

Preferences and Values for Treatment Goals in Patients with Acute Ischemic Stroke: Medical Staff Perspectives in China

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Abstract

Background: Individual values and beliefs vary according to cultural and social factors. To better understand clinical decision-making and inform future research, we undertook a survey of preferences in treatment goals for managing patients with acute ischemic stroke among medical professionals in China.

Methods: We designed a web-based survey through literature search, face-to-face interviews, pilot questionnaire development, and focus group meetings. Key outcomes explored were death, disability, quality of life, neurological impairments, cognitive dysfunction, and hemorrhagic transformation. Participants were asked to rate the importance of each outcome on a 5-point Likert scale to allow calculation of a weighted score of importance: higher scores indicating greater importance.

Results: During promotion among 2700 delegates at several major neurology conferences in 2018, 1189 participants (mean age 40 years, 53% female) completed the survey of whom 96% were clinicians, mainly from tertiary care hospitals located in 30 Provinces of China. For established therapies with bleeding risk (e.g. thrombolysis and thrombectomy), death was the most important outcome (weighted score 4.60), followed by disability (4.45), quality of life (4.45), neurological impairments (4.34), cognitive dysfunction (4.03), and hemorrhagic transformation (3.99). For other acute therapies without bleeding risk, quality of life ranked first (4.08), followed by disability (4.03), neurological impairment (3.92), death (3.79), cognitive dysfunction (3.78), and hemorrhagic transformation (3.51). Given a therapy with insufficient evidence of benefit, 845 (71%) participants thought it would be worth trying for potential to improve neurological recovery or quality of life.

Conclusions: From the perspective of Chinese medical staff, death is the most important outcome measure for patients with acute ischemic stroke. When reduction of death or disability were less likely to be achievable, the improvement in quality of life is an acceptable outcome measure. In contrast to the previously perceived high fear of bleeding in practice, hemorrhagic transformation was the least concerned even for therapies with a potential bleeding risk.

Introduction

While death and disability are the primary outcome measures used to assess the effects of therapies for acute ischemic stroke (AIS) in randomized controlled trials (RCTs)[1–3], the action of clinicians in interpreting such results depends upon many factors, such as the size, consistency and scope of net benefit over risks, and affordability of treatment. Guidelines recommend thrombolysis and thrombectomy for AIS based on a large body of evidence from RCTs[4, 5]. However, these therapies are only available to a small proportion (< 20%) of AIS patients worldwide, and even fewer (< 10%) in China and other parts of Asia[6–11], where neuroprotective agents, herbal products, and other therapies are more widely available and popular[6, 12, 13] despite insufficient supporting evidence. Reasons for the discrepancy between scientific evidence and clinical practice are complex.

The choice of treatment therapies is a joint decision between physicians and nurses, and patients and/or their families, where values and preferences over the importance of different outcomes from AIS vary across cultures, experiences and roles. The importance of patient-centered outcomes is now well accepted[14, 15], but few studies have been undertaken on the topic in China. The aim of our study was to determine the preferences and values of Chinese medical staff place upon key clinical outcomes used across treatments for AIS.

Methods

We conducted a staged study (Fig. 1), with approval from the Biomedical Research Ethics Committee of West China Hospital, Sichuan University [No. 2018(100)], and informed consent from all participants.

Stage 1: Face-to-face interviews

Two researchers independently undertook a literature search and identified 33 common outcome measures used in stroke RCTs (see Supplementary). Next, 31 stroke physicians from the West China Hospital, Sichuan University, participated in 1:1 face-to-face interviews, where they were asked to answer an open question: “which outcome measures do you think are important to assess the treatment effect for AIS during the acute phase” among the list of 33 outcome measures. Participants were required to provide at least 1 and no more than 10 responses, in rank order of clinical importance. A total of 306 responses were collected and these were categorized down to 20 outcome measures.

Stage 2: Pilot questionnaire development

A paper-based questionnaire was developed from the 20 outcome measures (Supplementary Table S1) for testing among 71 neurologists from 17 hospitals. In a round-table discussion, they had to choose 10 key outcome measures and provide feedback on design of the questionnaire.

Stage 3: Focus group meetings

A focus group of 4 stroke neurologists (ML, BW, SZ, and SW) finalized the survey content based upon the clinical importance of each outcome measure in sections: (i) baseline information; (ii) ranking importance of outcome measures in relation to established acute therapies with bleeding risk (thrombolysis, thrombectomy and antithrombotic agents) and other common therapies of neuroprotective agents, rehabilitation, acupuncture, Chinese patent medicine, and traditional Chinese medicine; (iii) three questions on “If an acute therapy may not reduce death or disability at 3 months but improves neurological deficits in short-term, do you think it is worth trying for stroke patients during the acute phase?” and if ‘Yes’, “which therapies would you like to use?” and “Please specify the outcome measures that you expect to improve with the chosen therapies”.

Stage 4: Web-based surveys

An online questionnaire developed by SurveyStar (Changsha, China) was delivered at 1 national and 6 regional academic, neurology conferences in China from April 2018 to September 2018. A two-

dimensional code linked to the questionnaire was promoted in lecture slide presentations and on postcards at the conference venues. Delegates were invited to scan the code and complete the questionnaire via mobile phones.

Statistical analysis

Two researchers (YW, SW) independently coded all interview data and performed thematic analysis of the pilot questionnaire[16]. The web questionnaire was then finalized after comparisons of the included categories with disagreements agreed through consensus. Quantitative data are presented as means and standard deviations for continuous variables, and percentage frequencies for categorical variables. To quantify the importance of each outcome measure ranked by participants, a 5-point Likert scale[17] was used: not important at all = 1, not important = 2, neutral = 3, important = 4, very important = 5. A weighted score was calculated using the following equation: $(1*a + 2*b + 3*c + 4*d + 5*e) / (a + b + c + d + e)$, where a, b, c, d, and e represent participants' numbers for ranked each outcome measure. A higher weighted score equated to greater clinical importance. All statistical analyses were performed in SPSS 25.0 (IBM, Chicago, IL, USA).

Results

Among 2700 delegates across seven conferences, 1895 accessed the web questionnaire and 1189 completed the survey. Of 1189 participants, the mean age was 40 ± 10 years and 53% participants were females. More than half had over 10 years clinical experience and 43% had research experience in stroke (Table 1).

Table 1
Baseline characteristics of 1189 participants from 30
provinces in China

Characteristics	
Age(years)	40 ± 10
Female	631 (53)
Highest academic degree	
Junior college degree or below	21 (2)
Bachelor's degree	540 (45)
Master's degree	471 (40)
Doctor's degree	157 (13)
Occupation	
Clinician	1141 (96)
Nurse	48 (4)
Clinical experience in stroke (years)	
None	62 (5)
≤ 5	253 (21)
6–10	245 (21)
11–19	280 (24)
≥ 20	349 (29)
Research experience in stroke (years)	
None	319 (27)
≤ 5	357 (30)
6–10	203 (17)
11–19	159 (13)
≥ 20	151 (13)
Teaching hospital	914(77)
Tertiary level hospital	946 (80)
Data are n (%) or mean (SD)	

Of the established acute therapies in AIS with potential bleeding risk, death was rated as the most important outcome measure (weighted score 4.60, 72.7% of participants ranked as 'very important'), followed by disability (weighted score 4.45, 56.4%) and quality of life (weighted score 4.45, 54.6%), neurological impairment (weighted score 4.34, 46.1%), cognitive dysfunction/dementia (weighted score 4.03, 30.1%), and hemorrhagic transformation (weighted score 3.99, 32.1%) (Fig. 2A). For other low-risk therapies, quality of life was ranked as most important outcome measure (weighted score 4.08, 35.2%), followed by disability (weighted score 4.03, 32.6%), neurological impairment (weighted score 3.92, 23.6%), death (weighted score 3.79, 33.4%), cognitive dysfunction/dementia (weighted score 3.78, 20.9%), and hemorrhagic transformation (weighted score 3.51, 16.6%) (Fig. 2B). Similar results were found in sensitivity analysis with the exclusion of responses from nurses (Supplementary appendix).

There were 845 (71%) participants who answered 'Yes' to the question on treatments with potential to improve neurological impairment but without a benefit on death or disability, with neuroprotective agents (57%), acupuncture (39%), Chinese patent medicine (24%), and traditional Chinese medicine (12%) being the most commonly chosen therapies. The key outcome measure targeted in the use of these therapies were limb function (77%), medical complication (defined as pneumonia, deep venous thrombosis or urinary tract infection) (65%), level of consciousness (64%), and pathological changes on brain imaging (defined as infarction volume expansion, reduction of hemorrhagic transformation, brain edema or middle shift) (56%) (Fig. 3).

Discussion

In our study of the preferences and values of health professionals involved in the management of AIS in China, we have shown that death is the outcome of most importance in the use of reperfusion therapies which are proven to reduce death and disability, whilst quality of life is also important. Hemorrhagic transformation had a low priority for these therapies which have a bleeding risk.

The finding that death had a higher priority than disability supports the old adage in Asian cultures that 'better to live than to die', whilst the ability to maintain functional independence in everyday life seems more important in Western culture. For example, as a life-saving intervention for malignant cerebral infarction, decompressive craniectomy was only acceptable to 7% of the general population in Germany, because the potential downside was the chance to continue living with severe disability[18]. However, recognition that people can change their views when affected is reflected in other studies in other countries showing higher rates of acceptance of decompressive hemicraniectomy: 28% in AIS patients, 47% in relatives[19], 16% in nurses[20], and 39% in physicians[21]. In regard to low-risk therapies, neuroprotection, rehabilitation, acupuncture, Chinese patent medicine, and traditional Chinese medicine, are all widely used alongside Western medicines in China[6], despite their limited evidence from RCTs. Our study shows these therapies are primarily used with the intent to improve quality of life.

Due to concerns over treatment-related hemorrhagic transformation, many Asian clinicians prefer to use lower doses of intravenous alteplase for thrombolysis treatment of AIS patients[22–24]. However, our

study suggests this adverse event is regarded as less important than the other clinical outcome measures, which is consistent with findings of dichotomized positive outcomes outweighing the risks of these treatments in RCTs. Education of doctors and patients over hemorrhagic transformation being an acceptable complication in the context of the poor prognosis of AIS may improve the update of reperfusion therapies.

Our web-based survey was able to gather opinions from a large number of health professionals at relatively low cost but is limited by selection bias from including those who were highly skilled and experienced, mainly clinicians, who had the opportunity to attend certain neurology conferences.

Conclusions

In summary, our survey of Chinese medical staff shows they rank death as the outcome of most importance for the use of proven reperfusion therapies, and contrary to current perceptions, the risk of hemorrhagic transformation had a low priority. When a therapy is unlikely to reduce the chances of death or disability, quality of life is more meaningful and acceptable outcome to target. These results may help improve the design of stroke RCTs and counselling of patients and families.

Abbreviations

AIS

acute ischemic stroke; RCTs: randomized controlled trials;

Declarations

Ethics approval and consent to participate

This study was approved by the Biomedical Research Ethics Committee of West China Hospital, Sichuan University [No. 2018(100)], and informed consent from all participants.

Consent for publication

Participants consent for publication: Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Author's Contributions

ML and SW conceived and designed the study. YW, SW and ML performed interviews and collected the data. SW and YW coded, analysed, and interpreted the data, and drafted the manuscript. ML, SW and YW revised and edited the manuscript. All authors interpreted the results, commented the manuscript and approved the final submission. ML is guarantor for the study. All authors revised the manuscript and approved the final version.

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Not applicable.

Availability of data and materials

The data used in this study are available from the corresponding author upon reasonable request.

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Figures

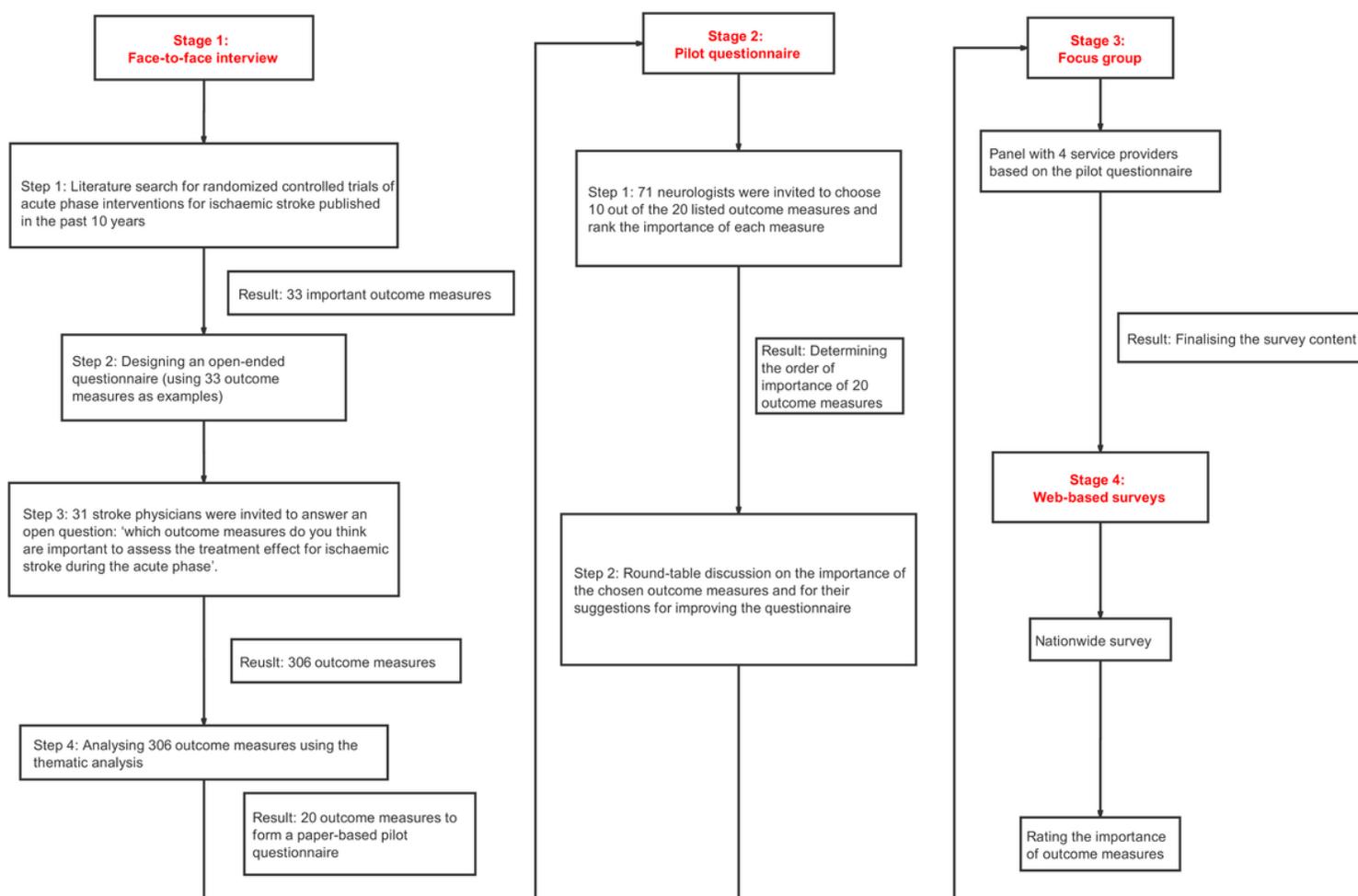


Figure 1

Key stages/steps of study

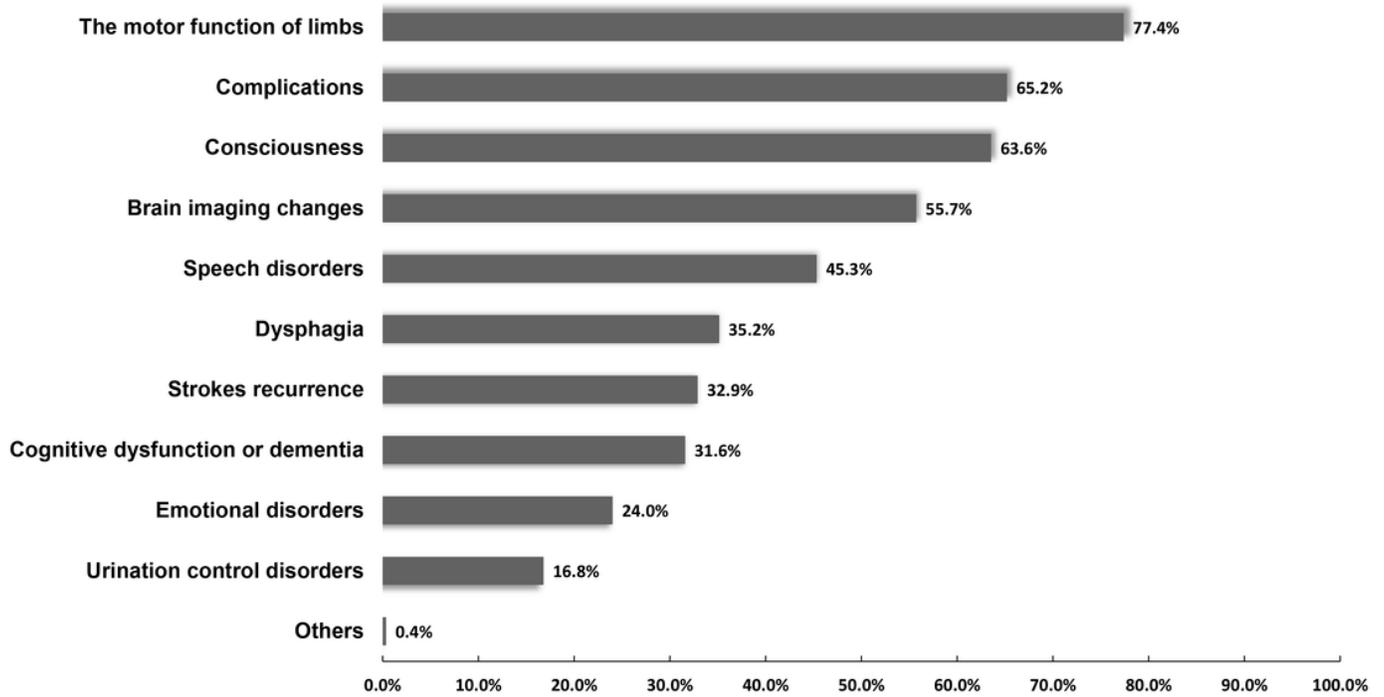


Figure 2

Participant rating importance of outcome measures for therapies with potential bleeding risk (A) and without potential bleeding risk (B).

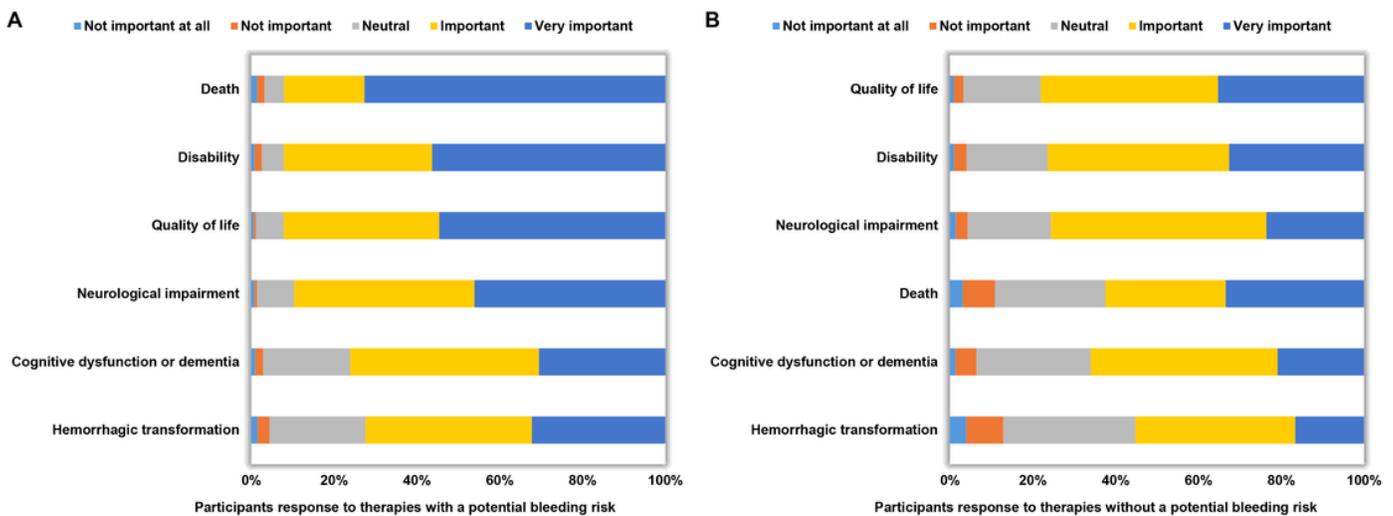


Figure 3

Participant responses for choosing outcome measures in regard to complications (pneumonia, deep venous thrombosis or urinary tract infection), and brain imaging changes on CT/MRI (infarction volume expansion, hemorrhagic transformation, brain oedema or middle shift), speech capability (aphasia or dysarthria) and emotional disorder (anxiety and depression)

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