performed by MedCalc Version 12.5.0.0 (Frank Schoonjans, Mariakerke, Belgium). All hypotheses were constructed two-tailed and $p \leq$ 0.05 was considered significant.

RESULTS

Patients Characteristics

A total of 70 patients were enrolled. Median age was 32 year (IQR 25-40), fifty five patients (78.6%) were males. Nineteen patients (27.1%) died, thirty six (51.4%) had unfavorable neurologic outcome (GOSE= 1-4), thirty six (70.6%) of the survivors had poor functional outcome (DRS ≥7). Patients characteristics are summarized at table 1.

Table 1: Patients characteristics

Study variable	Median (interquartile range) / frequency (%)
Age (years)	32 (25 – 40)
Male gender	55 (78.6)
GCS score	7 (5–9)
Marshall CT class	
Diffuse injury I	3 (4.3)
Diffuse injury II	20 (28.6)
Diffuse injury III (swelling)	11 (15.7)
Diffuse injury IV (shift)	10 (14.3)
Evacuated mass lesion	17 (24.3)
Non- Evacuated mass lesion	9 (12.9)
Rotterdam CT Score	
1	5 (7.1)
2	23 (32.9)
3	11 (15.7)
4	15 (21.4)
5	10 (14.3)
6	6 (8.6)

CT= Computerized Tomography, GCS= Glasgow Coma Score

Prediction of in-hospital mortality

Regarding Marshall CT classification, for every one point increase there was an estimated 199% increased odds of experiencing in-hospital mortality (OR = 2.99; 95% CI, 1.70– 5.27; $p < 0.001$). Similarly for every one point increase in Rotterdam CT score, there was an estimated 211% increased odds of experiencing in-hospital mortality (OR = 3.11; 95% CI, 1.78– 5.45; $p < 0.001$). These associations remained after adjustment for age, sex, and Glasgow Coma Score (Table 2).

Table 2: Logistic regression analyses in predicting hospital mortality, unfavourable neurologic outcome and poor functional outcome by Marshall CT Classification and Rotterdam CT Score

	Mortality		Neurologic Outcome		Functional Outcome	
	OR[a] (95% CI)	OR[b] (95% CI)	OR[a] (95% CI)	OR[b] (95% CI)	OR[a] (95% CI)	OR[b] (95% CI)
Marshall CT Classification	2.99 (1.70 – 5.27)	3.55 (1.70 – 7.44)	1.71 (1.20 – 2.42)	1.55 (1.03 – 2.33)	2.01 (1.12 – 3.58)	1.75 (0.90 – 3.41)
Rotterdam CT Score	3.11 (1.78 – 5.45)	3.02 (1.60 – 5.70)	2.28 (1.48 – 3.52)	2.08 (1.27 – 3.41)	3.10 (1.38 – 6.96)	2.60 (1.04 – 6.48)

[a] Unadjusted logistic regression model.
[b] Logistic regression model adjusted for age, sex, and Glasgow coma score
CI= Confidence Interval, OR= Odds Ratio.

Receiver operating characteristic (ROC) curves were estimated to compare prediction of in-hospital mortality by the two scores. The Marshall CT Classification area under the curve (AUC) was 0.848, the sum of sensitivity and specificity was maximized at a score of 4 (sensitivity = 0.73; specificity = 0.76). The Rotterdam CT score AUC was 0.850, the sum of sensitivity and specificity was maximized at a score of 4 (sensitivity = 0.68; specificity = 0.94) There difference between the two scores AUCs was not statistically significant ($p = 0.979$) (Fig 1).
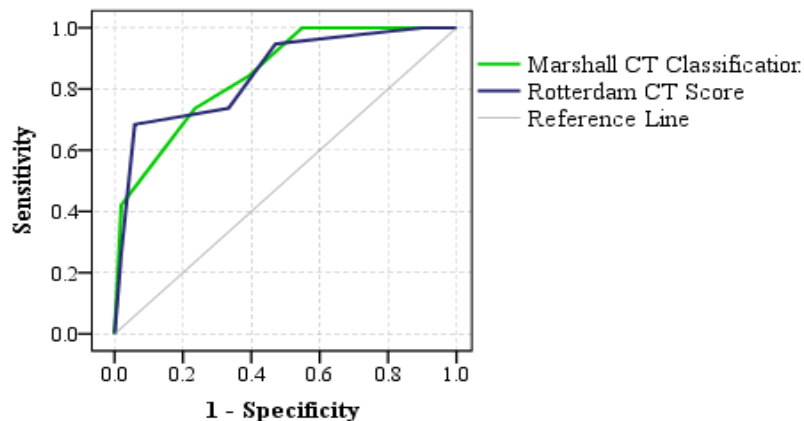

Figure (1): ROC curves comparing Marshall CT Classification and Rotterdam CT Score in predicting in-hospital mortality.

Prediction of unfavourable outcome (GOSE 1-4)

Regarding Marshall CT classification, for every one point increase there was an estimated 71% increased odds of experiencing unfavourable outcome (OR = 1.71; 95% CI, 1.20 – 2.42; p = 0.003). For every one point increase in Rotterdam CT score, there was an estimated 128% increased odds of experiencing in-hospital mortality (OR = 2.28; 95% CI, 1.48– 3.52; $p < 0.001$). These associations remained after adjustment for age, sex, and Glasgow Coma Score (Table 2).

Receiver operating characteristic (ROC) curves were estimated to compare prediction of unfavorable outcome by the two scores. The Marshall CT Classification area under the curve (AUC) was 0.712, the sum of sensitivity and specificity was maximized at a score of 2 (sensitivity = 0.80; specificity = 0.47). The Rotterdam CT score AUC was 0.771, the sum of sensitivity and specificity was maximized at a score of 4 (sensitivity = 0.41; specificity = 0.97). Although Rotterdam score showed higher AUC, this difference was not statistically significant ($p = 0.196$) (Fig 2).
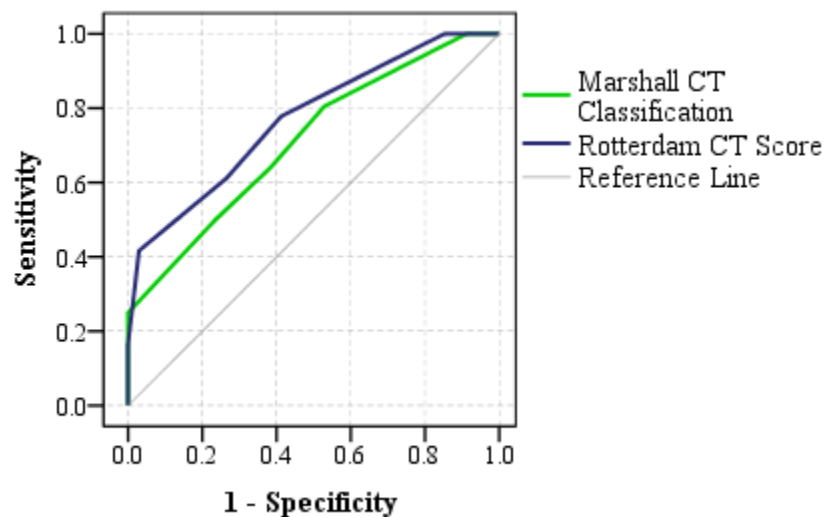

Figure (2): ROC curves comparing Marshall CT Classification and Rotterdam CT Score in predicting Unfavorable Neurologic Outcome.

Prediction of Poor Functional Outcome (DRS ≥7)

Regarding Marshall CT classification, for every one point increase there was an estimated 101% increased odds of experiencing poor functional outcome (OR = 2.01; 95% CI, 1.12 – 3.58; p =

0.018). For every one point increase in Rotterdam CT score, there was an estimated 210% increased odds of experiencing poor functional outcome (OR = 3.10; 95% CI, 1.38– 6.962; p = 0.006). However, after adjustment for age, sex, and Glasgow Coma Score only the Rotterdam CT score showed statistical significance (Table 2).

Receiver operating characteristic (ROC) curves were estimated to compare prediction of unfavorable outcome by the two scores (Table-8, Figure-8). The Marshall CT Classification area under the curve (AUC) was 0.717, the sum of sensitivity and specificity was maximized at a score of 3 (sensitivity = 0.50; specificity = 0.86). The Rotterdam CT score AUC was 0.769, the sum of sensitivity and specificity was maximized at a score of 2 (sensitivity = 0.58; specificity = 0.80). Although Rotterdam score showed higher AUC, this difference was not statistically significant (p = 0.349) (Fig 3).
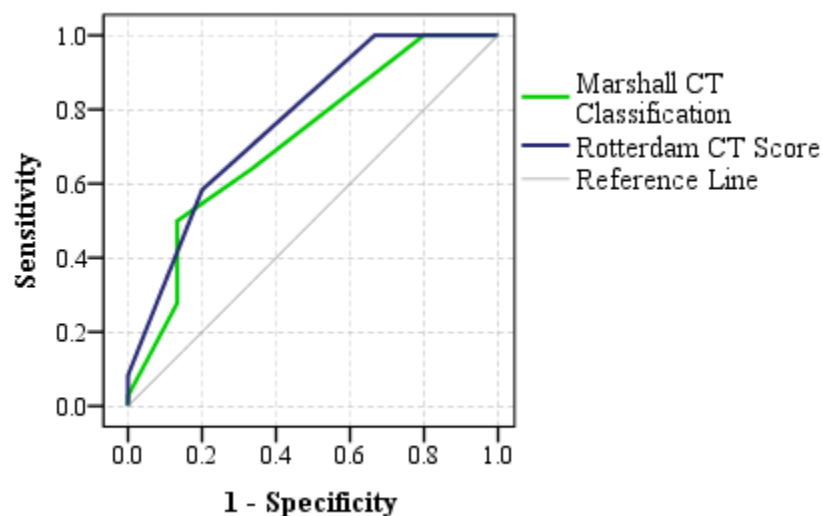

Figure (3): ROC curves comparing Marshall CT Classification and Rotterdam CT Score in predicting Poor Functional Outcome.

Prediction of ICU length of stay

There was a significant positive correlation between Marshall CT classification and ICU length of stay (r = 0.483; p < 0.001). (Table 9, Figure 9). Also, Rotterdam CT score showed a significant positive correlation with ICU length of stay (r = 0.586; *p < 0.001*).

DISCUSSION

Our results showed that both the Marshall and Rotterdam CT classifications were independent predictors of mortality and unfavourable neurologic outcome but the Rotterdam score alone was independent predictor of poor functional outcome after controlling for common confounders (Age, Sex, and GCS) via multiple logistic regression.

The severity of the injuries sustained in the present study population was high (median GCS = 7) with a 27% in-hospital mortality rate. The present study's in-hospital mortality rate is comparable to previous studies, whose patients were adults and all received intensive care, where the mortality rates were between 18% and 37%,[11-17] Abbassy et al. reported 23.1% mortality rate of TBI patients admitted to Alexandria Main University Hospital ICUs.[18]

Univariate analysis revealed that the Rotterdam CT score was significantly associated with mortality (OR: 3.11, 95% CI, 1.70– 5.27; $p < 0.001$). This associations remained after adjustment for age, sex, and GCS score (OR: 3.02, 95% CI, 1.50– 5.70; $p = 0.001$). This is consistent with Huang et al.[19] who reported unadjusted OR of 3.11 and adjusted OR of 2.6

Both classification system showed a moderate accuracy in predicting in-hospital mortality (Marshall score, AUC = 0.848 vs. Rotterdam score, AUC = 0.850). In accordance with that, Mata-mbemba et al.[20] found that both scores were significantly and positively associated with early death (AUC = 0.85 for both scores). They proposed that the positive relationships between the two scoring systems and early death can be explained by their inclusion of the two strongest predictors of early death on CT: basal cistern absence and positive midline shift. At variance with this Mass et al.[6] reported lower AUC for both scores (Marshall score, AUC = 0.67 vs. Rotterdam score, AUC = 0.71). Similarly, Bobinski et al.[21] reported AUC of 0.66 and 0.72 for Marshall score and Rotterdam score respectively. However, these studies included only patients with severe TBI and addressed late outcome (6 month after injury).

The present study found that diffuse injury IV (midline shift) was the optimal cutoff point on the Marshall classification. Midline shift was analyzed in various studies that found a strong association with worse outcome.[20, 22-24].

Univariate analysis revealed that the Rotterdam CT score was significantly associated with unfavourable outcome (OR = 2.28; 95% CI, 1.48– 3.52; $p < 0.001$). This associations remained

after adjustment for age, sex, and GCS score (OR: 2.08, 95% CI, 1.27– 3.41; $p = 0.004$). This is consistent with Huang et al.[19] who reported unadjusted OR of 2.61 and adjusted OR of 1.8. The Rotterdam score showed higher AUC than the Marshall score (0.77 vs. 0.71). In agreement with that, Nelson et al.[25] reported a relatively large-scale study wherein the performances of Rotterdam and Marshall scores were evaluated in patients with mild-to-severe TBI. These authors claimed that Rotterdam score was a better predictor than Marshall score of unfavorable outcome (AUC 0.76 vs. 0.73).

Although the GOS is the most commonly used TBI outcome measure in the literature, it may not be sensitive to more subtle, but potentially clinically relevant, changes in functioning. The DRS provides increased sensitivity to change by providing a greater range in possible scores and by addressing areas such as capability for productive activity and level of independence in the community.[26] However, the DRS is under-utilized in the literature and there is no study addressing the relation between CT characteristics and DRS.[26]

Length of stay (LOS) is an important measure of health care utilization and determinant of hospitalization costs. Health care providers and hospital administrators are interested in early and accurate LOS predictions for both economic and organizational reasons. In addition to these aspects of quality control, there is also patient interest in anticipated dates of discharge.[27]

The interpretation of LOS as a measure of patient outcome is problematic. For instance; a surviving patient discharged from the hospital after 5 days is not equivalent to a patient who dies on hospital Day 5, although the LOS would be the same. Thus in the present study the analysis was restricted to those patients who discharged alive. Although the type and severity of patients' illnesses can directly affect LOS, there are structural and managerial factors that influence ICU LOS.[13, 28, 29] ICUs vary greatly in geographic location, resources, organizational structure, and leadership. Also, clinical practices and availability of other observation facilities such as recovery room of intermediate care beds may also have influence on ICU LOS. These factors are difficult to control in predictive models.[27] Although many reports in the literature are available that determines risk factors for mortality and unfavorable outcome after TBI, at present little is published on factors influencing length of stay.

In the present study, the overall mean ICU LOS of 14.4 ± 7.8 days is very close to that reported by Bahloul et al.[12] (12.8 ± 15 days) and by Arabi et al.[11] (11.5 ± 7.3 days). Survivors' ICU LOS was a median of 11 days. Both classification systems showed a significant positive

correlation with ICU length of stay. However, the Rotterdam score showed higher correlation than the Marshall score (0.59 vs. 0.48)

A limitation of the present study is the analysis of data from the initial CT-scans only. Brain damage after TBI is a dynamic pathological process in which clinical and CT variables may change over time. Prediction of eventual outcome becomes more accurate using information from sequential rather than initial CT-scans.[30] However, the intent of the present study was to investigate the use of the CT classification and CT predictors toward a prognostic classification of TBI on admission. Such classification is considered useful to establish the baseline characteristics and prognostic risk of TBI patients on admission.

Competing Interests: The authors declare that they have no competing interests.

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