Perspectives on multidimensional assessment of post-stroke sequelae: from clinimetrics to holism

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**Competing interests**

The authors declare no conflicts of interest.

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**Abbreviations**

PSS, post-stroke sequelae; TCM-WM, traditional Chinese and Western medicine; CMs, Chinese medicines; NIHSS, National Institutes of Health Stroke Scale.

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**Abstract**

In this work, we intended to connect clinimetrics with holism in traditional Chinese medicine towards multidimensional assessment of post-stroke sequelae in real-world setting, as a bridge between inheritance and innovation. Firstly, a systematic search of current evidence that supported integrated treatment of traditional Chinese and Western medicine for post-stroke sequelae sufferers was performed. Secondly, on the basis of available evidence, we presented couples of implications. Lastly, as psychosomatic perspective is one of the main academic paradigms of traditional Chinese medicine holism, we chiefly proposed comprehensive assessment for both motor and non-motor severities to probably match consonance with traditional Chinese medicine practice that treats psycho-/somatic-complains simultaneously.

**Keywords:** clinimetrics; holism; integration of traditional Chinese and Western medicine; traditional Chinese medicine; post-stroke sequelae
Background

Acute ischemic stroke is a non-communicable disease that poses a substantial risk of mortality and morbidity worldwide, associated with leading causes of disability-adjusted life-years among Chinese population over 50 for the last decade [1–3]. According to the newest report from National Health Commission of the People's Republic of China [4], there was an increasing tendency for incidence as well as prevalence rate of ischemic stroke during the past 14 years, and the latter had reached up to 1256 per 100,000 person-years after age-standardized processing in 2019. Advanced interventions such as intravenous thrombolysis and endovascular therapies have manifestly improved the survival rate in acute phase of stroke, but simultaneously posed challenges to effective management of chronic post-stroke sequelae (PSS). In China, the integration of traditional Chinese and Western medicine (TCM-WM) is a routine therapy widely accepted by most patients in the clinical practice. For example, ultra-early acupuncture and massage could improve neurologic deficits, and herbal medicines can improve non-motor symptoms (e.g., post-stroke insomnia and depression), combined with conventional Western medicine therapies, which have greatly benefited patients with chronic PSS. And based on several current clinical guideline, acupuncture is recommended for advantageous rehabilitation among patients with PSS [5], while merging TCM-WM treatment into conventional nursing could promote better care of sensory disturbance [6]. However, due to insufficient evidence of high-level safety from large-sample investigation, the long-term combination of Chinese medicines (CMs), synthetic drugs and biological agents for chronic PSS may induce potential adverse drug reactions, especially when CM-injections were involved [7]. And it is challenging for physicians to make such a long-period risk-benefit appraisal under unknown mechanisms of interactions. In addition, there are a couple of challenges for evaluating efficacy of TCM-WM intervention among patients with PSS. For one thing, in the real-world settings, TCM-WM protocols always vary from practitioners to practitioners because of individual treatment. For instance, physicians form different department in the same hospital may choose distinct agents for the same PSS, which is probably dependent on their own experience or patients’ preference, while the outside doctors treat PSS would value regional custom and National Reimbursement Drug List; for another, the perception of traditional Chinese medicine (TCM) interventions in TCM-WM therapies for PSS treatment is different between TCM and Western medicine practitioners. For example, Xingnaojing injection is generally used for post-stroke disturbance of consciousness [5] and TCM physicians recommend for its prompt application, in contrast to early-stage thrombolysis in accord to Western medicine guidance. As a result, aforementioned interventions, namely reperfusion treatment and CM-injection, significantly overlap, leading to a temporal conflict during the same period [8]. Therefore, the specific standard protocol for PSS still lacks despite the existence of a few relevant TCM-WM clinical guidelines for reference.

Clinimetrics, an emerging recommended science of clinical measurements, provides a suitable conceptual and methodological framework to integrate the consistency of clinic and statistics with 3 quality-controlled indexes (viz. sensitivity, reliability and validity) [9, 10], which somehow promotes some hints that multi-dimensional evaluation from the perspective of clinimetric instruments and holistic concept in TCM.

Evidence and implications of available evidence

In this section, we systematically reviewed contemporary studies involved with TCM-WM interventions in ischemic PSS as an exemplification, in a bid to investigate common clinimetric instruments in clinical practice and to facilitate evidenced-based combination with TCM holism.

We conducted a literature survey of 7 databases (CNKI, VIP, WangFang, SinoMed, Embase, PubMed, Cochrane Library, Web of Science) from January 1st, 2017 to October 31, 2022 (Supplementary Table S1). Studies should be published in English or Chinese with Mesh and/or Entry terms including “Stroke”, “Ischemic”, “Embolic”, “Thrombotic”, “Sequeleae” “Integrative Medicine”, “Integrated Chinese and Western Medicine”). Further, unindexed journals and clinical trial registries were not searched. Our systematic retrieval returned 227 records and 51 eligible studies [11–61] were screened finally (Figure 1).

![Figure 1 Flowchart of screening eligible studies](image-url)
From our findings, a total of 19 instruments were used for objective assessment (Figure 2). As to evaluation content, both motor and non-motor symptoms of PSS were assessed. The former primarily included paralysis, limb spasm, ataxia, and dystaxia, while the latter mainly comprised depression, apathy, anxiety, cognitive or language dysfunction, constipation and insomnia, etc. In terms of evaluation methods, 13 of 19 were clinician-reported outcomes (viz. National Institutes of Health Stroke Scale (NIHSS), Stroke-Specific Quality of Life, Barthel Index of Daily Living, Modified Barthel Index Activities of Daily Living, Physical Self-maintenance Scale, Instrumental Activities of Daily Living, Fugl-Meyer Assessment, Lovett Scale Manual Muscle Testing, Hamilton Anxiety Scale), 5 of 19 were patient-reported outcomes (viz. Stroke-Specific Quality of Life, Nottingham Health Profile, Pittsburgh Sleep Quality Index, Self-Rating Anxiety Scale, Self-Rating Depression Scale) and the rest combined both patient-reported outcomes and clinician-reported outcomes. Regarding evaluation categories, broadly speaking, there were assessments for severity of neurological deficits assessment (e.g., NIHSS) as well as non-motor impairments (e.g., Montreal Cognitive Assessment), and individual-level-based daily living disability as well as social-level-based handicaps dysfunction (e.g., Modified Barthel Index Activities of Daily Living). Besides, 5 instruments served as measuring tools for TCM clinical core outcome [62, 63], namely NIHSS, Fugl-Meyer Assessment, Mini-mental State Examination, Barthel Index Activities of Daily Living and Lovett Scale Manual Muscle Testing. Furthermore, another 2 unexhibited instruments based on TCM syndromes and symptoms were also employed for PSS.

It is critical to choose appropriate instruments for measuring clinical efficiency. Whereas, in the context of individualized treatment, selecting endpoints towards the ideal settings of clinical trials might observe clinical efficiency of post-stroke sufferers treated with TCM-WM therapies to some degree, instead of full-scale angle. As a matter of fact, TCM holism highlights the spatio-temporal unification of “Environment-Individuals-Society”, with its complex scientific connotation that displays modern biologically holographic theory in another pattern [64, 65]. As stroke is an exemplar disabling long-term condition with potential multisystem impacts, more sophisticated assessments are required rather than simple dichotomous endpoints to fully capture daily living dysfunction in most post-stroke survivors.

![Figure 2 Overview diagram of 19 instruments. NIHSS, National Institute of Health Stroke Scale; CSS, China Stroke Scale; BI-ADL, Barthel Index Activities of Daily Living; MBI-ADL, Modified Barthel Index Activities of Daily Living; PSMS, Physical Self-maintenance Scale; IADL, Instrumental Activities of Daily Living; Lovett-MMT, Lovett Scale Manual Muscle Testing; FMA, Fugl-Meyer Assessment; HDS-R, Hasegawa Dementia Scale Revised; MMSE, Mini-mental State Examination; MoCA, Montreal Cognitive Assessment; HAMA, Hamilton Anxiety Scale; SAS, Self-Rating Anxiety Scale; SDS, Self-Rating Depression Scale; PSQI, Pittsburgh Sleep Quality Index; NHP, Nottingham Health Profile; SS-QoL, Stroke-Specific Quality of Life.](https://www.tmrjournals.com/imm)
Discussion

Adequate awareness of biopsychosocial domain

Although motor symptoms assessed by NIHSS or China Stroke Scale are essential to determine the post-stroke quality of life undeniably, patients’ subsequent PSS also deserves attention concerning clinimetrics-oriented evaluation. In clinical encounters, there is usually a mismatch between low NIHSS scores and severely impaired functioning. For instance, post-stroke depression or cognitive impairment may be important mediating variables, when a young male patient with few sequelae is unable to go to work. Likewise, TCM holds the opinion that body constituents and spirit are organically unified, which suggests that visible motor deficits often interact with invisible emotion or cognition. In other words, emotion-induced pathogenic factors known as interoception in modern psychology should be valued, which may be quantified by three-dimensional intervention model [66]. Furthermore, a number of TCM investigators applied “body-spirit syncrétism” to PSS treatment assimilated with modern rehabilitation techniques [67–71]. Thus, since psychosomatic perspective is one of main academic paradigms of TCM holism, comprehensive assessment for both motor and non-motor severities need to be enhanced, in line with “biopsychosocial medical model” that social, psychological and biological factors are underscored to jointly account for onset of illness [72, 73].

Merging long-term prognosis into full-cycle disease process towards TCM-oriented doctor-patient relationship

It is merging long-term prognosis with short-period efficacy that serves as another clinimetrics-oriented appraisal after stroke, according to TCM holism. Noteworthy, an interesting example is about the treatment adherence in secondary prevention of stroke whose benefits could not be totally understood by some patients, inevitably resulting in repeated discontinuation of medications and recurrent stroke. When they turned to TCM diagnosis attached to humanistic care, their mild complaints (e.g., constipation) will be captured and improved. The relief of this subjective distress indirect to acute/short-term prognosis (e.g., NIHSS scores) improvement, would significantly improve doctor-patient relationship that leads to increasing medication adherence and decreased stroke recurrences in turn, thereby obviously promoting preferable long-period prognosis, as an old saying goes that “doctor himself is the medicine”. Similarly, good prognosis largely depends on empathy competency from medical staff by verbal and non-verbal communication [66, 74]. Additionally, patient-reported outcomes as a supplement to clinician-reported outcomes could not only empower dominance of subjective experience in both TCM and TCM-WM practice, but also avoid pitfalls of conventional scales being inadequate for clinical challenges. Hence, from viewpoint of TCM holism, we recommend greater emphasis on TCM-oriented doctor-patient relationship during routine practice and systematic indexes of long-period prognosis based on clinimetric methodology, instead of solely using total effective rate as the composite outcome [75].

Concluding remarks

In summary, in the real-world settings, the integrative intervention of PSS is complex. And we are pleased to find both non-motor and motor complaints of PSS being well-addressed in eligible studies. TCM holism emphasizes interaction of human and his surroundings (viz. natural environment and social circumstance), harmony of inner and outer structures of individual body, and personalized complete course of disease, which suggests that core outcome set embracing a series of endpoints promisingly plays a multidimensional and long-term evaluation role [76] and is probably measured by clinimetric instruments. In accord with the guidance“non-discriminative judgment and complementary strengths” on TCM-WM therapies [77–79], incorporating clinimetrics into TCM holism will potentially promote evidence-based and clinic-oriented practice, where the latter is upholding classical principles as an inheritance while the former is breaking new ground for innovation.

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