

Use of Clinical Scales in Neurology – Implications for Researchers and Clinicians

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Conflicts of Interest

- None

Goals

- Issues in design of clinical trials
- Importance of clinical measures
- Used in all types of clinical research
- Examples of research in stroke

Evidence-Based Medicine

- Guidelines, which provide the foundation of evidence-based medicine, have created the standards for care
- Information for the guidelines largely comes from the results of modern clinical trials
- Responses by regulatory bodies and third party payers also are influenced by the results of clinical trials

Issues in Design of Trials

- Primary goals of trials vary and affect the design of the research program
- Prevention
- Slow progression
- Avoid recurrent events
- Prevent complications
- Reduce mortality
- Maximize recovery
- Improve or maintain quality of life

Issues in the Design of Clinical Trials

- Broad spectrum of diseases of brain, spinal cord, PNS, and muscle
- Wide variations in the extent and locations of disease
- Epidemiological variables and the presence of comorbid diseases
- Use of multiple concomitant therapies – “best medical care”
- Treatment goals and the nature of the intervention that is being tested in the trial

Randomization

- Crucial component of clinical trial
 - Avoids bias in patient recruitment
 - Baseline clinical features often used
 - History of illness and progression
 - Severity of impairments
 - Co-morbid diseases and treatments
- In multi-centers studies often centrally done

Surrogate Markers Trials in Neurology

- Imaging
 - Brain imaging: size, location, and evolution of disease
 - Brain functional imaging
 - Vascular imaging: recanalization
- Biomarkers
 - Variety of options: inflammatory, biochemical, genetic
- Electrophysiology studies
- Clinical outcomes remain the measure of success of any treatment

Blinding / Masking

- Also important for clinical trials
- Avoids bias in determining outcomes and events
- Use a wide range of clinical outcome measures
- Process varies depending on type of study
 - Patient is unaware of treatment
 - Patient and treating physician are unaware of treatment
 - Patient and rater are unaware of treatment
 - Independent rater or panel unaware of treatment

Clinical Rating Instruments

- Fundamental component of clinical research that now are used in practice because they provide important information for both researchers and clinicians
 - Eligibility for enrollment
 - Types and severity of neurological impairments
 - Changes in neurological status
 - Decisions about management
 - Responses to treatment
 - Outcomes

Requirements for a Useful Clinical Rating Instrument

- Inherent credibility- face validity
 - Germane to the clinical situation
 - Widely used and clinically useful
 - Results believable and make sense to both health care providers and the public
 - Understandable
 - A knowledgeable person should have a mental image of the patient's status when given the "score" on the scale

Steps in Development of a Clinical Rating Instrument

- Complex process that requires thought
 - Purpose of scale and information to be gained
 - Relevant to the assessment of patients
 - Assessed by history, examination, or diagnostic tests
 - Define how the scoring of a new scale will interdigitate with other rating instruments
- Need for a clear plan for testing and validating the instrument

Attributes of a Useful Clinical Rating Instrument

- Easy to administer for patients and assessors
 - Should not be time-consuming or burdensome
- Performance and scoring are straightforward
 - Clear instructions on the use
 - Administering and scoring of the scale
- Tested for reliability and reproducibility
 - Inter-rater agreement
 - Intra-rater reproducibility
- Educational and certification programs

Quality Control Measures in Clinical Trials

- Extra requirement in research studies, especially true in multi-center clinical trials
- Requirements
 - Scale is administered correctly
 - Scoring is accurate and consistent
- Well-validated scales should be used
 - Comparison with other research programs
 - Requirement of funding agents and regulators
- Programs to increase reliability and reproducibility
 - Education and certification
 - Central adjudication

Enthusiasm for New Clinical Rating Instruments

Researchers often have the desire to develop a new rating instrument

Time-consuming and may not be successful

Delays the primary goal of the project

Best to adopt/adapt current scales

NINDS Common Data Elements

- Developed to standardize research
- Wide variety of neurologic diseases
 - Degenerative disease, headache, trauma, stroke, etc.
- Well standardized instruments
- Allows comparison of different research studies

General Organization of Clinical Rating Instruments

- Usually based on history and direct examination
 - Impairments, disability, handicap
 - Some scale include results of diagnostic tests
 - Generally, two types of scales
 - Numerical scale - add components of assessment
 - Single score scale – aggregate of all information rather than scoring individual items

Numerical Scales

Several items assessed and scored

Scores of each item added to give a total score

Total score may represent a different combination of items

Depending on the scale, a high score can be good or bad

Example: NIH Stroke Scale

CHADS VASC Score

- Numerical scale to predict risk of stroke among patients with AF
- Based on history, epidemiology, and results of examination
- Higher score associated with highest risk

CHADS2 – VASc Score		
C	Congestive Heart Failure	1
H	Hypertension (>140/90 mmHg)	1
A	Age \geq 75	2
D	Diabetes Mellitus	1
S₂	Prior TIA or stroke	2
V	Vascular disease (MI, aortic plaque etc)	1
A	Age 65-74	1
Sc	Sex category (Female = 1 pt)	1

Glasgow Coma Scale

Feature	Response	Score
Best eye response	Open spontaneously	4
	Open to verbal command	3
	Open to pain	2
	No eye opening	1
Best verbal response	Orientated	5
	Confused	4
	Inappropriate words	3
	Incomprehensible sounds	2
	No verbal response	1
Best motor response	Obeys commands	6
	Localising pain	5
	Withdrawal from pain	4
	Flexion to pain	3
	Extension to pain	2
	No motor response	1

- Based on clinical findings
- Scores added from three components
- Low score poor prognosis
- Widely used in trauma

ICH Scale

- Used to assess patients with brain hemorrhage
- Combines epidemiology, imaging and clinical severity
- Prognosis

Component	ICH Score Points
GCS score	
3–4	2
5–12	1
13–15	0
ICH volume (cm ³)	
≥ 30	1
< 30	0
IVH	
Yes	1
No	0
Infratentorial origin of ICH	
Yes	1
No	0
Age (year)	
≥ 80	1
< 80	0
Total ICH Score	0–6

The GCS score refers to the GCS score at initial presentation (or after resuscitation); ICH volume, volume on initial CT calculated using the ABC/2 method; IVH, presence of any IVH on the initial CT.

GCS, Glasgow coma scale; ICH, intracerebral hemorrhage; CT, computed tomography; IVH, intraventricular hemorrhage.

Adapted from Hemphill JC 3rd, Bonovich DC, Besmertis L, Manley GT, Johnston SC. The ICH score: a simple, reliable grading scale for intracerebral hemorrhage. *Stroke* 2001;32:891–897.

NIH Stroke Scale

- 15 items of the neurological examination
- Each item independently scored
- Give a baseline severity of neurological impairments
- Could be used sequentially to monitor for worsening or improvement
- Range of scores 0 – 42
- Higher scores more severe stroke

NIH Stroke Scale

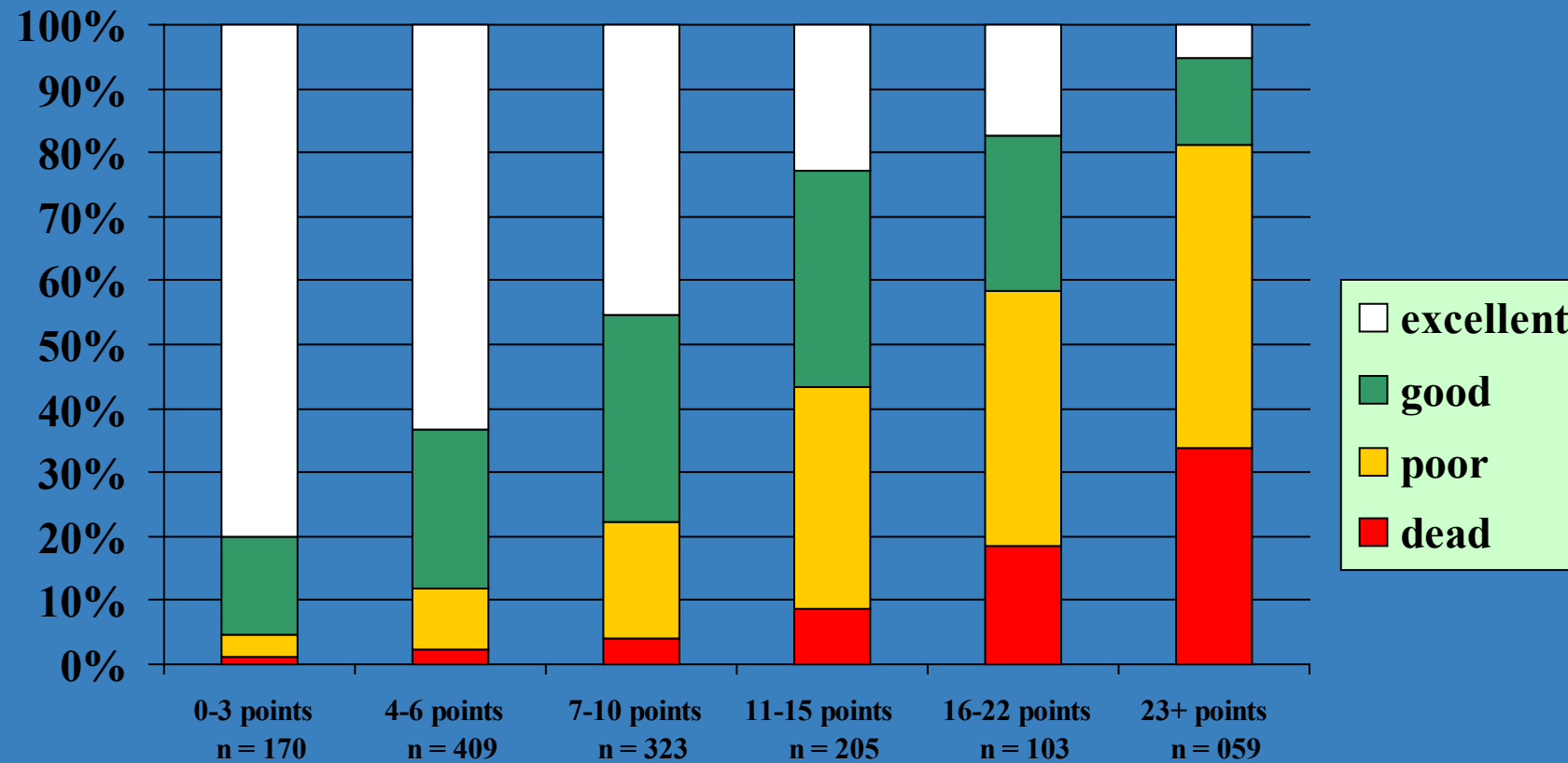
<i>Component</i>	<i>Scoring range</i>
Consciousness	0 – 3 points
Orientation	0 – 2 points
Commands	0 – 2 points
Best gaze	0 – 3 points
Visual fields	0 – 3 points
Facial motor function	0 – 3 points
Upper limb function (R/L)	0 – 4 (8) points
Lower limb function (R/L)	0 – 4 (8) points
Limb ataxia	0 – 2 points
Language	0 – 3 points
Articulation	0 – 2 points
Extinction	0 – 2 points

Brott et al, Stroke, 1989; 20: 864

Validation of NIH Stroke Scale

- Initial testing – high inter-rater agreement ($k = 0.69$) and test – retest reliability ($k = 0.66 - 0.77$)
- Prospectively assessed and total scores were compared to size of infarctions on CT and outcomes at 3 months
- Acceptable scale validity
- Scores correlated well with size of lesions and outcomes
- Tested in several other venues
- Now used internationally in wide range of stroke research
- Brott et al, Stroke, 1989: 20: 864

Prognosis by NIHSS Score



Increasing Reliability Scoring of NIH Stroke Scale

- Certification process using videotapes
- Used in clinical trials
- Available at several websites
- Components
- Education and testing
- Remediation
- Central adjudication of scores
- Albanese et al, Stroke; 1994; 25: 1748
- Lyden et al, Stroke; 1994; 25: 2250

Barthel Index

- Global outcome measure
- Assess level of independence
- Scores 0-100
- Individual items rated
- Score > 60 independent
- Score > 90 complete recovery

The Barthel Index		
Patient name	Rater name	Date
ACTIVITY		SCORE
Feeding		
0 = unable		
5 = needs cutting, spreading butter, etc, or requires modified diet		
10 = independent		_____
Bathing		
0 = dependent		
5 = independent (or in shower)		_____
Grooming		
0 = needs help with personal care		
5 = independent face/hair/teeth/shaving (implements provided)		_____
Dressing		
0 = dependent		
5 = needs help but can do about half unaided		
10 = independent (including buttons, zips, laces, etc)		_____
Bowels		
0 = incontinent (or needs to be given enemas)		
5 = occasional accident		
10 = continent		_____
Bladder		
0 = incontinent, or catheterised and unable to manage alone		
5 = occasional accident		
10 = continent		_____
Toilet use		
0 = dependent		
5 = needs some help, but can do something alone		
10 = independent (on and off, dressing, wiping)		_____
Transfers (bed to chair and back)		
0 = unable, no sitting balance		
5 = major help (one or two people, physical), can sit		
10 = minor help (verbal or physical)		
15 = independent		_____
Mobility (on level surfaces)		
0 = immobile or <50 yards		
5 = wheelchair independent, including corners, >50 yards		
10 = walks with help of one person (verbal or physical) >50 yards		
15 = independent (but may use any aid, eg. stick) >50 yards		_____
Stairs		
0 = unable		
5 = needs help (verbal, physical, carrying aid)		
10 = independent		_____
Total (0-100)		

Overall Assessment with a Single Score

All components of the assessment are summarized in a single score

Ranges to separate good from poor

Each score has specific and defined criteria

Generally, the higher the score, the poorer the situation

Hunt and Hess Scale

Grade	Criteria
0	Unruptured aneurysm
I	Asymptomatic or minimal headache and slight nuchal rigidity
II	Moderate-severe headache, nuchal rigidity, cranial nerve palsy
III	Drowsiness, confusion, or mild focal deficit
IV	Stupor, severe hemiparesis, vegetative disturbance
V	Deep coma, decerebrate rigidity, moribund appearance

Hypertension, diabetes, arteriosclerosis, chronic pulmonary disease, or vasospasm assigns patient to next less favorable category

- Single score
- Patients with aneurysms
- Clinical findings on admission
- Poor prognosis with higher score

Modified Rankin Scale

- Global outcome scale that is internationally accepted and used widely in stroke studies
- Status of the patient with an emphasis on motor limitations and walking
- Based on patient report
- Can be performed by a broad spectrum of health care providers
- Central adjudication
- Different scores (levels of recovery) are understood by physicians and governmental bodies

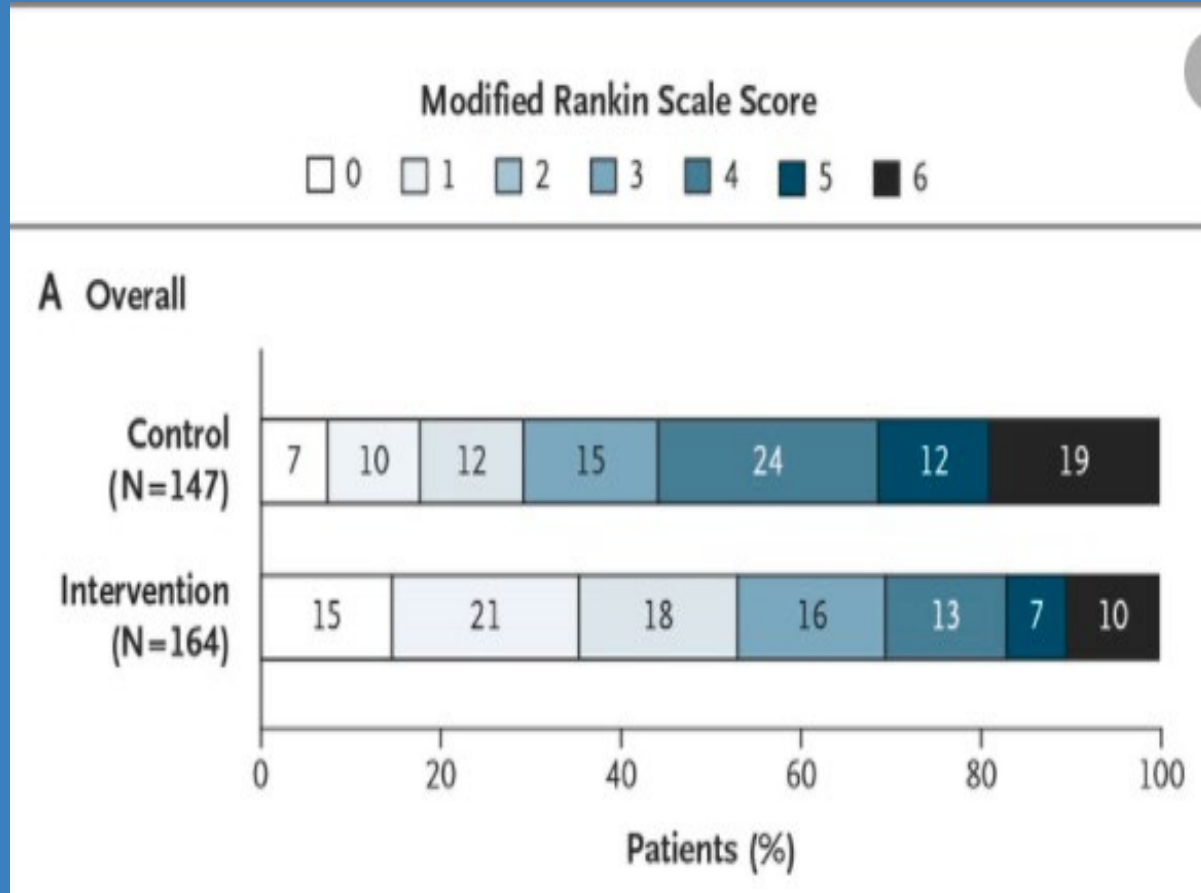
mRS Scores and Definitions

mRS score	Description
0	No symptoms at all
1	No significant disability despite symptoms; able to carry out all usual duties and activities
2	Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance
3	Moderate disability; requiring some help (e.g. with shopping/managing affairs) but able to walk without assistance
4	Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance
5	Severe disability; bedridden, incontinent and requiring constant nursing care and attention
6	Dead

Global Measures of Outcome

- Scales widely accepted by medical community, funding authorities, and governmental regulators
 - Broadly differentiate favorable from unfavorable outcomes
 - Used in both acute and recovery trials
 - Measure impact on multiple neurological impairments or disabilities
- May miss important neurological issues
 - Discrete areas of neurological disability
 - Over-emphasize some components of recovery
 - Often have ceiling- and floor- effects
- Require larger clinical trials

mRS Score for Outcomes



- Direct group comparisons
- Shift in outcomes

Glasgow Outcome Scale

GOS	GOSE	Interpretation
1 = Dead	1 = Dead	Dead
2 = Vegetative state	2 = Vegetative state	Absence of awareness of self and environment
3 = Severe disability	3 = Lower severe disability	Needs full assistance in ADL
	4 = Upper severe disability	Needs partial assistance in ADL
4 = Moderate disability	5 = Lower moderate disability	Independent, but cannot resume work/school or all previous social activities
	6 = Upper moderate disability	Some disability exists, but can partly resume work or previous activities
5 = Good recovery	7 = Lower good recovery	Minor physical or mental deficits that affects daily life
	8 = Upper good recovery	Full recovery or minor symptoms that do not affect daily life

ADL = activities of daily living.

- Originally five items
- Now expanded to nine
- Used primarily for head injuries
- Also used in other severe brain diseases

Complications

- Depression
- Anxiety
- Dementia
- Deep vein thrombosis
- Pneumonia
- Falls
- Nutrition
-

Test for Cognitive Impairments

MONTREAL COGNITIVE ASSESSMENT - PHILIPPINES (MOCA-P)

NAME: _____ Education: _____ Date of birth: _____
 Sex: _____ DATE: _____

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- Most common are Mini Mental Status and Montreal Cognitive Assessment
- Several items rated and total score

Quality of Life

- Several rating instruments
- Euro-qual 5
- Scores added

Attribute	Level	Description
Mobility	1	No problems in walking about
	2	Some problems in walking about
	3	Confined to bed
Self-care	1	No problems with self-care
	2	Some problems with washing or dressing self
	3	Unable to wash or dress self
Usual activities	1	No problems with performing usual activities (ie, work, study, housework)
	2	Some problems with performing usual activities
	3	Unable to perform usual activities
Pain or discomfort	1	No pain or discomfort
	2	Moderate pain or discomfort
	3	Extreme pain or discomfort
Anxiety or depression	1	Not anxious or depressed
	2	Moderately anxious or depressed
	3	Extremely anxious or depressed

Modality-Specific Scales

- Large number of rating instruments that are most used in rehabilitation and recovery research
- Emphasize recovery or compensation in a specific activity
 - Language and speech
 - Walking
 - Hand function
- Do not provide an assessment of the patient's autonomy

TICI Scale

- Used in patients with stroke having endovascular treatment
- Based on imaging findings following treatment
- Prognosis and recovery
- Adjunct to clinical outcomes

Thrombolysis in Cerebral Infarction (TICI) classification	
Grade 0	no perfusion
Grade 1	penetration with minimal perfusion
Grade 2a	partial filling $\frac{1}{3}$ of the entire vascular territory
Grade 2b	complete filling, but the filling is slower than normal
Grade 3	complete perfusion

Conclusion

- A wide variety of instruments have been developed for clinical research in neurology
 - Prevention
 - Acute care
 - Rehabilitation
 - Outcomes
 - Quality of life
- Some are modality-specific and others are more global
- No single clinical instrument will address all aspects of a patient's neurological disease

Conclusion Cont.

- Provide a quantitative element to a complex clinical situation
- Foster communication among health care professionals
- Results of clinical research are described using these instruments
- Both researchers and clinicians should understand the information conveyed using the instruments