# eTable 5. Quality appraisal of case reports and case series

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Domains** | | | | | | | | | | **Overall quality** | **OCEBM Level** |
| **Study ID** | **1** | **2** | **3** | **4** | **5** | **6** | **7: A** | | **7: P** | **8** |
| Corr et al. 20141 | Y | N | Y | N | NA | NA | Y | | − | N | Poor | 5 |
| Fang, Zheng & Zhang 20182 | Y | ? | Y | N | NA | NA | N | | − | N | Very poor | 5 |
| Fryer et al. 20163 | Y | ? | ? | N | NA | NA | N | | N | N | Very poor | 5 |
| Gagliardi et al. 20194 | Y | N | Y | Y | NA | N | ? | | Y | N | Good | 5 |
| González et al. 20205 | Y | N | Y | Y | NA | NA | Y | | N | ? | Good | 5 |
| Hayashi et al. 20206 | Y | ? | Y | N | NA | NA | Y | | Y | ? | Poor | 5 |
| Hovsepian et al. 20187 | Y | N | Y | N | NA | NA | N | | N | ? | Very poor | 5 |
| Ito et al. 20208 | Y | ? | Y | N | NA | NA | Y | | Y | ? | Poor | 5 |
| Kitamura et al. 20169 | Y | ? | Y | N | NA | NA | Y | | − | ? | Poor | 5 |
| Kubota et al. 200410 | Y | N | Y | N | NA | NA | N | | − | ? | Very poor | 5 |
| Lekoubou et al. 201111 | Y | N | Y | N | NA | NA | N | | Y | ? | Poor | 5 |
| Minobe et al. 2015 12 | Y | ? | Y | N | NA | NA | Y | | − | N | Poor | 5 |
| Mitani et al. 201313 | Y | ? | Y | N | NA | NA | Y 1st | N 2nd | N | N | 5 | 5 |
| Oyama et al. 202014 | Y | N | Y | N | NA | NA | Y | | − | N | Poor | 5 |
| Randhawa et al. 201615 | Y | N | Y | N | NA | NA | Y | | Y | N | Poor | 5 |
| Renard & Ion 202016 | Y | N | NR | NR | NA | NA | N | | − | N | Very poor | 5 |
| Sakai et al. 201817 | Y | N | Y | ? | NA | NA | N | | N | N | Very poor | 5 |
| Shigemi et al. 201118 | Y | N | Y | N | NA | NA | Y | | N | Y | Good | 5 |
| Shimizu et al. 202019 | Y | N | ? | Y | NA | NA | Y | | − | N | Poor | 5 |
| Siddiq, Widjaja & Tein 201520 | Y | ? | Y | N | NA | NA | N | | Y | ? | Poor | 5 |
| Sunde et al. 201621 | Y | N | ? | N | NA | NA | N | | Y | N | Very poor | 5 |
| Torre et al. 202022 | Y | N | N | N | NA | NA | N | | Y | ? | Very poor | 5 |
| Ueki et al. 202023 | Y | N | Y | Y | NA | NA | ?g | | − | N | Poor | 5 |
| Wang et al. 202024 | Y | ? | NR | NR | NA | NA | N | | − | N | Very poor | 5 |
| Wei, Cui & Pen 201925 | Y | N | Y | N | NA | NA | Y | | Y | Y | Good | 5 |
| Yoneda et al. 201226 | Y | ? | Y | N | NA | NA | N | | − | ? | Very poor | 5 |
| Koga et al. 200227 | Y | ? | Y | N | NA | NA | N | | N | Y | Poor | 4 |
| Calvaruso et al. 201128 | Y | ? | NR | ? | NA | NA | − | | N | N | Very poor | 5 |
| Cosentino et al. 201929 | Y | ? | NR | ? | NA | NA | − | | N | N | Very poor | 5 |
| Fukuda & Nagao 201930 | Y | ? | Y | N | NA | NA | − | | Y | N | Poor | 5 |
| Marques-Matos 201531 | Y | ? | N | N | NA | NA | − | | N | N | Very poor | 5 |
| Selim & Mehaney 201332 | Y | ? | NR | N | NA | NA | − | | N | N | Very poor | 5 |
| Sun et al. 201833 | Y | N | ? | N | NA | NA | − | | Y | N | Very poor | 5 |
| Suzuki et al. 201734 | Y | ? | N | N | NA | NA | − | | ? | N | Very poor | 5 |

Tool for evaluating the methodological quality of case reports and case series (Murad, et al. 2018) 35

Abbreviations: A, acute; NA, not applicable; N, no; NR, not reported; OCEBM, Oxford Centre for Evidence-Based Medicine Levels of Evidence; P, prophylactic; Y, yes; ?, unclear

article did not include acute or prophylactic treatment (therefore no follow up of respective regime reported).

The overall quality appraisal (within) for each article was classified according to the number of questions satisfied across any domains of Ascertainment, Causality, and Reporting; ≥ 3 questions satisfied= ‘good quality’; 2 questions= ‘poor quality’; one or fewer questions= ‘very poor'.

**Selection**

1. Does the patient(s) represent(s) the whole experience of the investigator (centre) or is the selection method unclear to the extent that other patients with similar presentation may not have been reported?

**Ascertainment**

2. Was the exposure adequately ascertained?a

3. Was the outcome adequately ascertained?b

**Causality**

4. Were other alternative causes that may explain the observation ruled out?c

5. Was there a challenge/rechallenge phenomenon?d

6. Was there a dose–response effect?

7. Was follow-up long enough for outcomes to occur?e

**Reporting**

8. Is the case(s) described with sufficient details to allow other investigators to replicate the research or to allow practitioners make inferences related to their own practice?f

*Items 4-6 are mostly relevant to cases of adverse drug events.*

1. ‘No, where anticonvulsants/antiepileptic drugs were used; ‘Unclear’ where any other treatments were used or where other treatments were not reported.
2. ‘Yes’ where outcomes included brain imaging or semi-quantitative measures; ‘No’ where response to treatment was measured via self-reported assessment, judgement, or description.
3. ‘No’ where the outcome (improvement or deterioration) could be explained by other exposures (i.e. other treatment/s).
4. ‘NA’ as adverse drug events with a rechallenge phenomenon was not applicable.
5. ‘Yes’ if follow-up was performed within an acceptable length of time; 2-4 weeks (Acute treatment). For prophylactic- there is no literature on an optimal follow up duration to determine the efficacy. ‘Yes’ refers to follow up of any length.
6. ‘No’ where route of administration or dose of L-arginine (acute or prophylactic treatment) was inadequately reported; ‘Unclear’ where the timing of treatment in relation to the stroke-like episode was not reported. ‘Unclear’ where details related to AED treatment were not reported i.e. type of AED, administration, or regime).
7. Route & regime (acute or prophylactic) treatment of L-arginine was not reported

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