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Early versus delayed mobilisation for aneurysmal subarachnoid haemorrhage (Review)

Ma Z, Wang Q, Liu M

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Early versus delayed mobilisation for aneurysmal subarachnoid haemorrhage.
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TABLE OF CONTENTS

[Intervention Review]

Early versus delayed mobilisation for aneurysmal subarachnoid haemorrhage

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ABSTRACT

Background

Rebleeding is an important cause of death and disability in patients with aneurysmal subarachnoid haemorrhage (SAH). In order to prevent rebleeding, the preferred strategy is aneurysm ablation (removal) as early as possible. However, in clinical practice some patients are not suitable for surgical treatment, or prefer conservative treatments. In some countries, therefore, total bedrest for four to six weeks has been considered one of the basic interventions to avoid rebleeding. However, the influence of bedrest on outcome in patients with SAH is not well known.

Objectives

To establish whether early mobilisation (less than four weeks after symptom onset) compared with delayed mobilisation (defined as patients staying in bed for at least four weeks after symptom onset) in patients with aneurysmal subarachnoid haemorrhage (SAH), who have not had or could not have any surgical treatment for the aneurysm, will increase the proportion of deaths from rebleeding.

Search methods

We searched the Cochrane Stroke Group Trials Register (May 2012), the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2012, Issue 6), the Chinese Stroke Trials Register (May 2012), MEDLINE (1950 to June 2012), EMBASE (1980 to June 2012), Web of Science Conference Proceedings (1990 to May 2012), CINAHL (1982 to June 2012), AMED (1985 to June 2012), PEDro (May 2012), REHABDATA (May 2012) and CIRRIE Database of International Rehabilitation Research (May 2012). In addition, we searched five Chinese databases, ongoing trials registers and relevant reference lists.

Selection criteria

We planned to include randomised controlled trials (RCTs) comparing early mobilisation (within four weeks after symptom onset) with delayed mobilisation (after four weeks).

Data collection and analysis

Two review authors independently selected trials for inclusion and exclusion. We resolved disagreements by discussion.

Main results

In the absence of any suitable RCTs addressing this topic, we were unable to perform a meta-analysis. Data from recent observational studies suggested the period of greatest risk for rebleeding occurs more frequently in the early period, especially within 24 hours of the initial SAH. The impact of bedrest on aneurysm care should be clarified.

Authors' conclusions

There are no RCTs or controlled trials that provide evidence for, or against, staying in bed for at least four weeks after symptom onset in patients with aneurysmal SAH, who have not had, or could not have, surgical treatment for the aneurysm. Treatment strategies to reduce the risk of rebleeding in SAH patients before aneurysm ablation, or in those not suitable for surgical treatment, or who prefer conservative treatments, deserve attention.

PLAIN LANGUAGE SUMMARY

Early versus delayed mobilisation to prevent further bleeding after spontaneous bleeding on the surface of the brain

Aneurysmal subarachnoid haemorrhage (SAH) is a serious event where spontaneous bleeding on the surface of the brain is usually caused by the rupture of an abnormal swelling of an artery (aneurysm). If effective treatment is not provided (e.g. surgery or drug therapy) rebleeding may occur, causing death or disability for the patient. Some researchers observed that the highest risk period for rebleeding in people with a SAH was between two and four weeks after symptom onset, if they did not receive effective treatment. Total bedrest for four to six weeks has, therefore, been considered to be one of the basic interventions to avoid rebleeding. However, despite comprehensive searching, we did not identify any suitable studies that provided evidence for or against staying in bed for at least four weeks after symptom onset in people who did not, or could not, have any treatment for their ruptured aneurysm. Treatment strategies to reduce the risk of rebleeding in SAH patients before aneurysm repair, or in those patients not suitable for surgical treatment, or who prefer conservative treatments, deserve further attention.

BACKGROUND

Description of the condition

Subarachnoid haemorrhage (SAH) is a subset of stroke that accounts for only 5% of all strokes (Van Gijn 2007). Most patients who have a SAH are less than 60 years old (Van Gijn 2001). The overall incidence of SAH is approximately nine per 100,000 person-years. Between 1950 and 2005, there was a decrease in incidence of 0.6% per year, which was relatively moderate compared with that for stroke in general (De Rooij 2007). Aneurysms (abnormal swellings of arteries that can rupture) are the cause of SAH in 85% of cases (Van Gijn 2007). Poor outcome (death or dependence) from aneurysmal SAH occurs in approximately 70% of patients (Hop 1997).

At present, critical care of a patient with SAH should focus on the prevention or immediate treatment of the common consequences of this disorder, such as vasospasm, rebleeding, hydrocephalus (increased intercranial pressure, previously called "water on the brain"), seizures, and other medical complications (Connolly 2012; King 1994). A series of complications in patients with SAH will cause a second attack. Theoretically, it is possible that improper management will lead to deterioration or even death. Rebleeding is an important cause of death and disability in patients with aneurysmal SAH. It has been shown that, without surgery or antifibrinolytic treatment,approximately 30% of patients have rebleeding within one month of the initial haemorrhage (Locksley 1966), and approximately 50% die directly because of the rebleeding (Hijdra 1987). Consequently, occlusion of the aneurysm should be considered a priority (Van Gijn 2001). The preferred strategy for preventing aneurysm rebleeding, in most hospitals around the world, is surgical or endovascular ablation of the aneurysm as soon as possible (Connolly 2012; Juvela 2006). However, in clinical practice some patients are not suitable for surgical treatment, or prefer medical or conservative treatments.

Description of the intervention

In theory, immobilisation could prevent the ruptured aneurysm from rebleeding. Some observational studies on the natural history of aneurysmal SAH have found the highest risk period for rebleeding to be two to four weeks after the initial SAH (Kassell 1983; Pakarinen 1967). Consequently, in order to avoid rebleeding, bedrest for four to six weeks has been considered one of the basic interventions, and is described in many textbooks in China (Wang 2005; Zhang 2003). Although surgical or endovascular treatment is recommended worldwide (Connolly 2012), bedrest might be included as a component of a broader treatment strategy for SAH that aims to reduce rebleeding (Bederson 2009; Henderson 1977), especially for patients who have not had, or could not have, surgical or endovascular treatment for the aneurysm (Bederson 2009; Nishioka 1984).

In contrast, early mobilisation and rehabilitation has been recommended for patients with ischaemic stroke or intracerebral haemorrhage who are clinically stable (Broderick 2007; EUSI 2006). It has been reported that interventions that promote recovery may reduce length of hospital stay (Sorbello 2009), and that very early mobilisation is associated with improved independence after stroke (Craig 2010). In addition, extended bedrest might lead to a number of complications (Marco 2012), such as venous thromboembolism (Barczyk 2001; Harvey 2003), pneumonia (Fukuyama 2010), urinary infections (Nickel 2005), etc.

Why it is important to do this review

In view of limited resources and increasing economic pressures, reducing duration of bedrest and length of hospital stay after SAH is an area of interest. However, the influence of bedrest and early mobilisation on outcomes in patients with SAH is unclear.

OBJECTIVES

To establish whether early mobilisation (less than four weeks after symptom onset) compared with delayed mobilisation (defined as patients staying in bed for at least four weeks after symptom onset) in patients with aneurysmal subarachnoid haemorrhage (SAH), who have not had, or could not have, any surgical treatment for the aneurysm, will increase the proportion of deaths from rebleeding.

METHODS

Criteria for considering studies for this review

Types of studies

We included randomised controlled trials (RCTs) comparing early mobilisation with delayed mobilisation.

Types of participants

Aneurysmal SAH is diagnosed by clinical symptoms and signs of SAH, with confirmation by the presence of subarachnoid blood on computerised tomography (CT) scan or, in cases with a negative CT, by the presence of xanthochromia in the cerebral spinal fluid (Suarea 2006). Recent SAH is defined as within seven days of symptom onset (CT showing high-density image).

Types of interventions

Delayed mobilisation (defined as patients staying in bed for at least four weeks after symptom onset) versus early mobilisation (defined as patients being able to move out of bed within four weeks or staying in bed for less than four weeks). Early mobilisation was defined as less than four weeks after symptom onset, based on observational studies on the natural history of aneurysmal SAH (Kassell 1983; Pakarinen 1967).

Types of outcome measures

Primary outcomes

1. Death from recurrent haemorrhage during the scheduled treatment period and the scheduled follow-up period. We planned to classify recurrent haemorrhage into two categories:
   a. a probable recurrent haemorrhage defined as sudden deterioration leading to death without confirmation of rebleeding by CT, magnetic resonance imaging (MRI) or post mortem;
   b. a definite recurrent haemorrhage defined as sudden clinical deterioration with rebleeding confirmed by CT, MRI or post mortem.
2. The proportion of recurrent haemorrhage.

Secondary outcomes

1. Death or dependence in daily activities during the scheduled follow-up period (modified Rankin scale 3 to 6 (Van Swieten 1988) or Glasgow outcome scale 1 to 3 (Jennett 1975)).
2. Death from any cause during the scheduled treatment period and the scheduled follow-up period.
3. Complications during hospital stay.
4. Duration of hospital stay.
5. Quality of life.
6. Anxiety during hospital stay.

Search methods for identification of studies

See the 'Specialized register' section in the Cochrane Stroke Group module. We searched for trials in all languages and arranged translation of relevant reports published in languages other than English and Chinese.

Electronic searches

We searched the Cochrane Stroke Group Trials Register, which was last searched by the Managing Editor in May 2012 . In addition, in collaboration with the Cochrane Stroke Group Trials Search Co-ordinator, we searched the following bibliographic databases:

- Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2012, issue 6);
- MEDLINE (1950 to June 2012) (Appendix 1);
- EMBASE (1980 to June 2012) (Appendix 2);
- CINAHL (1982 to June 2012) (Appendix 3);
- AMED (the Allied and Complementary Medicine Database (1985 to June 2012) (Appendix 4);
- Web of Science Conference Proceedings (1990 to May 2012);
- PEDro (Physiotherapy Evidence Database) (May 2012);
- REHABDATA (http://www.naric.com/research/rehab/default.cfm) (May 2012);
- CIRRIE Database of International Rehabilitation Research (http://cirrie.buffalo.edu/index.html) (May 2012);
- Chinese Stroke Trials Register (May 2012);
- China Biological Medicine Database (CBM) (1978 to May 2012);
- Chinese National Knowledge Infrastructure (CNKI) (1979 to May 2012);
- Chinese Science and Technique Journals Database (VIP) (1989 to May 2012);
- Wanfang Data (http://www.wanfangdata.com/) (1984 to May 2012);
- China Medical Academic Conferences (CMAC 1995 to May 2012).

We also searched the following international trials registers: ClinicalTrials.gov (http://www.clinicaltrials.gov/), Current Controlled Trials (http://www.controlled-trials.com), and the Stroke Trials Registry (http://www.strokecenter.org/trials/) (May 2012).

Searching other resources

We searched all reference lists of articles retrieved in full.

Data collection and analysis

Selection of studies

Two review authors (ZM, QW) independently scanned the title, abstract and keywords of records obtained from the electronic searches, and excluded obviously irrelevant studies. We then obtained the full text of the remaining studies, and the same two authors assessed these for inclusion based on the selection criteria outlined previously. We resolved any disagreements by discussion and, when necessary, in consultation with a third review author (ML). We planned to add any studies requiring further information to the Characteristics of studies awaiting classification section and to contact the study authors.

Data extraction and management

Two review authors (ZM, QW) planned, independently, to extract data relating to patient characteristics, methods, interventions, and outcomes, using a data extraction form. We planned to resolve disagreements by discussion. For dichotomous outcomes, we planned to extract the number of participants experiencing the event and the total number of participants in each arm of the trial. For continuous outcomes, we planned to extract the mean value and standard deviation for the changes in each arm of the trial, along with the total number in each group.

Assessment of risk of bias in included studies

We planned to assess the methodological quality of selected studies using The Cochrane Collaboration's tool for assessing risk of bias as described in the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011). We planned to create 'Risk of bias' tables and include a description and a judgement (low risk of bias, high risk of bias, or unclear risk of bias) for the following points for each of the included studies:

1. random sequence generation;
2. allocation concealment;
3. blinding of participants and personnel;
4. blinding of outcome assessment;
5. incomplete outcome data;
6. selective reporting;
7. other sources of bias.

Two review authors (ZM, QW) planned to perform quality assessment independently, and any disagreements arising at any stage, were to be resolved by discussion or with a third review author (ML) when necessary.

Data synthesis

We planned to perform statistical analysis using the Cochrane Review Manager software, RevMan 5.1 (RevMan 2011). We intended to express results for dichotomous outcomes as risk ratios (RR) with 95% confidence intervals (CI), and express the results for continuous outcomes as mean difference (MD) or standardised mean difference (SMD). We planned to use a random-effects model to combine individual results regardless of heterogeneity, and we planned to quantify inconsistency across studies or subgroups using the I^2 statistic. We considered that an I^2 value greater than 50% would represent substantial heterogeneity.

Subgroup analysis and investigation of heterogeneity

We planned a priori subgroup analyses based on:

1. the severity of the SAH (according to Hunt and Hess (Hunt 1968) or the Glasgow Coma Scale (Teasdale 1974));
2. different duration of bedrest.

Sensitivity analysis

We planned sensitivity analyses as follows:

1. excluding studies with inadequate concealment of allocation;
2. excluding studies in which outcome evaluation was not blinded;
3. excluding studies in which loss to follow-up was not reported or was more than10%.

RESULTS

Description of studies

Results of the search

After reading1359 titles and abstracts in EMBASE, CINAHL, and AMED; 11492 in MEDLINE; and 15 in CENTRAL and a number of other databases, we identified nine potentially eligible trials for further assessment (Ando 1989; Blissitt 2006; Hunger 1984; Kara 2007; Mazzucchi 1998; McKissock 1960; McKissock 1962; Nibbelink 1977; Yap 2002). However, we excluded all of them after full assessment. We did not identify any ongoing trials.

Included studies

We did not include any RCTs.

Excluded studies

We excluded four trials because they were not RCTs (Ando 1989; Hunger 1984; Nibbelink 1977; Yap 2002). We excluded others because the interventions did not meet our pre-stated inclusion criteria, including the following interventions: elevations of the head of the bed (Blissitt 2006), management of rehabilitation before surgery (Mazzucchi 1998), conservative and surgical treatment (McKissock 1960; McKissock 1962), and supervised exercise at admission and at home (Kara 2007). More details are provided in the Characteristics of excluded studies table.

Risk of bias in included studies

We did not identify any suitable studies for inclusion.

Effects of interventions

In the absence of any suitable RCTs in this area, we were unable to perform any analyses.

DISCUSSION

Summary of main results

At present, there are no RCTs providing evidence for or against staying in bed for at least four weeks after symptom onset in patients with aneurysmal SAH, who have not had, or could not have, any surgical treatment for the aneurysm.

Overall completeness and applicability of evidence

In the past, bedrest for at least four weeks had been considered one of the basic interventions to avoid rebleeding due to the natural history of aneurysmal SAH. The highest risk period for rebleeding was found to be between two and four weeks after symptom onset. However, disagreement existed about the period of greatest risk for rebleeding. In one study, it was reported that, after onset of SAH, the rate of rebleeding was 10% for one week,12% for two weeks, 7% for three weeks, 8% for four weeks, and 25% for five to 12 weeks. The accumulated rebleeding rate in two weeks was 25%. The peak time of rebleeding was the ninth day after onset (Locksley 1966). Furthermore, another study reported that the rate of rebleeding within eight weeks after onset of SAH was 32.3%, the second week was 10.1% and the third week was 8.0% (Pakarinen 1967). Juvela et al reported that the first weekend had the highest rebleeding incidence (4.5%), and the rate was 4.1% within 24 hours after onset of SAH, which accumulated to 20% within two weeks (Juvela 2006).

Several studies showed the highest risk of rerupture to be within the first 24 hours. In one study that included 661 cases of ruptured intracranial aneurysms, rebleeding occurred in 65 cases (10%), and, within this group, 43 cases (70%) rebled within the first six hours after initial SAH (Ando 1989). Kassell et al reported that rebleeding was most likely to happen within 24 hours after onset, with an incidence of the 4.1%, which decreased to 1.5% in the following 48 hours. The accumulated rate of rebleeding was 19% within two weeks (Kassell 1983). Tanno et al found rebleeding after hospitalisation in 181 patients with ruptured intracranial aneurysms (out of 5612 cases), in whom rebleeding occurred in 65 (35.9%) within three hours and in 88 (48.6%) within six hours after the initial SAH (Tanno 2007). Given that death resulting from SAH often occurs before hospital admission, the true incidence of rebleeding might be even higher in the ultra-early period after the initial SAH. These findings suggest aneurysmal rebleeding occurs more frequently in the earlier period after the initial SAH than previous reports indicated.

The different rates of rebleeding are most probably because previous studies missed rebleeding occurring in the ultra-early period after the initial SAH. In addition, impact of early surgical or endovascular treatment on rebleeding in the modern era of aneurysm care was not ignored.

Recent studies showed that the highest risk of rebleeding was in earlier periods, especially the first days after symptom onset, rather than weeks post haemorrhage, and we made our inference that prolonged bedrest might not be necessary. However, this should be clarified in further studies.

Potential biases in the review process

Although we have carried out extensive searching to identify studies for inclusion, it is possible that we have missed potentially relevant trials.

Agreements and disagreements with other studies or reviews

We did not find any other relevant studies or reviews of this topic.

AUTHORS' CONCLUSIONS

Implications for practice

There is no evidence from RCTs for or against patients with aneurysmal subarachnoid haemorrhage (SAH), who have not had, or could not have, any surgical treatment for the aneurysm, staying in bed for at least four weeks after symptom onset.

Implications for research

Based on our knowledge of the current literature, it is fair to say that treatment strategies to reduce the risk of rebleeding in SAH patients before aneurysm repair, or in those not suitable for surgical treatment, or in those who prefer conservative treatments, deserve further attention. Optimal periods of bedrest for these patients should be clarified. We consider that observational studies should be carried out prior to conducting future randomised controlled trials.

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We thank Mrs Hazel Fraser for providing relevant trials from the Cochrane Stroke Group Trials Register and her efforts related to the review, and Mrs Brenda Thomas for her help with developing the search strategy and searching for data for us. We also appreciate the help provided by Dr Zilong Hao in the design of our review and his practical advice during its development. Thanks to all the other editors of the Cochrane Stroke Group for their valuable help and advice on writing this review. Thanks also to all the attending staff of the West China Hospital.

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CHARACTERISTICS OF STUDIES

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Ando 1989	Not an RCT
Blissitt 2006	Intervention did not meet our pre-stated inclusion criteria (elevations of the head of the bed of 20° versus 45°)
Hunger 1984	Not an RCT
Kara 2007	Intervention did not meet our pre-stated inclusion criteria (regular supervised exercise versus home exercise)
Mazzucchi 1998	Intervention did not meet our pre-stated inclusion criteria (different strategies of rehabilitation were compared before surgery)
McKissock 1960	Intervention did not meet our pre-stated inclusion criteria (controlled trial of conservative and surgical treatment in posterior-communicating aneurysms)
McKissock 1962	Intervention did not meet our pre-stated inclusion criteria (controlled trial of conservative and surgical treatment in middle cerebral aneurysms)
Nibbelink 1977	Not an RCT
Yap 2002	Not an RCT

RCT: randomised controlled trial

APPENDICES

Appendix 1. MEDLINE search strategy

We used the following search strategy for MEDLINE (Ovid) and adapted it for CENTRAL.

1. subarachnoid hemorrhage/
2. intracranial hemorrhages/ or cerebral hemorrhage/
3. intracranial aneurysm/
4. rupture, spontaneous/
5. 3 and 4
6. aneurysm, ruptured/
7. exp brain/ or exp meninges/
8. 6 and 7
9. ((subarachnoid or arachnoid) adj6 (haemorrhage$ or hemorrhage$ or bleed$ or blood$)).tw.
10. vasospasm, intracranial/
11. ((cerebral or intracranial or cerebrovascular) adj6 (vasospasm or spasm)).tw.
12. sah.tw.
13. 1 or 2 or 5 or 8 or 9 or 10 or 11 or 12
14. bed rest/ or immobilization/ or rest/
15. (bed rest or bed-rest or bedrest or bed bound or bed-bound or bedbound or immobili$).tw.
16. (confined adj5 bed).tw.

17. early ambulation/
18. physical therapy modalities/ or "physical therapy (specialty)"/
19. rehabilitation/ or "activities of daily living"/ or recovery of function/
20. movement/ or locomotion/ or walking/ or motor activity/
21. exercise movement techniques/ or exercise/ or exercise therapy/
22. 18 or 19 or 20 or 21
23. time factors/ or time/ or early.tw.
24. 22 and 23
25. ((early or earlie$ or accelerat$ or immediate or fast-track or timing or rapid) adj10 (mobil$ or ambulat$ or rehab$ or physiotherapy or physical therapy or physical activity or movement or sitting or standing or walking or semi-recumb$ or out of bed)).tw.
26. (stroke unit$ or mobility protocol).tw.
27. 14 or 15 or 16 or 17 or 24 or 25 or 26
28. 13 and 27
29. subarachnoid hemorrhage/nu, rh [Nursing, Rehabilitation]
30. 28 or 29

Appendix 2. EMBASE search strategy

We used the following search strategy for EMBASE (Ovid).

1. subarachnoid hemorrhage/
2. brain artery aneurysm rupture/ or brain hemorrhage/ or brain vasospasm/
3. (intracranial aneurysm/ or brain artery aneurysm/) and (rupture/ or artery rupture/ or rupture$.tw.)
4. aneurysm rupture/ and (exp brain/ or exp meninx/)
5. ((subarachnoid or arachnoid$) adj6 (haemorrhage$ or hemorrhage$ or haematoma$ or hematoma$ or bleed$ or blood$)).tw.
6. ((brain or cereb$ or intracranial) adj3 aneurysm$ adj3 ruptur$).tw.
7. ((cerebral or intracranial or cerebrovascular) adj6 (vasospasm or spasm)).tw.
8. sah.tw.
9. or/1-8
10. bed rest/ or immobilization/ or rest/
11. (bed rest or bed-rest or bedrest or bed bound or bed-bound or bedbound or immobili$).tw.
12. (confined adj5 bed).tw.
13. mobilization/ or patient mobility/ or physical mobility/
14. exp physiotherapy/ or physiotherapist/ or exp rehabilitation/ or daily life activity/ or convalescence/ or "movement (physiology)"/ or exp locomotion/ or motor activity/ or exp exercise/ or exp kinesiotherapy/
15. early intervention/ or time/ or (early or earlier).tw.
16. 14 and 15
17. ((early or earlie$ or accelerat$ or immediate or fast-track or timing or rapid) adj10 (mobil$ or ambulat$ or rehab$ or physiotherapy or physical therapy or physical activity or movement or sitting or standing or walking or semi-recumb$ or out of bed)).tw.
18. (stroke unit$ or mobility protocol).tw.
19. 10 or 11 or 12 or 13 or 16 or 17 or 18
20. 9 and 19
21. subarachnoid hemorrhage/rh [Rehabilitation]
22. 20 or 21

Appendix 3. CINAHL search strategy

We used the following search strategy for CINAHL (Ebsco).

S35 .S33 or S34
S34 .(MH "Subarachnoid Hemorrhage/RH")
S33 .S13 and S32
S32 .S14 or S15 or S16 or S17 or S18 or S19 or S29 or S30 or S31
S31 .TI (stroke unit* or mobility protocol) OR AB (stroke unit* or mobility protocol)
S30 .TI ((early or earlie* or accelerat* or immediate or fast-track or timing or rapid) N10 (mobil* or ambulat* or rehab* or physiotherapy or physical therapy or physical activity or movement or sitting or standing or walking or semi-recumb* or out of bed)) OR AB ((early or earlie* or accelerat* or immediate or fast-track or timing or rapid) N10 (mobil* or ambulat* or rehab* or physiotherapy or physical therapy or physical activity or movement or sitting or standing or walking or semi-recumb* or out of bed))
S29 .S25 and S28
S28 .S26 or S27
S27 .TI (early or earlier) OR AB (early or earlier)
S26 .(MH "Time+") OR (MH "Early Intervention")
S25 .S20 or S21 or S22 or S23 or S24

S24 .(MH "Movement+")
S23 .(MH "Rehabilitation")
S22 .(MH "Physical Therapy+")
S21 .(MH "Activities of Daily Living+")
S20 .(MH "Ambulation Aids+") OR (MH "Ambulation Therapy (Saba CCC)") OR (MH "Exercise Therapy: Ambulation (Iowa NIC)") OR (MH "Ambulation: Walking (Iowa NOC)") OR (MH "Walking+")
S19 .TI confined N5 bed OR AB confined N5 bed
S18 .TI (bed rest or bed-rest or bedrest or bed bound or bed-bound or bedbound or immobili*) OR AB (bed rest or bed-rest or bedrest or bed bound or bed-bound or bedbound or immobili*)
S17 .(MH "Immobilization")
S16 .(MH "Bed Rest") OR (MH "Bed Rest Care (Iowa NIC)") OR (MH "Rest (Iowa NOC)")
S15 .(MH "Physical Mobility") OR (MH "Mobility Therapy (Saba CCC)")
S14 .(MH "Early Ambulation")
S13 .S1 or S4 or S5 or S8 or S11 or S12
S12 .TI sah OR AB sah
S11 .S9 and S10
S10 .TI (vasospasm or spasm) OR AB (vasospasm or spasm)
S9 .TI (cerebral or intracranial or cerebrovascular) OR AB (cerebral or intracranial or cerebrovascular)
S8 . S6 and S7
S7 .TI (haemorrhage* or hemorrhage* or bleed* or blood*) OR AB (haemorrhage* or hemorrhage* or bleed* or blood*)
S6 .TI (subarachnoid or arachnoid) OR AB (subarachnoid or arachnoid)
S5 .(MH "Cerebral Vasospasm")
S4 .S2 and S3
S3 .(MH "Rupture") OR "rupture" OR (MH "Rupture, Spontaneous")
S2 .(MH "Cerebral Aneurysm")
S1 .(MH "Intracranial Hemorrhage") OR (MH "Cerebral Hemorrhage") OR (MH "Subarachnoid Hemorrhage")

Appendix 4. AMED search strategy

We used the following search strategy for AMED (Ovid)

1. cerebral hemorrhage/
2. brain disease/ and hemorrhage/
3. (exp brain/ or meninges/) and aneurysm/
4. rupture/ or ruptur$.tw.
5. 3 and 4
6. ((subarachnoid or arachnoid$) adj6 (haemorrhage$ or hemorrhage$ or haematoma$ or hematoma$ or bleed$ or blood$)).tw.
7. ((brain or cereb$ or intracranial) adj3 aneurysm$ adj3 ruptur$).tw.
8. ((cerebral or intracranial or cerebrovascular) adj6 (vasospasm or spasm)).tw.
9. sah.tw.
10. 1 or 2 or 5 or 6 or 7 or 8 or 9
11. bed rest/ or immobilization/ or rest/
12. (bed rest or bed-rest or bedrest or bed bound or bed-bound or bedbound or immobili$).tw.
13. (confined adj5 bed).tw.
14. mobilisation/
15. physical therapy modalities/ or physiotherapists/ or exp exercise therapy/ or rehabilitation/ or exp locomotion/ or movement/ or motor activity/ or "activities of daily living"/
16. time/ or (early or earlier).tw.
17. 15 and 16
18. ((early or earlie$ or accelerat$ or immediate or fast-track or timing or rapid) adj10 (mobil$ or ambulat$ or rehab$ or physiotherapy or physical therapy or physical activity or movement or sitting or standing or walking or semi-recumb$ or out of bed)).tw.
19. (stroke unit$ or mobility protocol).tw.
20. 11 or 12 or 13 or 14 or 17 or 18 or 19
21. 10 and 20

CONTRIBUTIONS OF AUTHORS

Zhenxing Ma: designed the review, developed the search strategy, undertook searches, obtained copies of relevant references, appraised studies and selected trials for inclusion/exclusion, and drafted the review.

Qiuxiao Wang: designed the review, developed the search strategy, undertook searches, obtained copies of relevant references, appraised studies and selected trials for inclusion/exclusion, and drafted the review.

Zhenxing Ma and Qiuxiao Wang contributed equally to this review, and they are joint first authors.

Ming Liu: designed the review, developed the search strategy, selected trials for inclusion, and drafted the review.

The review will be updated by Zhenxing Ma and Qiuxiao Wang.

DECLARATIONS OF INTEREST

None known

INDEX TERMS

Medical Subject Headings (MeSH)

*Bed Rest [mortality]; *Early Ambulation [mortality]; Secondary Prevention; Subarachnoid Hemorrhage [mortality] [*prevention & control]; Time Factors; Treatment Outcome

MeSH check words

Humans