

The reporting quality of acupuncture for neurogenesis in experimental ischemic stroke study

Zheng-Xiang Li¹, Yan Li², Wen-Ting Yang², Min Wang¹, Meng-Bei Xu², Xiao-Li Zhou², Pei-Qing Rong², Ting-Yu Jin², Wen-Jin Yi¹, Guo-Qing Zheng²

¹Department of Acupuncture and Tuina, Wenling Hospital of Traditional Chinese Medicine of Zhejiang Province, Taizhou 317500, China;

²Department of Neurology, the Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, Wenzhou 325027, China

Contributions: (I) Conception and design: GQ Zheng, ZX Li; (II) Administrative support: GQ Zheng; (III) Provision of study materials or patients: MB Xu, XL Zhou; (IV) Collection and assembly of data: PQ Rong, TY Jin, WJ Yi; (V) Data analysis and interpretation: Y Li, WT Yang, M Wang; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Guoqing Zheng. Department of Neurology, the Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, Wenzhou 325027, China. Email: gq_zheng@sohu.com.

Background: There is increasing evidence demonstrating the highly inadequate reporting of preclinical research in multiple scientific publications. The purpose of this study is to systematically investigate the reporting quality of acupuncture for neurogenesis in animal models of acute ischemic stroke.

Methods: We searched eight databases, including PubMed, EMBASE, CINAHL, AMED, Chinese National Knowledge Infrastructure, VIP information database, Wanfang data Information Site, and Chinese Biomedical Literature Database. The methodological quality of included studies was assessed by using the CAMARADES 10-item checklist. The STRICTA statement was modified to gear to animal acupuncture research. The reporting quality was assessed according to the ARRIVE guidelines and the modified STRICTA statement. Data were analyzed with descriptive statistics.

Results: Ultimately, 44 studies containing 2,411 subjects were identified. The overall compliance with the CAMARADES 10-item checklist has a mean of 4.3. The reporting quality indicated that the overall compliance with ARRIVE guidelines has a mean of 59.9% and with the modified STRICTA statement a mean of 71.8%. The findings suggest that the reporting quality of acupuncture for preclinical stroke was generally poor.

Conclusions: Full compliance with ARRIVE guidelines and/or modified STRICTA statement in designing, conducting and reporting preclinical acupuncture research is urgently needed in the future.

Keywords: Reporting quality; acupuncture; neurogenesis; Animal Research: Reporting In Vivo Experiments guidelines (ARRIVE guidelines); modified Standards for Reporting Interventions in Clinical Trials of Acupuncture statement (modified STRICTA statement)

Submitted Aug 02, 2018. Accepted for publication Feb 18, 2019.

doi: 10.21037/atm.2019.02.16

View this article at: <http://dx.doi.org/10.21037/atm.2019.02.16>

Introduction

More and more evidence demonstrate the highly insufficient reporting of animal research in multiple scientific publications. Even as the animal studies published in seven leading journals (*Cell*, *Nature*, *Science*, *Nature Medicine*, *Nature Immunology*, *Nature Genetics*, and *Nature*

Biotechnology) with >500 citations, the randomization processes or blinding were reported in only less than 20% of the studies (1). Consequently, there are increasing concerns that lack of transparent reporting and poor experimental design contribute to the frequent failure of translating preclinical discoveries into novel treatments for human disease (2). Reporting guidelines set a checklist

format of pre-determined criteria for more complete and transparent reports of biomedical research, and thus increasing their value to inform policy, scientific practice and clinical practice (3). The Animal Research: Reporting In Vivo Experiments (ARRIVE) guidelines (4) provide guidance on complete and transparent reporting of *in vivo* animal research, which aims to improve the quality of research reports. Up to 2014, the ARRIVE guidelines have been endorsed by over 300 research journals around the world, including the Nature Publishing Group, BioMed Central, and PLoS (2). Quality of reporting and adherence to ARRIVE guidelines in animal studies has been studied in many specialized areas or diseases such as critical care (5), Neoplasms (6), implant dentistry (7), Chagas Disease (8) and rheumatology (9). However, up to now there was no assessment of the reporting quality of complementary and alternative medicine (CAM) in animal studies.

Acupuncture, one component of CAM therapy, has been well utilized for thousands of years in China and elsewhere in East Asia (10). Acupuncture has also been used in stroke therapy for thousands of years and is still being used in modern time (11). Ischemic stroke was a major cause of death and disability worldwide (12). However, rt-PA, the only pharmacological treatment thrombolytic for ischemic stroke approved by the Food and Drug Administration, is limited by its time window and severe adverse events (13). Thus, alternative medicines such as acupuncture are increasingly used in stroke patient adjunct to conventional treatment. Up to 2013, at least 24 systematic reviews of acupuncture for stroke have been published (14).

Regenerative strategies, particularly with regard to neurogenesis, offer long-term hope for many patients who have suffered a stroke. The potential beneficial results of acupuncture for neurogenesis in experimental ischemic stroke have been reported in a preclinical systematic review, suggesting that acupuncture is a prospective therapy that could enhance endogenous neurogenesis for ischemic stroke through decreasing infarct volume and ameliorating neurological impairment (15). However, the reporting quality of acupuncture for neurogenesis in experimental ischemic stroke has not been evaluated. In addition, no guideline has yet been developed for transparent reporting of the acupuncture intervention in the animal study, although the Revised Standards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA) statement are well developed (16). Thus, the purpose of this study is to evaluate the reporting quality of acupuncture for neurogenesis in experimental ischemic stroke study by

using the ARRIVE guidelines and the modified STRICTA statement.

Methods

Search strategy

Studies of acupuncture for neurogenesis treatment in animal models of acute ischemic stroke were searched from PubMed, EMBASE, CINAHL, AMED, Chinese National Knowledge Infrastructure (CNKI), VIP information database, Wanfang data Information Site and Chinese Biomedical Literature Database. We also manually searched abstracts of academic seminars and reference lists from identified publications. The publication time is from the inception of each database up to December 2018. The search terms used were (acupuncture OR electroacupuncture) AND (stroke OR cerebral ischemia OR middle cerebral occlusion OR MCAO) AND (neurogenesis OR neural regeneration OR neurotization) in English or in Chinese. All searches were limited to studies on animals.

Eligibility

We included all controlled studies on the effect of acupuncture in neurogenesis in experimental ischemic stroke. Inclusion criteria were pre-specified as follows: (I) animal experimental studies; (II) focal cerebral ischemia; (III) acupuncture or electroacupuncture treatment; and (IV) outcome was measured as neuronal nuclear antigen (NeuN) and/or Nestin and/or polysialylate form of the neural cell adhesion molecule (PSA-NCAM) and/or bromodeoxyuridine (BrdU) and/or glial fibrillary acidic protein (GFAP).

Data extraction

The following information was extracted from each study: (I) general information: the first author's name, publication year, language; (II) animal details: species, and number of animals in every groups; (III) the reporting quality of each included study was assessed by using the modified STRICTA 2010 checklist and ARRIVE 2010 checklist. Each item was assigned a "yes" (Y, scored as 1) or "no" (N, scored as 0) response, depending on whether the author reported it. Each item was weighted with equal importance. All articles were evaluated independently by two reviewers (Y Li and WT Yang). Any disagreement was discussed

and resolved through consultation with the corresponding author (GQ Zheng).

Quality assessment

The methodological quality of the included studies was assessed using the CAMARADES 10-item checklist (17) as follows: (I) publication after peer review; (II) statement of control of temperature; (III) randomization to treatment or control; (IV) blinded induction of ischemia; (V) blinded assessment of outcome; (VI) anesthetic without marked intrinsic neuroprotective activity; (VII) appropriate animal model (aged, diabetic, or hypertensive); (VIII) sample size calculation; (IX) statement of compliance with animal welfare regulations; (X) declared any potential conflict of interest. Each study was given a quality score out of a possible total of 10 points; subsequently the group median was calculated. Two authors evaluated study quality independently and any disagreements were settled through consultation with the corresponding author (G Zheng).

Data analyses

Microsoft Excel 2007 was used for the descriptive statistical analysis of all included articles. The accumulated number and proportion of each item of the CAMARADES 10-item checklist or STRICTA 2010 checklist or ARRIVE 2010 checklist in the included articles were calculated.

Results

Study selection

We identified 3,411 potentially relevant articles from eight databases. After removing duplicate articles, 1,324 articles were left. Through screening titles and abstracts, 1,057 papers were excluded because they were not relevant to acupuncture. After full-text evaluation on the remaining 267 articles, a total of 223 studies were excluded for the following reasons: outcome measures not marked with the following neurogenesis indicators, i.e., Brdu, Nestin, PSA-NCAM, NeuN and GFAP (n=92); meeting abstract (n=27); review (n=22); duplicate publication (n=21); letter (n=18); editorial material (n=16); historical article (n=15); commentary (n=12). Finally, 44 eligible studies involved a total of 2,411 experimental subjects were identified. Thirty-four studies are in Chinese and 10 studies are in English. The screening process is summarized in a flow

diagram (*Figure 1*).

The methodological quality of included studies

The methodological quality of included studies was evaluated by using the CAMARADES 10-item checklist statement (*Table 1*). The methodological quality score of the included studies ranged from 2 to 7 out of a total of 10 points, and the median was 4.3. Among these 44 studies, 2 studies (4.5%) got 2 point (21,27); 11 studies (25.0%) got 3 points (22,23,25,26,28,31,34,35,38,43,46); 11 studies (25.0%) got 4 points (24,30,33,36,39,40,44,47,56,57,61); 13 studies (29.5%) got 5 points (18-20,29,32,37,41,42,45,49,51,53,58) and 6 studies (13.6%) got 6 points (48,50,52,55,59,60); 1 study (2.3%) got 7 point (54) (*Table 1*). The detailed information is listed below:

- (I) Thirty-two studies (72.7%) were published in peer-reviewed journals; and 12 studies (27.3%) were online master's theses or PhD theses that were not formally published (18,20,22,24,36-40,47,53,58);
- (II) Twenty-six studies (59.1%) described control of the temperature;
- (III) Thirty-nine studies (88.6%) reported random allocation to treatment group;
- (IV) None of the studies described masked induction of stroke model;
- (V) Four studies (9.1%) reported blinded assessment of outcome (41,54-56);
- (VI) Forty-three studies (97.7%) used anesthetic without significant intrinsic neuroprotective activity;
- (VII) Five studies (11.4%) used appropriate animal model (aged, diabetic, or hypertensive); hyperlipemia rats were used in one study (20) (2.3%), aged rats in two studies (21,59) (4.5%), and hypertensive rats in two studies (37,41) (4.5%);
- (VIII) None of the studies declared the sample size calculation;
- (IX) Twenty-five studies (56.8%) mentioned compliance with animal welfare regulations (18-20,24,29,32,36-40,42,44,45,47-55,58,60);
- (X) Fifteen studies (34.1%) contained statements of potential conflict of interests (18,20,22,24,47-54,58-60).

The reporting quality according to ARRIVE guidelines

The reporting quality of acupuncture for neurogenesis in experimental ischemic stroke was evaluated by the ARRIVE

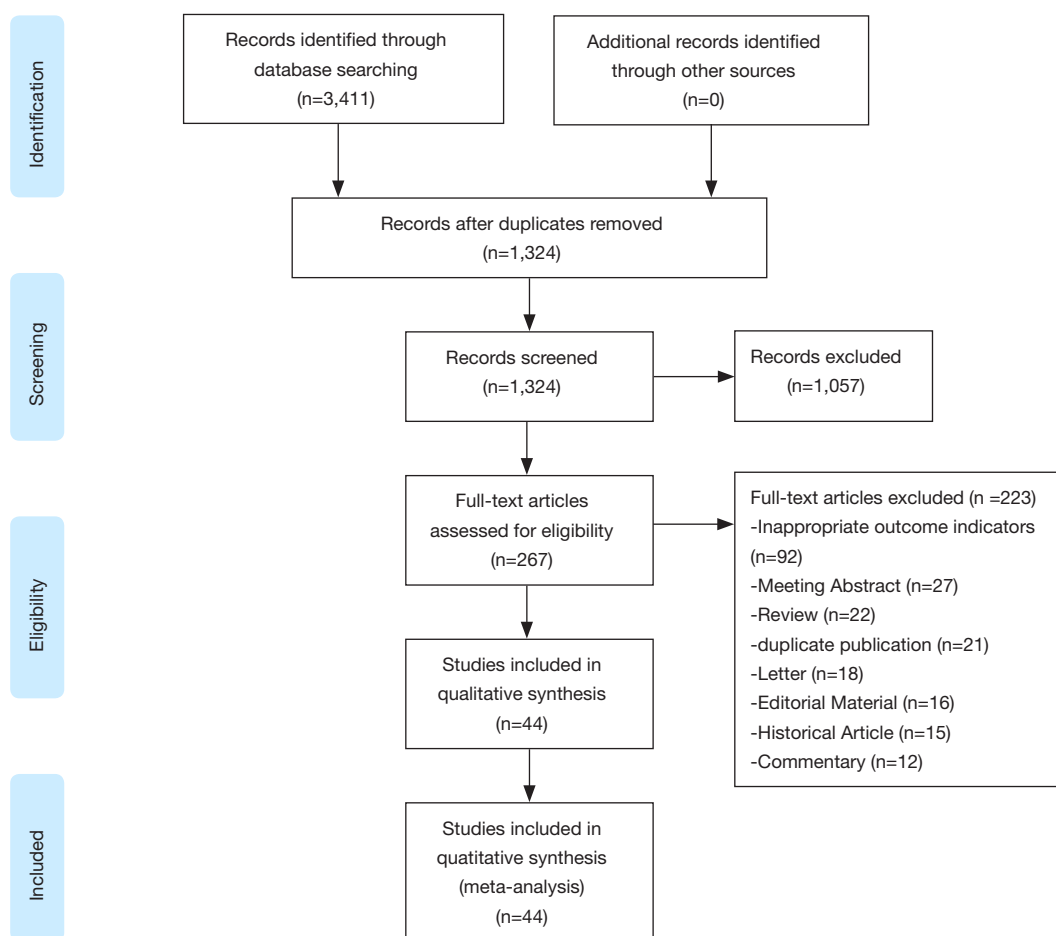


Figure 1 Flow diagram of study selection process.

Table 1 The methodological quality according to CAMARADES 10-item checklist

Author	Years	A	B	C	D	E	F	G	H	I	J	Total
Huang <i>et al.</i> (18)	2009		√	√			√			√	√	5
Yan <i>et al.</i> (19)	2008	√	√	√			√			√		5
Ren <i>et al.</i> (20)	2007			√			√	√		√	√	5
Gao <i>et al.</i> (21)	2010	√						√				2
Luo <i>et al.</i> (22)	2007			√			√				√	3
Yang <i>et al.</i> (23)	2010	√		√			√					3
Rui <i>et al.</i> (24)	2011			√			√			√	√	4
Li <i>et al.</i> (25)	2012	√		√			√					3
Wang <i>et al.</i> (26)	2013	√		√			√					3
Tang <i>et al.</i> (27)	2008	√					√					2
Liu <i>et al.</i> (28)	2001	√		√			√					3

Table 1 (continued)

Table 1 (continued)

Author	Years	A	B	C	D	E	F	G	H	I	J	Total
Tao <i>et al.</i> (29)	2008	√	√	√			√			√		5
Diao <i>et al.</i> (30)	2008	√	√	√			√					4
Yang <i>et al.</i> (31)	2006	√		√			√					3
Song <i>et al.</i> (32)	2008	√	√	√			√			√		5
Yang <i>et al.</i> (33)	2008	√	√	√			√					4
Pi <i>et al.</i> (34)	2006	√	√				√					3
Fei <i>et al.</i> (35)	2012	√		√			√					3
Li <i>et al.</i> (36)	2008		√	√			√			√		4
You <i>et al.</i> (37)	2012		√	√			√	√		√		5
Mi <i>et al.</i> (38)	2010			√			√			√		3
Bao <i>et al.</i> (39)	2007		√	√			√			√		4
Chen <i>et al.</i> (40)	2003		√	√			√			√		4
Li <i>et al.</i> (41)	2004	√		√		√	√	√				5
Zhang <i>et al.</i> (42)	2011	√	√	√			√			√		5
Zhao <i>et al.</i> (43)	2006	√		√			√					3
Liu <i>et al.</i> (44)	2005	√		√			√			√		4
Yu <i>et al.</i> (45)	2010	√	√	√			√			√		5
Wan <i>et al.</i> (46)	2010	√		√			√					3
Zhao <i>et al.</i> (47)	2004		√				√			√	√	4
Tao <i>et al.</i> (48)	2010	√	√	√			√			√	√	6
Yang <i>et al.</i> (49)	2005	√		√			√			√	√	5
Cheng <i>et al.</i> (50)	2009	√	√	√			√			√	√	6
Kim <i>et al.</i> (51)	2014	√	√				√			√	√	5
Tao <i>et al.</i> (52)	2015	√	√	√			√			√	√	6
Jian <i>et al.</i> (53)	2015		√	√			√			√	√	5
Tao <i>et al.</i> (54)	2015	√	√	√		√	√			√	√	7
Zhao <i>et al.</i> (55)	2015	√	√	√		√	√			√		6
Chen <i>et al.</i> (56)	2015	√		√		√	√					4
Cao <i>et al.</i> (57)	2016	√	√	√			√					4
Yao <i>et al.</i> (58)	2015		√	√			√			√	√	5
Li <i>et al.</i> (59)	2015	√	√	√			√	√			√	6
Tan <i>et al.</i> (60)	2018	√	√	√			√			√	√	6
Mi <i>et al.</i> (61)	2018	√	√	√			√					4

Studies fulfilling the criteria of: A: peer reviewed publication; B: control of temperature; C: random allocation to treatment or control; D: blinded induction of model; E: blinded assessment of outcome; F: use of anesthetic without significant intrinsic neuroprotective activity; G: appropriate animal model (aged, diabetic, or hypertensive); H: sample size calculation; I: compliance with animal welfare regulations; J: statement of potential conflict of interests.

guidelines (<http://fp.amegroups.cn/cms/atm.2019.02.16-1.pdf>) as follows:

- (I) Item 1 (Title): 44 (100.0%) studies provided a concise and accurate description of the content of the article;
- (II) Item 2 (Abstract): 43 studies (97.7%) provided a precise summary of the background, research objectives, key methods, principal findings and conclusions of the study;
- (III) Item 3 (Background): (a) 38 articles (86.4%) included an adequate scientific background and explained the experimental method and rationale; (b) 15 articles (34.1%) introduced the reason how and why the animal species and model being used could address the scientific objectives and, where appropriate, the study's relevance to human biology;
- (IV) Item 4 (Objectives): 44 studies (100%) described the primary and secondary objectives of the study;
- (V) Item 5 (Ethical statement): 15 articles (34.1%) indicated the nature of the ethical review permissions, relevant licenses, and national or institutional guidelines for the care and use of animals, that cover the research;
- (VI) Item 6 (Study design): (a) 42 articles (95.5%) provided the number of experimental and control groups; (b) 39 articles (88.6%) reported that randomization was conducted to minimize the effects of subjective bias when allocating animals to treatment; (c) 44 studies (100%) mentioned experimental unit;
- (VII) Item 7 (Experimental procedures): (a) 44 studies (100%) provided precise details of drug formulation and dose, site and route of administration, anesthesia used, surgical procedure, and method of euthanasia; (b) 43 studies (97.7%) provided the time when these procedures were implemented; (c) 18 articles (40.9%) described the places where the experimental procedures were carried out; (d) 1 article (2.3%) explained why the route of administration and the drug dose were selected;
- (VIII) Item 8 (Experimental animals): (a) 42 reports (95.5%) provided the details of the animals used, including species, strain, sex, developmental stage and weight; (b) 41 reports (93.2%) provided further relevant information such as the source of animals and international strain nomenclature;
- (IX) Item 9 (Housing and husbandry): (a) 16 articles (36.4%) gave the number of cage companions; (b) 26 articles (59.1%) described the husbandry conditions including light/dark cycle, temperature, type of food, access to food and water; (c) 26 studies (59.1%) mentioned welfare-related assessments and interventions that were carried out prior to, during, or after the experiment;
- (X) Item 10 (Sample size): (a) 34 articles (77.3%) specified the total number of animals used in each experiment, and the number of animals in each experimental group; (b) none of the articles explained how the number of animals was determined or provided details of sample size calculation used; (c) none of the articles indicated the number of independent replications of each experiment.
- (XI) Item 11 (Allocating animals to experimental groups): (a) 11 articles (25.0%) mentioned randomization for allocating animals to experimental groups; (b) all of the included articles (100%) described the order in which the animals in different experimental groups were treated and assessed;
- (XII) Item 12 (Experimental outcomes): all of the included articles (100%) clearly defined the primary and secondary experimental outcomes;
- (XIII) Item 13 (Statistical methods): (a) 42 articles (95.5%) provided details of the statistical methods used for each analysis; (b) 38 articles (86.4%) specified the group of animals as a unit of analysis for each dataset; (c) 30 articles (68.2%) described the methods used to assess whether the data met the assumptions of the statistical approach;
- (XIV) Item 14 (Baseline data): 7 articles (15.9%) offered the baseline data such as characteristics and health status of animals.
- (XV) Item 15 (Numbers analysed): (a) 35 articles (79.5%) report the number of animals in each group included in each analysis; (b) 10 articles (22.7%) described if any animals or data were not included in the analysis;
- (XVI) Item 16 (Outcomes and estimation): 43 articles (97.7%) reported the results for each analysis

carried out, with a measure of precision;

- (XVII) Item 17 (Adverse events): (a) no study give details of all important adverse events in each experimental group; (b) no study described any modifications to the experimental protocols made to reduce adverse events;
- (XVIII) Item 18 (Interpretation/scientific implications): (a) all articles (100%) interpreted the results, taking into account the study objectives and hypotheses, current theory and other relevant studies; (b) 4 articles (9.1%) commented on the study limitations; (c) 2 studies (4.5%) described the implications of experimental methods or findings for the replacement, refinement or reduction (the 3Rs) of the use of animals in research;
- (XIX) Item 19 (Generalisability/translation): 7 studies (15.9%) commented on whether, and how, the findings of this study are likely to translate to other species or systems, including any relevance to human biology;
- (XX) Item 20 (Funding): 26 studies (59.1%) list all funding sources (including grant number) and the role of the funder(s) in the study.

The reporting quality according to the modified STRICTA statement

The reporting quality of experimental ischemic stroke for acupuncture was evaluated by the modified STRICTA statement (Table 2).

Acupuncture rationale

Thirty-two articles (72.7%) provided reasons for treatment based on historical context, literature sources, citing references where appropriate, and so on (item 1).

Needling details

Forty-three articles (97.7%) recorded the number of needle insertions per subject per session (item 2a). All of the 44 articles listed names (or location) of points used (item 2b). Twenty-three articles (52.3%) mentioned the depth of needle insertion (item 2c). Eighteen articles (40.9%) described muscle twitch response as the response sought (item 2d). All the articles (100%) described the type of needle stimulation, including manual and electrical (item 2e). Forty-one articles (93.2%) mentioned the needle retention time (item 2f). Forty-three articles (97.7%)

provided the information of needle type (item 2g).

Treatment regimen

All of the articles (100%) provided the number of treatment sessions (item 3a) and mentioned the frequency and duration of treatment sessions (item 3b).

Control intervention(s)

The proportion of the quoted data to elucidate the control in the context of the research question was 0% (item 4a). Three articles (6.8%) reported precise descriptions of the control (item 4b).

Discussion

Principal findings

In the present study, 44 articles of acupuncture for neurogenesis in animal research were identified. To our knowledge, this is the first research which assessed the reporting quality of both CAM and acupuncture in animal research based on the ARRIVE guidelines and/or modified STRICTA statement. The mean methodological quality score of the included primary studies was 4.3 according to the CAMARADES 10-item checklist. The reporting quality of acupuncture for neurogenesis in experimental ischemic stroke studies indicated that the mean overall compliance with ARRIVE guidelines was 59.9% and with the modified STRICTA statement was 71.8%.

Comparison with other studies

Up to now, a few studies have assessed the quality of healthcare reporting by evaluating the compliance with various assessment instruments. The ARRIVE guidelines (4) published in 2010 promote substantial improvements in methods used for animal studies. However, the reporting of the animal researches is still inadequate. Although no study has assessed the reporting quality of animal research in acupuncture by using ARRIVE guidelines, the quality of reporting of animal research in specific diseases found that the items of animal strain, sex, and weight or age was reported in 68% (52/77); the randomization and randomization procedure was reported 61% and 2% respectively; type of blinding was reported in 40%, including disease induction (7%), intervention (23%), and/or subjective outcomes (55%); the sample size calculation was reported in 5% of the related animal researches published in three prominent

Table 2 The reporting quality according to the modified STRICTA statement.

Item	Detail	N (%) (n=44)	95% CI
Acupuncture rationale (explanations and examples)	Reasoning for treatment provided, based on historical context, literature sources, and/or consensus methods, with references where appropriate	32 (72.7)	57%, 85%
Details of needling (explanations and examples)	a) Number of needle insertions per subject per session (mean and range where relevant);	43 (97.7)	88%, 100%
	b) Names (or location if no standard name) of points used (uni-/bilateral);	44 (100.0)	92%, 100%
	c) Depth of insertion, based on a specified unit of measurement, or on a particular tissue level;	23 (52.3)	37%, 68%
	d) Response sought (e.g., <i>de qi</i> or muscle twitch response);	18 (40.9)	26%, 57%
	e) Needle stimulation (e.g., manual, electrical);	44 (100.0)	92%, 100%
	f) Needle retention time;	41 (93.2)	81%, 99%
	g) Needle type (diameter, length, and manufacturer or material).	43 (97.7)	88%, 100%
Treatment regimen (explanations and examples)	a) Number of treatment sessions;	44 (100.0)	92%, 100%
	b) Frequency and duration of treatment sessions.	44 (100.0)	92%, 100%
Control or comparator interventions (explanations and examples)	a) Rationale for the control or comparator in the context of the research question, with sources that justify this choice;	0 (0.0)	0%, 8%
	b) Precise description of the control or comparator. If sham acupuncture or any other type of acupuncture-like control is used, provide details as for Items 1 to 3 above.	3 (6.8)	1%, 19%

critical care journals during 6 months of the year 2012 (5). Furthermore, in 396 articles for animal experiments of neoplasms published between 2010 and 2012 in Chinese journals, the reporting of items of adequate randomization methods, adequate blinding, sample size calculation was 91.67%, 0.25%, and 0%, respectively (6). In present study, the ARRIVE score for the included studies varied from 14 to 28; the mean score was 22.8 out of a maximum of 38 points. In particular, the randomization and randomization procedure were reported in 88.6% and 25.0% of included studies, respectively; 9.1% reported that the procedure of outcome assessment was in a blinded manner; 0% reported a sample size calculation. Thus, the reporting quality of preclinical acupuncture research in the present study is similar to that in the animal studies on neoplasms in Chinese journals (6), whereas it is lower than that in the selected three prominent critical care journals (5).

One of the hallmarks of a good quality study is that it should have an adequate sample size with sufficient statistical power to detect statistical differences between treatment groups. Studies with inadequate sample sizes often run the risk of overestimating intervention benefits (62). However, no study conducted pre-trial

estimation of sample size, suggesting that the lack of statistical power to ensure appropriate estimation of the therapeutic effect (63). Randomization and blinding are also the core standards of rigorous study design (64). Inflated estimates of treatment efficacy were found when the studies with inadequate randomization or blinding (65), and the possibility of investigator committing fallacy of incomplete evidence is increased when the experiment is conducted in an unblinded manner (66).

Implications

Reporting guidelines such as ARRIVE aim to increase the reporting quality of bioscience research, but to date these guidelines are still much less endorsed and adhered to than they should be (4,67). This study attempts to warn about the weak reporting quality in animal research of acupuncture and has a teaching intention to encourage the scientific community to adopt ARRIVE guidelines to completely report their preclinical results and to unify animal models in order to maximize obtained information and to be more transparent inside and outside the academic field. The availability of guidelines only is not sufficient to

improve the completeness of reporting: concerted efforts clearly play a major role (68). Strong recommendation of the endorsement and adoption of ARRIVE guidelines by all the stakeholders, including peer reviewers, prospective authors, journal editors, implementation scientists, and guideline developers is needed to increase the completeness of reporting in animal research of acupuncture. Especially, the support of and collaboration with influential biomedical journals are crucial for the success of the project (69). To date, no specific reporting guidelines for acupuncture animal research has been developed. The STRICTA statement (16) was developed to address reporting issues of controlled trials with acupuncture therapy. Therefore, in the present study, we modified the STRICTA statement to gear to preclinical research on acupuncture, and thereby promoting their quality of reporting, interpretation and replication. In this study, the reporting of the items in STRICTA of acupuncture rationale is item 1 (72.7%); of needling details 2a (97.7%), 2b (100%), 2c (52.3%), 2d (40.9%), 2e (100%), 2f (93.2%) and 2g (97.7%); of treatment regimen 3a (100%) and 3b (100%); of control intervention(s) 4a (0%) and 4b (6.8%). Most of the items were reported consistently, but several items were inadequately reported. In particular, no study applied the quoted data to elucidate the control in the context of the research question, and few animal studies on acupuncture used sham acupuncture as the control. Thus, development of appropriate sham acupuncture method in animal study and reporting of the control in the context of the research question is urgently needed. Therefore, to tailor the STRICTA statement to the objectives of this study, a modified version of the STRICTA statement was used allowing assessments of the quality of reporting in animal studies. It is hoped that, over time, use of the modified STRICTA statement recommendations will lead to more rigorous preclinical design, more robust conclusions and better data to determine future policy and practice.

Limitations of study

The study has some limitations. First, we only described the reporting of items on quality of the published paper. It may very well be that what was not reported was actually done. Thus, it is possible that the methodological quality was actually good, and only the reporting quality was poor. Second, this study only included a small number of publications. However, a large number of articles should be assessed for their reporting quality if a more comprehensive

evaluation is undertaken. Thus, the results should be interpreted with caution. Third, it should be noted that some journals have more restrictions than others in terms of word count, and these restrictions may be related with undetailed descriptions of eligibility criteria, abstract, process of consent acquisition, and blinding methods. Finally, whether the researchers have referred to ARRIVE guidelines was not investigated in present study; therefore, we are not sure whether these scores might be related to the impact of these resources.

Conclusions

The findings of this study are significant in that they revealed the reporting quality of the studies on acupuncture for neurogenesis in animal models of acute ischemic stroke was generally poor. These findings would alert the researchers, journal editors, clinicians and reviewers, and funding agencies to be more focused on the design, conduct and report of preclinical acupuncture research. Reporting and accounting for all details of animal research is indispensable for reducing publication bias, assisting to replication, justifying the research, and translating to human medicine. The reporting quality of animal research on acupuncture can be improved through adopting and adhering to well-developed reporting guidelines: the ARRIVE guidelines and modified STRACTA statement.

Acknowledgements

Funding: This project was supported by the grant of National Natural Science Foundation of China (81573750/81473491/81173395/H2902); the Young and Middle-Aged University Discipline Leaders of Zhejiang Province, China (2013277); Zhejiang Provincial Program for the Cultivation of High-level Health talents (2015).

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

References

1. Hackam DG, Redelmeier DA. Translation of research evidence from animals to humans. *JAMA* 2006;296:1731-2.
2. Baker D, Lidster K, Sottomayor A, et al. Two years later: journals are not yet enforcing the ARRIVE guidelines on

- reporting standards for pre-clinical animal studies. *PLoS Biol* 2014;12:e1001756.
3. Moher D, Avey M, Antes G, et al. The National Institutes of Health and guidance for reporting preclinical research. *BMC Med* 2015;13:34.
 4. Kilkenny C, Browne WJ, Cuthill IC, et al. Improving Bioscience Research Reporting: The ARRIVE Guidelines for Reporting Animal Research. *PLoS Biol* 2010;8:e1000412.
 5. Bara M, Joffe AR. The methodological quality of animal research in critical care: the public face of science. *Ann Intensive Care* 2014;4:26.
 6. Liu Y, Zhao X, Mai Y, et al. Adherence to ARRIVE Guidelines in Chinese Journal Reports on Neoplasms in Animals. *PLoS One* 2016;11:e0154657.
 7. Vignoletti F, Abrahamsson I. Quality of reporting of experimental research in implant dentistry. Critical aspects in design, outcome assessment and model validation. *J Clin Periodontol* 2012;39:6-27.
 8. Gulin JE, Rocco DM, García-Bournissen F. Quality of Reporting and Adherence to ARRIVE Guidelines in Animal Studies for Chagas Disease Preclinical Drug Research: A Systematic Review. *PLoS Negl Trop Dis* 2015;9:e0004194.
 9. Ting KH, Hill CL, Whittle SL. Quality of reporting of interventional animal studies in rheumatology: a systematic review using the ARRIVE guidelines. *Int J Rheum Dis* 2015;18:488-94.
 10. PDQ® Integrative, Alternative, and Complementary Therapies Editorial Board. Acupuncture (PDQ®) Health Professional Version. Available online: <http://www.ncbi.nlm.nih.gov/books/NBK65714/>
 11. Liu Z, Guan L, Wang Y, et al. History and mechanism for treatment of intracerebral hemorrhage with scalp acupuncture. *Evid Based Complement Alternat Med* 2012;2012:895032.
 12. Donnan GA, Fisher M, Macleod M, et al. Stroke. *Lancet* 2008;371:1612-23.
 13. Jauch EC, Saver JL, Adams HP Jr, et al. Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke association. *Stroke* 2013;44:870-947.
 14. Zhang JH, Wang D, Liu M. Overview of systematic reviews and meta-analyses of acupuncture for stroke. *Neuroepidemiology* 2014;42:50-8.
 15. Lu L, Zhang XG, Zhong LL, et al. Acupuncture for neurogenesis in experimental ischemic stroke: a systematic review and meta-analysis. *Sci Rep* 2016;6:19521.
 16. MacPherson H, Altman DG, Hammerschlag R, et al. Revised STAndards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA): Extending the CONSORT statement. *J Evid Based Med* 2010;3:140-55.
 17. Macleod MR, O'Collins T, Howells DW, et al. Pooling of animal experimental data reveals influence of study design and publication bias. *Stroke* 2004;35:1203-8.
 18. Huang GF. Role of CREB Phosphorylation in Neurogenesis in vivo Activated by Electro-acupuncture Combined with rTMS after focal Cerebral Ischemia (in Chinese) (Thesis). Wuhan: Huazhong University of Science and Technology, 2009.
 19. Yan CQ, Huang GY, Zhan KB, et al. The effects of acupuncture on reactive gliosis after focal cerebral ischemia (in Chinese). *Cent Chin Med J* 2008;32:81-5.
 20. Ren XJ. The effects of acupuncture on the NSC and neurotrophin of the hyperlipemia with cerebral ischemia rats (in Chinese) (Thesis). Beijing: Beijing University of Chinese Medicine, 2007.
 21. Gao JF, LV FH, Zhu CL. Effect of electroacupuncture on cell proliferation and differentiation in dentate gyrus of aged rats with focal cerebral ischemia reperfusion injury (in Chinese). *Chin J Traditional Chin Medic Pharm* 2010;25:1076-9.
 22. Luo WS. Effect of ERK Signal Transduction Pathway and Differentiation and Proliferation of Neural Stem Cells by Electroacupuncture Ren and Du Meridians in Brain Ischemia Rat (in Chinese) (Thesis). Guangzhou: Traditional Chinese Medicine University of Guangzhou, 2007.
 23. Yang FX, Yang ZX, Yu HB, et al. Effect of electroacupuncture ren meridian on the proliferation of neural stem cells in brain ischemia rats (in Chinese). *Chin J Tradit Med Sci Technol* 2010;17:188-9.
 24. Jun R. Effects of Electroacupuncture on Differentiation of Nerve Stem Cells in Rats with Cerebral Ischemia (in Chinese) (Thesis). Qingdao: Qingdao University, 2011.
 25. Li P, Zhang S. Effect of electroacupuncture stimulation on endogenous neural stem cells activation in ischemia rats (in Chinese). *Zhongguo Ying Yong Sheng Li Xue Za Zhi* 2011;27:450-1.
 26. Wang F, Yang N, Wang BG, et al. Influence of Electroacupuncture Eu meridian Combined with Etem Cells Transplantation on Nerve Regeneration of Rats after Cerebral Infarct (in Chinese). *Chin J Chin Med* 2013;28:1843-5.
 27. Tang Q, Xu ZH, Bai J. The effect of electroacupuncture

- on proliferation and migration of neural stem cells after rat cerebral infarction (in Chinese). *J Clin Acup Moxib* 2008;24:49-51.
28. Liu Z, Lai XS. Effects of electro-acupuncture on proliferation of endogenous neural stem cells after focal cerebral ischemia in adult rats (in Chinese). *Chin J Rehab Med* 2007;22:218-21.
 29. Tao J, Chen LD, Xue XH, Yan SL. Effects of electroacupuncture on proliferation and differentiation of nerve stem cells in the adult rats after brain ischemic injury (in Chinese). *Chin J Rehab Med* 2008;23:1061-3.
 30. Diao LH, Yu HB, Pi M, et al. Effects of electroacupuncture at the Ren channel and basic fibroblast growth factor injection on in situ neural stem cell proliferation in subventricular zone of cerebral ischemic rats (in Chinese). *J Clin Rehab Tissue Eng Res* 2008;12:1435-9.
 31. Yang ZX, Yu HB, Rao X, et al. Effects of electroacupuncture at the conception vessel on proliferation and differentiation of nerve stem cells in subventricular zone of the lateral ventricle of cerebral ischemia rats (in Chinese). *J Tradit Chin Med* 2006;47:429-32.
 32. Song TS, Zhou MF. The effects of acupuncture on astrocyte proliferation after cerebral ischemia-reperfusion injury in rats (in Chinese). *Chin J Physi Med Rehab* 2008;30:244-7.
 33. Yang ZX, Yu HB, Luo WS, et al. The effect of electroacupuncture at Ren and Du vessels on hippocampus horizontal cells of focal cerebral ischemia (in Chinese). *Chin Med Her* 2008;5:7-9.
 34. Pi M, Diao L, Yu H, et al. Electroacupuncture at Ren channel point combined with injection of basic fibroblast growth factors for neural stem cell proliferation in subventricular zone of cerebral ischemic side. *Neural Regen Res* 2006;5:424-7.
 35. Ye F, Yu JJ, Deng XL, et al. Electroacupuncture for promoting endogenous neural stem cell proliferation and neurological rehabilitation early after cerebral infarction (in Chinese). *Chin J Physi Med Rehab* 2012;34:801-5.
 36. Li JG. The influence on electroacupuncture towards neurogenesis and neurofunctional re-establishment after cerebral ischemia reperfusion (in Chinese) (Thesis). Tai'an: Taishan Medical College, 2005.
 37. You HL. Effects of Electroacupuncture on hypertension induced cerebral infarction in rats proliferation of neural precursor cells in brain and nerve regeneration in rats (in Chinese) (Thesis). Shanxi: Shanxi Medical University, 2012.
 38. Mi XJ. Effects of electroacupuncture on hypertension induced cerebral infarction in rats proliferation of neural precursor cells in brain and nerve regeneration in rats (in Chinese) (Thesis). Chongqing: Chongqing Medical University, 2010.
 39. Bao DP. Possible mechanism of electroacupuncture on inherent neural stem cells after cerebral ischemic injury in rats (in Chinese) (Thesis). Harbin: Heilongjiang University of Chinese Medicine, 2007.
 40. Chen H. Effect of electroacupuncture on neural stem cell proliferation, migration after brain ischemic injury in rats (in Chinese) (Thesis). Shanghai: Fudan University, 2003.
 41. Li CX. Experimental Study of Proliferation, Migration and Differentiation of Neural Precursor Cells after Acute Cerebral Infarction and the Effect of Electroacupuncture on Hypertensive Cerebral Infarction (in Chinese) (Thesis). Guangzhou: Zhong Shan University, 2004.
 42. Zhang HX, Zhang XY, Zhou L. Effect of scalp-acupuncture on the proliferation and migration of neural stem cells in acute cerebral ischemia/reperfusion injury rats (in Chinese). *Zhongguo Zhong Xi Yi Jie He Za Zhi* 2011;31:951-4.
 43. Zhao WS. To explore the mechanism of acupuncture and moxibustion in treating ischemic stroke from inherent neural stem cells (in Chinese) (Thesis). Harbin: Heilongjiang University of Chinese Medicine, 2006.
 44. Liu Z, Lai XS. Influence of electroacupuncture on expression of nestin of neural stem cells in ischemic sides of adult rats with cerebral ischemia (in Chinese). *Chin J Rehab Med* 2005;9:89-91.
 45. Yu DQ, Pei HT, Zhang PH, et al. Effects of electroacupuncture on the expression of nestin in endogenous neural stem cell in hippocampus in rats with focal cerebral ischemia-reperfusion (in Chinese). *Zhongguo Zhen Jiu* 2010;30:929-32.
 46. Wan SY, Tan F, Wu HK, et al. Effects of electric acupuncture on glial fibrillary acidic protein and vascular endothelial growth factor expressions and ultrastructure of gliavascular net of cerebral ischemic tissue in hypertensive rats (in Chinese). *Chin J TCM WM Crit Care* 2010;17:226-9.
 47. Zhao ZQ. Effects of electroacupuncture at 'Hegu' points (LI4) on proliferation, migration of neural stem cells after focal ischemia/reperfusion (in Chinese) (Thesis). Chongqing: Chongqing Medical University, 2004.
 48. Tao J, Xue XH, Chen LD, et al. Electroacupuncture improves neurological deficits and enhances proliferation and differentiation of endogenous nerve stem cells in rats

- with focal cerebral ischemia. *Neurol Res* 2010;32:198-204.
49. Yang ZJ, Shen DH, Guo X, et al. Electroacupuncture enhances striatal neurogenesis in adult rat brains after a transient cerebral middle artery occlusion. *Acupunct Electrother Res* 2005;30:185.
 50. Cheng S, Ma M, Ma Y, et al. Combination therapy with intranasal NGF and electroacupuncture enhanced cell proliferation and survival in rats after stroke. *Neurol Res* 2009;31:753-8.
 51. Kim YR, Kim HN, Ahn SM, et al. Electroacupuncture promotes post-stroke functional recovery via enhancing endogenous neurogenesis in mouse focal cerebral ischemia. *PLoS One* 2014;9:e90000.
 52. Tao J, Liu W, Huang J, et al. Electroacupuncture at Quchi and Zusanli enhances the proliferation of cortex and SVZ-derived neural stem cell in cerebral ischemia-reperfusion injured rats via activation of Notch1 signaling pathway. *Rehab Med* 2015;25:23-34.
 53. Jiang YJ. Exploration of the mechanism of opposing needling for improving neural functional recovery in middle cerebral artery occlusion rats through the expression of GABAB receptor mediated cAMP-PKA-CREB signaling pathway (in Chinese) (Thesis). Fuzhou: Fujian University of Traditional Chinese Medicine, 2015.
 54. Tao J, Zheng Y, Liu W, et al. Electro-acupuncture at LI11 and ST36 acupoints exerts neuroprotective effects via reactive astrocyte proliferation after ischemia and reperfusion injury in rats. *Brain Res Bull* 2016;120:14-24.
 55. Zhao J, Sui M, Lü X, et al. Electroacupuncture promotes neural stem cell proliferation and neurogenesis in the dentate gyrus of rats following stroke via upregulation of Notch1 expression. *Mol Med Rep* 2015;12:6911-7.
 56. Chen B, Tao J, Lin Y, et al. Electro-acupuncture exerts beneficial effects against cerebral ischemia and promotes the proliferation of neural progenitor cells in the cortical peri-infarct area through the Wnt/ β -catenin signaling pathway. *Int J Mol Med* 2015;36:1215-22.
 57. Cao X, Shi XH, Zhang SL, et al. Exploration of effects of opposing needling on stem cell in the ischemia/reperfusion injured rats (in Chinese). *Lishizhen Med Mater Med Res* 2016;27:993-5.
 58. Yao JN. Exploration of the effects of electro-acupuncture on the proliferation of endogenous neural stem cells through microRNA-9 regulated Notch1 signaling pathway after cerebral ischemia and reperfusion injury in rats (in Chinese) (Thesis). Fuzhou: Fujian University of Traditional Chinese Medicine, 2015.
 59. Li QP, Han YS, HanYZ, et al. Effects of the “Xingnao Kaiqiao” acupuncture therapy on expressions of vascular endothelial growth factor and glial fibrillary acidic protein after cerebral ischemia reperfusion in rats at early stage. *Chin J Rehab Med* 2015;30:645-50.
 60. Tan F, Wang J, Liu JX, et al. Electroacupuncture stimulates the proliferation and differentiation of endogenous neural stem cells in a rat model of ischemic stroke. *Exp Ther Med* 2018;16:4943-50.
 61. Mi D, Pan C, Chen X. Effect of Eye Acupuncture on the Expression Nesting and GAP43 of Rats after Cerebral Ischemia-reperfusion Injury. *J Liaoning Univ TCM* 2018;20:119-22.
 62. Kjaergard LL, Villumsen J, Gluud C. Reported methodologic quality and discrepancies between large and small randomized trials in meta-analyses. *Ann Intern Med* 2001;135:982-9.
 63. Schulz KF, Grimes DA. Sample size calculations in randomised trials: mandatory and mystical. *Lancet* 2005;365:1348-53.
 64. Landis SC, Amara SG, Asadullah K, et al. A call for transparent reporting to optimize the predictive value of preclinical research. *Nature* 2012;490:187-91.
 65. Beberta V, Luyten D, Heard K. Emergency medicine animal research: does use of randomization and blinding affect the results? *Acad Emerg Med* 2003;10:684-7.
 66. Baginskait J. Scientific Quality Issues in the Design and Reporting of Bioscience Research: A Systematic Study of Randomly Selected Original InVitro, In Vivo and Clinical Study Articles Listed in the PubMed Database. Available online: <http://www.dcn.ed.ac.uk/camarades/files/Camarades%20Monograph%20201201>
 67. Liu L, LSkinner M, McDonough SM, et al. STRICTA: is it time to do more? *BMC Complement Altern Med* 2015;15:190.
 68. Simera I, Moher D, Hirst A, et al. Transparent and accurate reporting increases reliability, utility, and impact of your research: reporting guidelines and the EQUATOR Network. *BMC Med* 2010;8:24.
 69. Altman DG, Simera I, Hoey J, et al. EQUATOR: reporting guidelines for health research. *Lancet* 2008;371:1149-50.

Cite this article as: Li ZX, Li Y, Yang WT, Wang M, Xu MB, Zhou XL, Rong PQ, Jin TY, Yi WJ, Zheng GQ. The reporting quality of acupuncture for neurogenesis in experimental ischemic stroke study. *Ann Transl Med* 2019;7(6):123. doi: 10.21037/atm.2019.02.16