TITLE:

Presentation of a regression equation to predict the Glasgow verbal score from the Glasgow eye and best motor score in patients with traumatic brain injury – a pilot study.

Georgios Matis[1], Theodossios Birbilis[1], Nikolaos Lyratzopoulos[2], Georgios Minopoulos[2], Konstantinos Manolas[2]

[1] Neurosurgery Department – Democritus University of Thrace (DUTH), University General Hospital of Alexandroupolis, Greece

[2] 1st Department of Surgery – Democritus University of Thrace (DUTH), University General Hospital of Alexandroupolis, Greece

Corresponding author:

G. K. MATIS

Megalou Alexandrou 43-45

55133 Thessaloniki

Tel: 2310446785 – 2310998957 – 6977990208

gkmatis@yahoo.gr

SUMMARY

Presentation of a regression equation to predict the Glasgow verbal score from the Glasgow eye and best motor score in patients with traumatic brain injury – a pilot study.

Matis G.[1], Birbilis T.[1], Lyratzopoulos N.[2], Minopoulos G.[2], Manolas K.[2]

[1] Neurosurgery Department – Democritus University of Thrace (DUTH), University General Hospital of Alexandroupolis, Greece

[2] 1st Department of Surgery – Democritus University of Thrace (DUTH), University General Hospital of Alexandroupolis, Greece

The Glasgow Coma Scale (GCS) represents an international model of recording neurological findings, comparing patients and predicting outcome. It is the sum of three components, namely the best motor response, the best verbal response, and eye opening. However, calculating its verbal component in specific patients' subgroups (intoxication, medications, dementia, psychiatric diseases, developmental impairments, intubation, tracheostomy, laryngectomy, edema of tongue, facial trauma, mutism, hearing impairments) is extremely difficult. The aim of this pilot study was to derive a regression equation to accurately predict the verbal score based on the eye and motor scores. The data from 74 patients with traumatic brain injury who were admitted to the Intensive Care Unit (ICU) of University Hospital of Alexandroupolis, Greece (a tertiary care university hospital) during the decade 1994-2003 were obtained. The mean age and APACHE-II score was 45.19±2.555 and 15.91±0.890

respectively with the majority of the patients being male (87.8%) and living in an urban environment (58.1%). The main causes of injury were car accidents (75.7%) and falls (23%) and subjects were mainly conservatively treated (88.3%). The mean ICU length of stay was 11.5±2.051 days. 61.67% of patients presented a GCS score of 3 (all of whom were diagnosed with intraventricular hemorrhage), 10% a GCS score of 15 and 6.67% a GCS score of 14. With the aid of the statistical package SPSS (Statistical Package for Social Sciences) v. 14.0, the stepwise regression method was performed and the following equation was obtained: GCS-Verbal = 0.963 + (0.029*GCS-Eyes*GCS-Motor^2). This equation presented an adjusted R^2 value of 0.916, a standard error of estimate value of 0.46 and a F value of 795.509, p=0.000. Correlation between actual and predicted verbal and total scores was calculated using the Pearson correlation coefficient and the Spearman rank correlation coefficient. The same question was addressed for other 3 regression equations which were proposed by other authors: (a) GCS-Verbal = -0.3756 + (GCS-Motor*0.5713) + (GCS-Eyes*0.4233), (b) GCS-Verbal = 2.3976 + (GCS-Motor*(-0.9253)) + (GCS-Eyes*(-0.9214)) + (GCS-Motor^2*0.2208) + (GCS-Eyes^2*0.2318), and (c) GCS-Verbal = 0.2095 + (GCS-Motor*(-2.1238)) + (GCS-Eyes*3.9897) + (GCS-Motor^2*0.6048) + (GCS-Eyes)^2*(-1.9077) + (GCS-Motor)^2*(-0.0344) + (GCS-Eyes)^3*0.2748. The discriminative ability of all 4 equations was tested using the Receiver Operating Characteristic curves (ROC). Various GCS scores (depending on the equation employed) were defined as test variables and outcome was defined as the state variable. The mean actual verbal and total Glasgow coma score was 1.9865±0.1861 and 6.3919±0.554 respectively. In the derived equation the corresponding mean values were 1.9865±0.178 and 6.3919±0.551 (r=0.958, r_S=0.916, p=0.000 and r=0.995, r_S=0.998, p=0.000). For the other 3 equations the mean predicted verbal

score was 1.8732±0.195 (r=0.922, r_S=0.920, p=0.000), 1.8726±0.160 (r=0.950, r_S=0.924, p=0.000) and 1.9147±0.162 (r=0.951, r_S=0.923, p=0.000), while the mean predicted total score was 6.2786±0.572 (r=0.991, r_S=0.999, p=0.000), 6.2780±0.531 (r=0.995, r_S=0.999, p=0.000) and 6.3201±0.534 (r=0.995, r_S=0.999, p=0.000). The area under the ROC curves of total Glasgow coma scores for predicting survival was 0.545±0.076 (p=0.547) for the derived equation and 0.543±0.076 (p=0.567) for the other three equations. The corresponding value for actual ROC curve was 0.548±0.076 (p=0.523). The analysis of results demonstrates that the proposed equation predicts with great accuracy the verbal component in patients with traumatic brain injury, produces similar results with other regression equations brought forward by other authors and is simpler and less time consuming to solve. As drawbacks of this pilot study one should mention the relatively small sample size, the large number of patients with a GCS score of 3 (61.67%), the small number of patients with a GCS score within the intermediate values of this scale (where the mathematical relationship among its constituents is not so obvious and the predictive ability is more limited), and the lack of data collectors' experience (residents). However, the study is still in progress; it is our scope to include more than 200 patients with GCS scores other than 3. Final results will be available within 12 months.

Key words: equations, Glasgow Coma Scale, regression, traumatic brain injury

INTRODUCTION

Traumatic Brain Injury (TBI) constitutes a major public health problem confronted by trauma centers. In USA, one TBI is sustained every 21 seconds, that is 1.5 million annually[11]. Glasgow Coma Scale (GCS) is considered as a practical scale for evaluating the severity and length of impaired consciousness and coma in TBI patients[25]. It assesses the ability of patients to open eyes (1-4 points), communicate verbally (1-5 points) and execute commands and move their limbs (1-6 points)[10]. The derived score is crucial for clinical decisions such as defining the time of intubation, computed tomography application or operation[9]. GCS represents an international standardized approach of recording neurological findings[1] and is incorporated in various other scales (APACHE-II, ASCOT, CRAMS, RTS, TRISS)[13,17].

Yet, its calculation is some times cumbersome (Table 1)[6,7]. More specifically, in order to surpass such obstacles, researchers have used regression models, especially in computing the verbal component [22]. These models are capable of predicting with great accuracy the score of GCS-Verbal from eye response (GCS-Eyes) and motor response (GCS-Motor)[16]. It is thus possible to rate GCS in intubated TBI patients too [16,22].

The scope of the present study was: (a) the construction of a regression equation for accurate prediction of GCS-Verbal score based on GCS-Eyes and GCS-Motor scores and (b) the comparison of this equation with similar equations provided by other reports.

MATERIAL – METHOD

The medical records of TBI patients admitted to the Intensive Care Unit (ICU) of General Hospital of Alexandroupolis, Greece, during the decade 1994-2003 were

retrospectively reviewed. In total, complete data (total GCS, GCS components, physiological variables, imaging findings, and outcome) were available for 74 patients. Of note, these were not homogenous, since some of them were sedated, while others were recovering from general anesthesia, a finding common in many papers[22].

For statistical analysis SPSS (Statistical Package for Social Sciences) v.14.0 was used. Stepwise regression was employed; GCS-Verbal was the dependent variable and GCS-Eyes and GCS-Motor the independent ones. Moreover, several transformations of the last two variables were performed (such as involutions, products, reciprocals). Finally, the best multiple linear regression equation was chosen.

Correlation between observed and predicted (by the equation) mean values of GCS-Verbal and total GCS was explored with the aid of the Pearsonian χ^2 (r) coefficient and Spearman's r_S[28]. Same calculations were carried out for other 3 regression equations published in the literature and applied to these 74 patients[22]:

GCS-Verbal = -0.3756 + (GCS-Motor*0.5713) + (GCS-Eyes*0.4233) (Equation 1).

GCS-Verbal = 2.3976 + (GCS-Motor*(-0.9253)) + (GCS-Eyes*(-0.9214)) + (GCS-Motor^2*0.2208) + (GCS-Eyes^2*0.2318) (Equation 2).

GCS-Verbal = 0.2095 + (GCS-Motor*(-2.1238)) + (GCS-Eyes*3.9897) + (GCS-Motor^2*0.6048) + (GCS-Eyes^2*(-1.9077) + (GCS-Motor^2*(-0.0344)) + (GCS-Eyes^3*0.2748) (Equation 3).

The discriminative ability of all equations was verified with ROC *(Receiver Operating Characteristic curves)*[18]. These curves represent the graphical illustration of the observed exchange between sensitivity (Y axis – percentage of true positive

results) and 1-specificity (X axis – percentage of false positive results) for cutoff points ranging from 0 to 100[12]. The GCS values (derived from all equations) were consecutively defined as test variables and outcome was defined as state variable. The next step was to compute and compare the areas under the ROCs (AUC) for all four equations.

RESULTS

Patients' demographics are presented in Table 2. Most of them were male (87.8%), from urban areas (58.1%), involved in traffic accidents (75.7%), and treated conservatively (88.3%). The bar chart of GCS and outcome is illustrated in Figure 1. One could notice the large number of patients with a GCS score of 3 (61.67%) and unfavourable outcome (1=death). In Table 3 the frequency of GCS score of 3 (depending on brain CT findings) is presented. It is noteworthy that this score was observed in 100% of patients with intraventricular hemorrhage.

Totally, 61.67% of patients have a GCS of 3, 10% a GCS of 15 and 6.67% a GCS of 14. More specifically, GCS-Eyes for survivors takes more often the value 1 (62.96%), followed by 4 (25.93%) and 2 (7.41%). For non-survivors, the scores of GCS-Eyes present similar frequency (75.76% for score 1, 15.15% for score 4, and 6.06% for score 2).

The most frequent score for GCS-Verbal for survivors is 1 (66.67%), followed by score 5 (22.22%). For non-survivors, the scores of GCS-Verbal show similar frequency (75.76% for score 1, and 9.09% for score 5).

The most frequent score for GCS-Motor in survivors is 1 (59.26%), followed by scores 5 (18.52%), and 6 (14.81%). Non-survivors exhibit similar frequencies (63.63% for score 1, 15.15% for score 5 and 9.09% for score 6).

The derived multiple regression equation is:

GCS-Verbal = 0.963 + (0.029*GCS-Eyes*GCS-Motor^2) (Equation 4).

The equation has the following characteristics: adjusted correlation coefficient R^2=0.916, standard error of estimation of theoretical values=0.46 and F=795.509, p=0.000. For simplicity reasons a table to predict (according to Equation 4) GCS-Verbal scores was constructed (Table 4). These scores are illustrated in Figure 2.

The mean observed verbal response and total GCS was 1.9865±0.1861 and 6.3919±0.554 respectively. For observed GCS scores, AUC was found to be 0.548±0.076 (p=0.523). For Equations 1-4, the corresponding values and the r και r_S coefficients are shown in Table 5. Finally, in Figure 3 the ROCs for predicted total GCS for all four equations are presented.

DISCUSSION

The GCS is used for assessment of level of consciousness and severity of injury, but also in outcome prediction[3,17]. The prognostic ability of APACHE system is mainly attributed to this scale[1,15]. It is the sum of three components: verbal, eye and motor response[25].

It has been proposed in the clinical practice to apply the 3 scores (GCS-Eyes, GCS-Verbal and GCS-Motor) separately and not as a sum, because otherwise they are weighted the same and they don't fully reflect the clinical condition[7]. Several researchers state that GCS-Motor alone is sufficient to predict short-term outcome[8], others use both GCS-Eyes and GCS-Motor scores[19], while others calculate the sum of the three scores[17]. However, it has been observed that patients with the same total score exhibit different danger of dying due to rating differences in the three

components[26]. Mortality is significantly different for different combinations that produce the following total scores: 7, 9, 11, and 14[27].

The reliability and accuracy of GCS have been disputed, especially when raters are not adequately trained and mainly in the intermediate level of consciousness (GCS 7-11)[14]. Residents, physicians in surgical specialties and participants in ATLS *(Advanced Trauma Life Support)* program seem to be better raters[20]. Many reasons for the attributed reduced reliability have been proposed; no reference to brainstem reflexes, skewness to motor response, difficulty in application in intubated patients, and time of beginning of GCS calculation (accident site, emergency department, ICU)[23,24]. Studies suggest that rating should be performed before sedation[15] and preferably at the accident site[5].

Analytically, it is difficult to calculate total GCS in intubated patients because GCS-Verbal cannot be measured[16]. Difficulties are related, among others, to cases of laryngectomy, tracheostomy, edema of tongue, aphasia and craniofacial injuries (Table 1)[2,6,7]. In an attempt to overcome these problems, several approaches have been established: (a) calculation based on clinical picture (low ratings, considerable effect of sedation), (b) attribution of score 1, (c) computing the mean value of GCS-Verbal of other non-intubated patients, and (d) use of letter «T» (rendering GCS calculation not possible)[15,16,19]. In addition, literature proposes the use of letter «P» (pharmaceutical paralysis), of «S» (sedation), of «C» (closed eyes), and of «U» (untestable variables)[2,13].

It is of interest that a study focused on rating methods of intubated patients concluded that: 26% of trauma centers applied 1 point to GCS-Verbal score, 23% gave 3 points to total GCS, 16% noted the letter «T» and 10% calculated always a

score of 15[2]. Another report stated the percentage of correct GCS ratings was only 51%[4].

Parallelly, several regression models are brought forward, with the Equations 1, 2 and 3 being an illustrative example[22]. The application of Equation 1 in 24,085 patients gave a predicted GCS-Verbal score of 4.3±1.2, with mean observed score of 4.4±1.3 (r=0.90, p=0.0001) and total GCS 13.7±3.4, with observed score of 13.6±3.5 (r=0.97, p=0.0001). The AUC for predicting outcome for both GCS scores (predicted and observed) was 0.850 and 0.868[16]. Based on data from the specific 74 patients, for computing of GCS-Verbal from GCS-Eyes and GCS-Motor, Equation 4 was chosen as the simplest one.

Equation 4 provides the biggest adjusted coefficient of determination (0.916), followed by Equations 3, 2 and 1 (0.832, 0.830 and 0.76 respectively). Rutledge et al reported in their sample the following correlation coefficients: r=0.76 (Equation 1), r=0.9179 (Equation 2) and r=0.9194 (Equation 3)[22]. In our sample, the application of Equation 4 gave a higher r that equaled to 0.958, while the corresponding values after the application of Equations 1, 2 and 3 were 0.922, 0.950, and 0.951. Reversely, Equation 4 gave a smaller r_S (0.916). The bigger r_S related to Equation 2 (0.924), followed by Equations 3 (0.923) and 1 (0.920). In conclusion, all four equations when applied to the specific 74 patients gave very good and comparable results. Advantages attributed to Equation 4 are its simplicity and the limited time needed for its calculation.

At this point, some drawbacks of the present study should be highlighted: (a) the relatively small sample, (b) the big number of patients with a GCS score of 3 (61.67%), (c) the limited number of patients with intermediate GCS scores (where the mathematical relationship among its components might not be so obvious and the

predictive ability of GCS diminished), and (d) the lack of raters' experience (residents). Similar limiting factors are reported in the literature[21,22]. However, the study is still in progress; it is our scope to include more than 200 patients with GCS scores other than 3. Final results will be available within 12 months.

In this report a regression equation to accurately predict GCS-Verbal score from GCS-Eyes and GCS-Motor scores was proposed. We confirmed the conclusions of other studies suggesting the existence of a mathematical relationship among GCS components and the positive correlation between GCS-Eyes and GCS-Motor scores from the one hand, and GCS-Verbal score from the other[16,22]. The utility of such an equation in calculating GCS in intubated patients is obvious. Yet, further validation of the equation in bigger samples is warranted.

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TABLE 1. Situations that affect GCS calculation.

EYE OPENING
- Periorbital edema - Inujury of eyes / cranial nerves - Pain
MOTOR RESPONSE
- Injury of spine / peripheral nerves / limbs - Alcohol / drugs - Psychiatric disease / dementia - Developmental disabilities - Lack of spoken language comprehension - Pain
VERBAL RESPONSE
- Intubation / tracheostomy / laryngectomy / edema of tongue - Craniofacial injuries - Alcohol / drugs (sedatives, neuromuscular-blocking agents) - Psychiatric disease / dementia - Developmental disabilities - Lack of spoken language comprehension / aphasia / hearing impairment - Pain

TABLE 2. Patients' demographics.

Age (years) *(range)*	45.19±2.555 *(3-87)*
Sex *(%)*	Male: 65 *(87.8)* Female: 9 *(12.2)*
Location *(%)*	Rural: 21 *(28.4)* Semi-urban: 10 *(13.5)* Urban: 43 *(58.1)*
Cause of TBI *(%)*	Traffic accidents: 56 *(75.7)* Falls: 17 *(23)* Physical violence: 1 *(1.3)*
GCS *(range)*	6.39±0.554 *(3-15)*
GCS-Eyes *(range)*	1.81±0.146 *(1-4)*
GCS-Verbal *(range)*	1.99±0.186 *(1-5)*
GCS-Motor *(range)*	2.59±0.241 *(1-6)*
APACHE-II *(range)*	15.91±0.890 *(1-39)*
Length of stay in ICU (days) *(range)*	11.5±2.051 *(1-106)*
Treatment *(%)*	Conservative: 67 *(88.3)* Surgical: 7 *(11.7)*

TABLE 3. The frequency of GCS score of 3 depending on brain CT findings.

FINDING	PERCENTAGE (%)
Intraventricular hemorrhage	100
Presence of blood in paranasal sinuses	80.95
Injuries of extracranial soft tissues	76.19
Intracerebral hemorrhage	71.43
Pneumocephalus	70.59
Edema	69.44
Subarachnoid hemorrhage	67.74
Epidural hematoma	66.67
Subdural hematoma	60.71
Fracture	54.17
Contusion	42.11

TABLE 4. Predicted GCS-Verbal scores from GCS-Eyes and GCS-Motor scores (according to Equation 4).

GCS-Motor	**GCS-Eyes**			
	1	**2**	**3**	**4**
1	*1*	*1*	*1*	*1*
2	*1*	*1*	*1*	*1*
3	*1*	*1*	*2*	*2*
4	*1*	*2*	*2*	*3*
5	*2*	*2*	*3*	*4*
6	*2*	*3*	*4*	*5*

ΠΙΝΑΚΑΣ 5. Results of the Equations 1-4.

EQUATION / FINDING	1	2	3	4
R^2 *(p)*	**0.76** *(0.0001)*	**0.83** *(0.0001)*	**0.832** *(0.0001)*	**0.916** *(0.000)*
GCS-Verbal	**1.8732±0.1948**	**1.8726±0.1596**	**1.9147±0.1622**	**1.9865±0.1782**
	r=0.922 r_S*=0.920*	*r=0.950* r_S*=0.924*	*r=0.951* r_S*=0.923*	*r=0.958* r_S*=0.916*
	p=0.000			
GCS	**6.2786±0.57175**	**6.2780±0.53060**	**6.3201±0.53405**	**6.3919±0.55084**
	r=0.991 r_S*=0.999*	*r=0.995* r_S*=0.999*	*r=0.995* r_S*=0.999*	*r=0.995* r_S*=0.998*
	p=0.000			
AUC *(p)* *(range)*	**0.543±0.076** *(0.567)* *(0.394–0.692)*	**0.543±0.076** *(0.567)* *(0.394–0.692)*	**0.543±0.076** *(0.567)* *(0.394–0.692)*	**0.545±0.076** *(0.547)* *(0.396–0.695)*

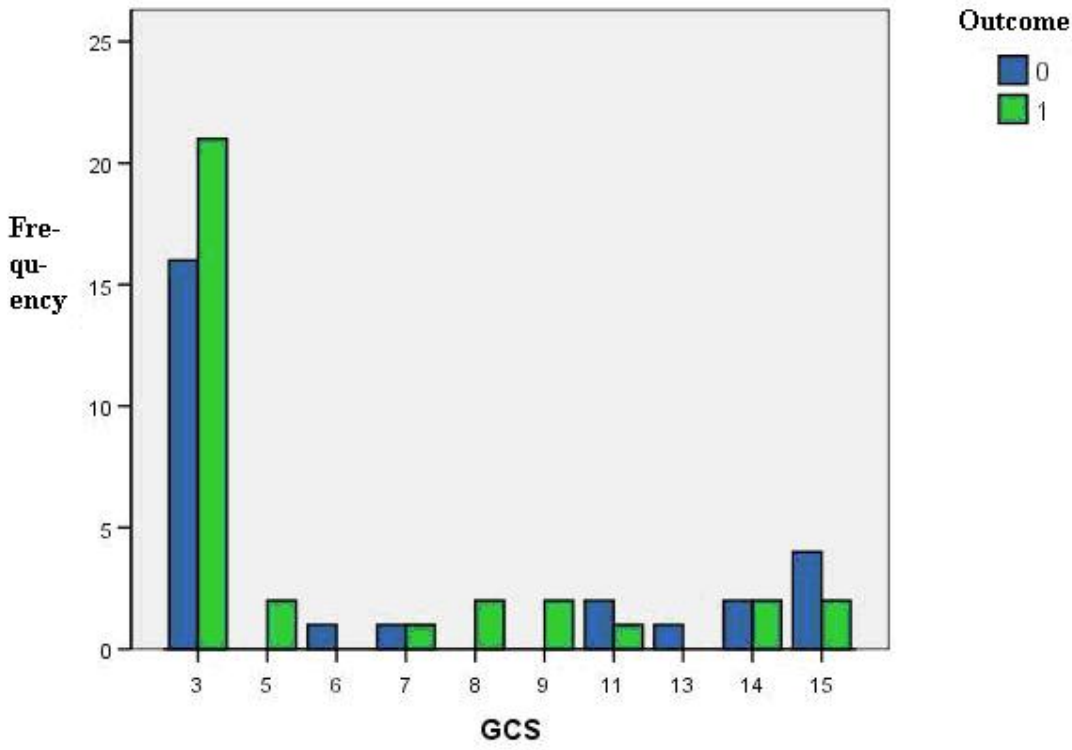

FIGURE 1. Barchart of GCS and outcome (0: survival, 1: death).

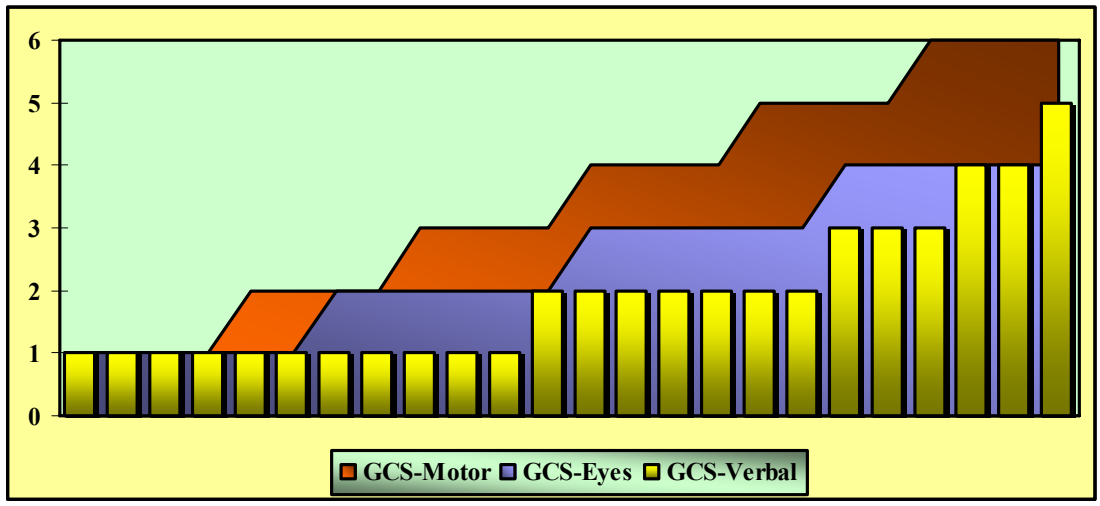

FIGURE 2. Predicted GCS-Verbal scores from GCS-Eyes and GCS-Motor scores (according to Equation 4).

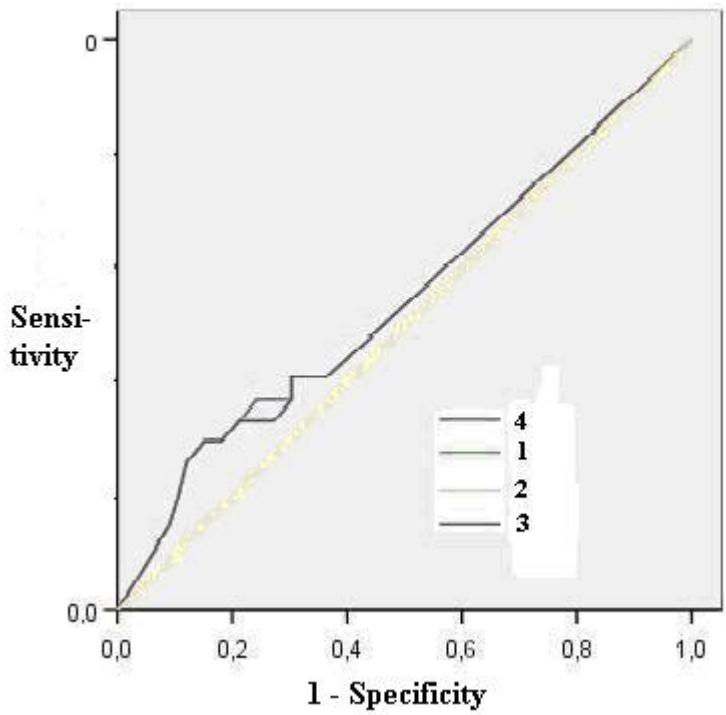

FIGURE 3. ROC curves of total GCS for the four equations.