**Additional file 3: Risk of bias evaluation form**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Domain** | **Description** | **Judgment** | **Risk of bias** | **Direction** |
| **Selection bias** |
| Inclusion and exclusion criteria |
| Were inclusion and exclusion criteria specified?  | *.* | □ yes □ no □ unclear |  | □ overestimation □ underestimation□ unclear |
| Were inadequate eligibility criteria avoided? |  | □ yes □ no □ unclear |  | □ overestimation □ underestimation□ unclear |
| Randomization |
| Was randomization reported?  |  | □ yes □ no □ unclear |  | □ overestimation □ underestimation□ unclear |
| Was the method specified and done after lesion? |  | □ yes □ no □ unclear |  | □ overestimation □ underestimation□ unclear |
| Overall |  |  | □ high □ low □ unclear | □ major overestimation □ overestimation □ underestimation□ major underestimation□ unclear |
| **Information bias** |
| Blinding of outcome assessment |
| Were outcome assessment blinded to treatment allocation? |  | □ yes □ no □ unclear |  | □ overestimation □ underestimation□ unclear |
| Overall |  |  | □ high □ low □ unclear | □ major overestimation□ overestimation □ underestimation□ major underestimation□ unclear |
| **Confounding** |
| Blinding of care |
| Were induction of cerebral lesions, maintenance, decision regarding care blinded to treatment allocation? |  | □ yes □ no □ unclear |  | □ overestimation □ underestimation□ unclear |
| Comorbidities |
| Were animals with comorbidities included? |  | □ yes □ no □ unclear |  | □ overestimation □ underestimation□ unclear |
| Temperature |
| Animal temperature controlled?  |  | □ yes □ no □ unclear |  | □ overestimation □ underestimation□ unclear |
| Was the method to control temperature adequate? |  | □ yes □ no □ unclear |  | □ overestimation □ underestimation□ unclear |
| Anesthesia |  |  |  |  |
| Agents known for important neuroprotective activity? |  | □ yes □ no □ unclear |  | □ overestimation □ underestimation□ unclear |
| Overall |  |  | □ high □ low □ unclear | □ major overestimation □ overestimation □ underestimation□ major underestimation□ unclear |
| **Other treats to internal validity** |
| Conflict of interest |
| Was a statement of conflict of interest was reported?  |  | □ yes □ no □ unclear |  | □ overestimation □ underestimation□ unclear |
| Did authors report a conflict of interest? |  | □ yes □ no □ unclear |  | □ overestimation □ underestimation□ unclear |
| Random error / Sampling error |
| Was the sample size calculation reported?  |  | □ yes □ no □ unclear |  | □ overestimation □ underestimation□ unclear |
| Was the precision of the estimate sufficient? |  | □ yes □ no □ unclear |  | □ overestimation □ underestimation□ unclear |
| Internal publication bias |
| Are reports of the study free of suggestions of selective outcome reporting?  |  | □ yes □ no □ unclear | □ high □ low □ unclear | □ overestimation □ underestimation□ unclear |
| Were outcomes and statistical analysis described in a protocol published a priori? |  | □ yes □ no □ unclear | □ high □ low □ unclear | □ overestimation □ underestimation□ unclear |
| **Other methodological quality concerns** |
| Peer review |
| Was the study report peer reviewed? |  | □ yes □ no □ unclear | □ high □ low □ unclear | □ overestimation □ underestimation□ unclear |
| Animal welfare |
| Was there a statement of compliance with animal welfare explicitly stated? |  | □ yes □ no □ unclear | □ high □ low □ unclear | □ overestimation □ underestimation□ unclear |