Reconsidering the logic of World Federation of Neurosurgical Societies grading in patients with severe subarachnoid hemorrhage

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OBJECTIVE Current data show a favorable outcome in up to 50% of patients with World Federation of Neurosurgical Societies (WFNS) Grade V subarachnoid hemorrhage (SAH) and a rather poor prediction of worst cases. Thus, the usefulness of the current WFNS grading system for identifying the worst scenarios for clinical studies and for making treatment decisions is limited. One reason for this lack of differentiation is the use of “negative” or “silent” diagnostic signs as part of the WFNS Grade V definition. The authors therefore reevaluated the WFNS scale by using “positive” clinical signs and the logic of the Glasgow Coma Scale as a progressive herniation score.

METHODS The authors performed a retrospective analysis of 182 patients with SAH who had poor grades on the WFNS scale. Patients were graded according to the original WFNS scale and additionally according to a modified classification, the WFNS herniation (hWFNS) scale (Grade IV, no clinical signs of herniation; Grade V, clinical signs of herniation). The prediction of poor outcome was compared between these two grading systems.

RESULTS The positive predictive values of Grade V for poor outcome were 74.3% (OR 3.79, 95% CI 1.94–7.54) for WFNS Grade V and 85.7% (OR 8.27, 95% CI 3.78–19.47) for hWFNS Grade V. With respect to mortality, the positive predictive values were 68.3% (OR 3.9, 95% CI 2.01–7.69) for WFNS Grade V and 77.9% (OR 6.22, 95% CI 3.07–13.14) for hWFNS Grade V.

CONCLUSIONS Limiting WFNS Grade V to the positive clinical signs of the Glasgow Coma Scale such as flexion, extension, and pupillary abnormalities instead of including “no motor response” increases the prediction of mortality and poor outcome in patients with severe SAH.

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KEY WORDS Glasgow Coma Scale; subarachnoid hemorrhage; World Federation of Neurosurgical Societies grading; vascular disorders

Death and severe disability after spontaneous subarachnoid hemorrhage (SAH) are related to the initial severity of the hemorrhage. The scale most often used and recommended is the World Federation of Neurosurgical Societies (WFNS) scale, in which the clinical condition is primarily graded by the Glasgow Coma Scale (GCS).13 Despite low GCS scores in poor-grade SAH, 35%–50% of aggressively treated patients show a favorable outcome.1,4,12,13,15,18,22 Until now there has been no validated triage scheme to identify which patients with SAH will most likely not benefit from aggressive treatment based on WFNS scores.22 Even in the most severe SAH (i.e., WFNS Grade V), a good outcome is observed in 24%–50% of patients treated aggressively.1,12,15,32

In comatose patients the motor score of the GCS (mGCS) is the best indicator of clinical outcome.22,30 According to the original description and the contemporary use of the GCS, patients with an mGCS of 3 or 2 exhibit...
that included all patients with spontaneous SAH who were first contact with medical personnel, at admission to the hospital between January 2005 and December 2010. By thorough chart review we identified GCS scores recorded at admission. Because the motor equivalent for the next stage of progressive herniation is flaccidity, a GCS score of 3 means that the patient shows no motor response. This, however, is a well-known cause of misclassification.27,31 Logically, as herniation proceeds, decerebrate posturing (which indicates midbrain or pontine compression) is followed not only by flaccidity but also by signs of medullary compression such as third cranial nerve dysfunction and progressive loss of brainstem reflexes.

The usefulness of including brainstem reflexes and third nerve dysfunction to identify different stages of herniation in comatose patients has been previously shown.34 In-hospital mortality was highly associated with signs of herniation. Because the GCS is the basis for WFNS grading, information about progressive herniation beyond the motor response and posturing—e.g., third nerve dysfunction or loss of brainstem reflexes—is unfortunately not incorporated in routine SAH grading. As a known consequence, patients who are sedated and treated with ventilation who do not exhibit a motor response but have symmetrically reactive pupils and intact brainstem reflexes may be wrongly classified as having a GCS score of 3 and thus WFNS Grade V, which leads to inaccuracies in the prognostic power of the WFNS in poor-grade patients.

In this study we applied the concept by following the logic of the original GCS design and the pathophysiological concept behind the scale. During the progression of brain herniation, abnormal flexion (decorticate rigidity, late diencephalic syndrome) is followed by abnormal extension posturing (decerebrate rigidity, mesencephalic syndrome). Both are “positive” signs; i.e., signs that can be observed by the examiner. If herniation progresses further, damage occurs to the medulla, and the typical signs are flaccidity; no response to pain, mydriasis, and no reaction to light. Using the latter positive signs would help to verify a patient with a true GCS score of 3.

Our purpose was to reevaluate the prognostic power of the WFNS Grade V classification, particularly with regard to poor-grade patients. We compared the existing WFNS grading system with a modified WFNS herniation grading model (hWFNS) with respect to predicting poor outcome and death.

Methods

We performed a single-center retrospective analysis that included all patients with spontaneous SAH who were admitted to the Neurosurgical Unit of the Bern University Hospital between January 2005 and December 2010. The local ethics committee approved the study. By thorough chart review we identified GCS scores recorded at first contact with medical personnel, at admission to the neurosurgical unit, and after diversion of CSF. The GCS score after CSF diversion was used for grading the severity of SAH according to the WFNS scale.29 If continuous sedation was required for patient care, the last GCS score before intubation was used for WFNS grading. Demographic and clinical data were recorded. Signs of herniation (anisocoric pupils, bilaterally dilated pupils, no corneal reflexes, posturing) were recorded up to the time of aneurysm treatment. Admission imaging was used to assess Fisher grade, ventricular dilatation, and intracerebral hemorrhage.29 A CSF shunt was placed if a patient showed clinical and radiological signs of hydrocephalus, defined as decreased level of consciousness and ventricular dilatation. In comatose patients an external ventricular drain was placed, which was also used for monitoring intracranial pressure. Patients were treated according to standard SAH guidelines, which included early angiography and transfer to an intensive care unit. Aggressive treatment of poor-grade patients was at the discretion of the treating surgeon and was based on parameters like clinical presentation, age, pretreatment morbidities, and the patient’s expressed wishes. Outcome was assessed according to the modified Rankin Scale (mRS) at 6 months post-SAH, when patients were hospitalized for a control angiography, or during visits to the outpatient clinic. Outcome was dichotomized into good (mRS Score 0–3) and poor (mRS Score 4–6).

The WFNS and hWFNS Grading Models

Patients were graded according to the original WFNS scale, in which GCS Score 3–6 corresponds to WFNS Grade V and GCS Score 7–12 corresponds to WFNS Grade IV.

To test our hypothesis, these patients were also graded according to our modified WFNS classification, the hWFNS. In this modification of Grade V, we only included patients with signs of flexion or extension or positive clinical signs of brainstem dysfunction (anisocoric pupils, bilaterally dilated pupils, no corneal reflexes). Thus, patients with a GCS score of 6–12 or those with no motor response but otherwise intact brainstem function were graded hWFNS Grade IV. Thus, a patient graded as GCS 3 (no motor response) but with 3-mm symmetrical pupils with prompt reaction to light and intact corneal reflex was assigned hWFNS Grade IV instead of WFNS Grade V. In summary, contrary to patients with hWFNS IV, those with hWFNS V showed at least one of the following signs of brainstem dysfunction or herniation: anisocoric pupils, bilaterally dilated pupils, no corneal reflexes, or posturing (flexion, extension). The two classification methods were compared with respect to predicting poor outcome and death.

Statistical Analysis

Comparison between the WFNS and hWFNS grading systems was done using OR, positive predictive value (PPV), sensitivity, and specificity. The OR and PPV for poor outcomes were calculated using contingency tables. The 95% CIs for ORs were obtained according to the efficient-score method.29 The Fisher exact test was used to calculate 2-sided p values. We also created likelihood ra-
Results

This retrospective analysis included 428 patients with spontaneous SAH who were admitted to the Neurosurgical Department of the Bern University Hospital between January 2005 and December 2010. We identified 182 patients with poor-grade SAH, of whom 80 were assigned WFNS Grade IV and 102 were WFNS Grade V. The study included 56 men and 126 women (ratio 1:2.3), with a median age of 60 years (interquartile range 53–69 years). According to initial imaging, 6 patients (3.3%) were Fisher Grade 2, 137 (75.3%) were Fisher Grade 3, and 39 (21.4%) were Fisher Grade 4. One hundred sixty-four patients (90.1%) had intraventricular and/or intraparenchymatous hemorrhage. Thirty-eight patients (20.9%) received aneurysm clipping and 67 (36.8%) received coil intervention. Two patients were lost to follow-up. The distribution of patients according to the two different WFNS classifications and outcome parameters is displayed in Table 1. Both WFNS scores showed a highly significant association with respect to mortality and outcome at 6 months. According to the two classification methods, 101 patients (WFNS) and 77 patients (hWFNS) were assigned SAH Grade V. According to the WFNS classification, 75 of 101 patients with Grade V had a poor outcome after 6 months, which resulted in a PPV for poor outcome of 74.3% (OR 3.79, 95% CI 1.94–7.54) (Table 1, Fig. 1). According to the hWFNS classification, 66 of 77 patients with Grade V had a poor outcome: PPV 85.7% (OR 8.27, 95% CI 3.78–19.47).

Sixty-nine of 101 patients with WFNS Grade V died: PPV 68.3% (OR 3.9, 95% CI 2.01–7.69), compared with 60 of 77 patients with hWFNS Grade V: PPV 77.9% (OR 6.22, 95% CI 3.07–13.14). Figure 1 shows that the hWFNS scale has an overall better diagnostic quality with respect to poor outcome. With respect to mortality after 6 months, the two scales (WFNS and hWFNS) are equal (Fig. 2).

Discussion

The Pathophysiological Concept and Logic Behind the Lower GCS Scores

The GCS was originally designed to classify different states of impaired consciousness. Impaired consciousness as an expression of brain dysfunction can be caused by focal or diffusely acting agents. Supratentorial lesions can cause impaired consciousness by two major clinical herniation syndromes: the uncal herniation syndrome causes an early third nerve compression and a lateral midbrain compression, and the central herniation syndrome begins with bilateral diencephalic impairment. Although they have different starting points, if herniation progresses both syndromes proceed to a final stage of mesencephalic and upper medullary involvement. During central herniation in its late diencephalic stage, stretching and compression of feeding vessels and impairment of the ascending arousal system causes coma, flexor posturing (decorticate posturing), and yet small reactive pupils. The diencephalic stage is followed by the midbrain stage, where pupils become fixed at midposition. Motor responses show extensor posturing (decerebrate posturing), either spontaneously or in response to stimuli. Extensor posturing is believed to be due to a release of vestibulospinal postural reflexes from forebrain control, and the fixed position of the pupils is presumably caused by central impairment of both the sympathetic and parasympathetic central pathways. Next the patient enters the pontine stage, where motor tone becomes flaccid, pupils dilated and irregular, and breathing irregular and shallow due to destruction of upper pontine structures. Finally, in the medullary stage, the pupils are maximally dilated and breathing fails, with no chance of useful recovery.

In early uncal herniation the pupil is dilated but still reacts to light, which is abolished in the late uncal herniation syndrome. Pupillary dilation in uncal herniation syndrome is caused, in contrast to the central herniation syndrome, by direct compression of the oculomotor nerve by herniated tissue. As uncal herniation proceeds, the next stage is the midbrain stage (see above), skipping the diencephalic stage. With progressive herniation, the subsequent stages are equivalent to the central herniation syndrome. Including this pathophysiology of progressive herniation in the current WFNS grading system, our data show that discrimination and outcome predictions improve when clinical signs of brainstem dysfunction are used as additional criteria for assigning a GCS score of 3.

Weakness of the Current WFNS Grade V Definition

The so-called brainstem sign modification avoids labeling patients who might actually have a better prognosis.

<p>| Table 1. Outcome at 6 months according to the mRS: comparison of WFNS and hWFNS scales |
|--------------------------------------------|---|---|-----------------|-----------------|---|---|-----------------|-----------------|</p>
<table>
<thead>
<tr>
<th>Scale</th>
<th>Outcome</th>
<th>ppv</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
<th>Alive</th>
<th>Dead</th>
<th>PPV</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>WFNS</td>
<td>Grade IV</td>
<td>45</td>
<td>34</td>
<td>51</td>
<td>28</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>74.3</td>
<td>0.69 (0.59–0.77)</td>
<td>0.63 (0.51–0.75)</td>
<td>32</td>
<td>69</td>
<td>68.3</td>
<td>0.71 (0.61–0.8)</td>
<td>0.61 (0.5–0.72)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Grade V</td>
<td>26</td>
<td>75</td>
<td>43</td>
<td>66</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>85.7</td>
<td>0.61 (0.51–0.7)</td>
<td>0.85 (0.74–0.92)</td>
<td>17</td>
<td>60</td>
<td>77.9</td>
<td>0.62 (0.51–0.72)</td>
<td>0.8 (0.7–0.9)</td>
<td></td>
</tr>
<tr>
<td>hWFNS</td>
<td>Grade IV</td>
<td>60</td>
<td>43</td>
<td>66</td>
<td>37</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Grade V</td>
<td>11</td>
<td>66</td>
<td>51</td>
<td>28</td>
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</table>

* Good outcome: mRS Score 0–3; poor outcome: mRS Score 4–6.
† PPV refers to the prediction of poor outcome and death in patients newly classified as WFNS Grade V.
but are included in the original WFNS Grade V with a GCS score of 6 or a misclassified GCS score of 3. Comparable results have been published for mGCS in patients with poor-grade SAH who do not improve above an mGCS score of 3,13 and for prediction of morbidity and mortality in childhood drowning or near-drowning.10,14 In these cases, unreactive pupils, decorticate, decerebrate, or flaccid posture (GCS score ≤ 5) were the best independent predictors of poor neurological outcome and death.10,14

Although diffuse ischemic or hypoxic brain damage after SAH is less reliably graded with the GCS, this flaw applies more to the original WFNS scale, because the hWFNS scale incorporates these signs. Major shortcomings of the GCS score are as follows: 1) the difficulty in assessing verbal response in intubated patients; 2) a “missing sign”—no motor response—to allocate the worst grade, which is of poor specificity and is not a pathological finding per se; and 3) the lack of attention...
to abnormal brainstem reflexes and signs of herniation. The degree of oculomotor dysfunction has even been described as the most valuable indicator of the progress and extent of the herniation. In addition, recent publications on traumatic brain injury have pointed to the problem of early intubated patients and reliable GCS assessment as well as the lack of an association between GCS score and outcome. Besides the shortcomings of the GCS, the clinical status of patients with poor-grade SAH and the quality of assessments can be obscured by intubation, sedation, hydrocephalus, or seizures. In summary, these factors might negatively influence the predictive value of the WFNS grade.

Modification of WFNS Grade V

Use of the hWFNS scale improved the predictive value of the original WFNS grading. The hWFNS Grade V is based on clearly defined positive pathological findings; i.e., visible signs of herniation or brainstem dysfunction. Using positive signs augments the level of differentiation between WFNS Grades IV and V. Comparable results were presented in earlier studies.

Van den Berg et al. showed that neurological improvement > GCS Score 5 (which corresponds to hWFNS Grade IV) is associated with favorable outcome in 39% of patients, whereas those without improvement (which corresponds to hWFNS Grade V) showed a worse outcome. Starke et al. showed that each point increase in motor examination score predicted a 1.8-fold increased odds of favorable outcome. Both methods reflect signs for a beneficial outcome and, according to both methods, a good outcome can only be predicted after clinical improvement (e.g., improvement in mGCS score) either has or has not taken place up to a certain point in time. Mack et al. provided evidence for a clinical sign that predicted negative outcome. They showed a better mid- and long-term recovery in patients who had intact pupillary reactivity compared with those with uni- or bilateral nonreactive pupils. The hWFNS scale, as in the latter study, predicts poor outcome using only positive clinical signs, which includes posturing (mGCS Scores 2 and 3) in its grading scale.

The WFNS scale is widely accepted and our modification would only affect the definition of poor-grade patients (i.e., Grades IV and V). The acceptance of a modification of an existing grading system is not predictable, but mainly depends on the following features: 1) its simplicity; 2) its pathophysiologic logic; 3) its accuracy in describing a patient’s clinical status; and 4) its relevance for clinical management. The presence of a brainstem sign often has management consequences. Most neurosurgeons already use brainstem signs, when present, in addition to a WFNS Grade V diagnosis when reporting about a patient’s neurological status or when deciding about the individual management of a patient.

To validate the findings of this retrospective study, we have initiated a multicenter prospective trial that will start patient recruitment in 2015 (ClinicalTrials.gov, registration no. NCT02304328).

Conclusions

Demanding positive signs of brainstem herniation or dysfunction before assigning a GCS score of 3 in patients with poor-grade SAH helps to identify patients with “true” WFNS Grade V, and significantly improves prediction of outcome at 6 months. These criteria could easily be implemented into the WFNS grading system.

References


Disclosure
The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

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