### STROBE Checklist

| Item No. | Recommendation | Page No. | Relevant text from manuscript |
|----------|----------------|----------|------------------------------|
| **Title and abstract** | 1 | (a) Indicate the study’s design with a commonly used term in the title or the abstract | 1 | Bi-frontal pneumocephalus is an independent risk factor for early postoperative agitation in adult patients after elective craniotomy for brain tumor. A prospective cohort study |
|  | | (b) Provide in the abstract an informative and balanced summary of what was done and what was found | 2-3 | Adult intensive care unit admitted patients after elective craniotomy under general anesthesia were consecutively enrolled. After adjustment for confounding, agitation was independently associated with worse neurologic outcome (odd ratio: 5.4, 95% confidential interval: 1.1–28.9, P = 0.048). |
| **Introduction** | 2 | Explain the scientific background and rationale for the investigation being reported | 4 | Postoperative agitation after general anesthesia has been reported to occur in 3.7 to 29% of patients. Therefore, we conducted this prospective cohort study of adult patients who had undergone elective craniotomy for brain tumors. |
| **Objectives** | 3 | State specific objectives, including any prespecified hypotheses | 5 | We aimed to investigate the risk factors for agitation, specifically focusing on the association between postoperative pneumocephalus and agitation. The association of agitation with long-term outcomes was also analyzed. |
| **Methods** | 4 | Present key elements of study design early in the paper | 6 | Study design, ethics and patient population. This prospective cohort study was approved by the Institutional Review Board of Beijing Tiantan Hospital, Beijing, China (KY2014-034-01). |
| **Study design** | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | 6 | The study was conducted in a neurosurgical ICU of University affiliated hospital (Beijing, China) between Jan 1 and Aug 31, 2015. |
| **Setting** | 6 | (a) Cohort study—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up | 6 | The inclusion criterion was adult patients who had undergone elective craniotomy for brain tumors. The exclusion criteria included:…… |
### Case-control Study

Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls.

### Cross-sectional Study

Give the eligibility criteria, and the sources and methods of selection of participants.

### (b) Cohort Study

For matched studies, give matching criteria and number of exposed and unexposed

### Case-control Study

For matched studies, give matching criteria and the number of controls per case.

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| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | 9-12 | Agitation assessment and definition Assessment of postoperative CT scans Data collection |
|-----------|---|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Data sources/measurement | 8* | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group | 9-12 | The patients were divided into two groups based on their maximal SAS score: the agitation group (maximal SAS ≥ 5) and the non-agitation group (maximal SAS ≤ 4). |
| Bias | 9 | Describe any efforts to address potential sources of bias | 9-12 | Two attending neuroradiologists who were blinded to agitation status retrospectively reviewed each patient’s first postoperative CT scans. Two neuroradiologists independently reviewed the CT scans. Discrepancies were resolved by discussion until consensus was reached. |
| Study size | 10 | Explain how the study size was arrived at | | According to standard recommendations, 10 cases of interest (agitation) would be required. We anticipated an average incidence of agitation in the present cohort using data from previous reports (11%), and planned to enroll 400 cases to identify risk factors for postoperative agitation. |

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Continued on next page
Quantitative variables 11

Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why

Categorical variables are expressed as counts (percentages), and continuous data are reported as medians with interquartile ranges (IQRs).

Statistical methods 12

(a) Describe all statistical methods, including those used to control for confounding

(b) Describe any methods used to examine subgroups and interactions

(c) Explain how missing data were addressed

(d) Cohort study—If applicable, explain how loss to follow-up was addressed

Case-control study—If applicable, explain how matching of cases and controls was addressed

Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy

(e) Describe any sensitivity analyses

Missing data and loss to follow-up were documented.

Results

Participants 13*

(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed

(b) Give reasons for non-participation at each stage

(c) Consider use of a flow diagram

Descriptive data 14*

(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders

(b) Indicate number of participants with missing data for each variable of interest

(c) Cohort study—Summarise follow-up time (eg, average and total amount)

Outcome data 15*

Cohort study—Report numbers of outcome events or summary measures over time

Case-control study—Report numbers in each exposure category, or summary measures of exposure

Cross-sectional study—Report numbers of outcome events or summary measures

Main results 16

(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included

(b) Report category boundaries when continuous variables were categorized

(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period

The Hosmer-Lemeshow test was used to determine whether the model fitted the data adequately well.
| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses | 23 | Table 4 |
|----------------|----|-----------------------------------------------------------------------------------------------|----|---------|

**Discussion**

| Key results | 18 | Summarise key results with reference to study objectives | 30 | Our main findings were:…….. |
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| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias | 33-34 | There are limitations to the present study…….. |
|------------|----|-----------------------------------------------------------------------------------------------|----|-----------------------------|

| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | 33 | Thus, our patients represented a population that was at high-risk of postoperative agitation, and our results may limit the generalization to the entire population of patients undergoing craniotomy for brain tumors. |
|----------------|----|-----------------------------------------------------------------------------------------------|----|-----------------------------|

| Generalisability | 21 | Discuss the generalisability (external validity) of the study results | 33 | Thus, our patients represented a population that was at high-risk of postoperative agitation, and our results may limit the generalization to the entire population of patients undergoing craniotomy for brain tumors. |
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**Other information**

| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based | In the submission window |
|---------|----|-----------------------------------------------------------------------------------------------|-------------------------|

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.