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ESO Guidelines on Moyamoya angiopathy

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Background

Moyamoya angiopathy (MMA): a rare condition and multiple questions

Natural Course

- Not well known
- Prognostic value of vascular and haemodynamic assessment ?
- Need of long-term imaging assessment ?

Pathogenesis

- Poorly understood
- Strong genetic component in MMD cases (RNF213)
- Prognostic value of RNF213 variants ?

Treatment

- No treatment reducing the progression of the disease
- Aspirin efficacy for reducing ischemic events (CVE) undetermined
- Lack of guidelines for cerebral revascularization surgery used to prevent clinical manifestations:
  - indication criteria ?
  - best technique of revascularization ?
  - timing for surgery ?
  - patient management in the perioperative period ?

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European Stroke Organisation (ESO) Standard Operating Procedure

- **Evidence-based recommendations** based on the GRADE evidence methodology:
  - Formulation of 9 PICO questions (imaging assessment x3, genetic x1, treatment x5)
  - Identification of main outcomes and rating of their relative importance
  - Systematic literature review for each PICO question
  - Assessment of the risk of bias
  - Grading of the quality of evidence for each question and outcome (very low - low - high)
  - Grading of the strength of recommendation (weak- strong)

- **Expert Consensus Statement**
  - When insufficient evidence to provide evidence-based recommendation
  - Secret ballot voting, Delphi method

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Expert Consensus Statement: Haemodynamic assessment

PICO 1: In patients with Moyamoya angiopathy (MMA), does haemodynamic assessment (by CT, MRI, SPECT, PET and ultrasound) compared with no haemodynamic assessment improve the identification of patients at higher risk of unfavourable outcome ?

Expert consensus statements

- **For all patients,** we suggest **performing haemodynamic assessment during the diagnostic workup** in order to help decision-making. (9/9).
- **In patients with asymptomatic MMA**, and where symptoms are not clearly associated with haemodynamic triggers, **haemodynamic assessment should be performed to identify hemispheres at risk** (9/9)
- **For patients with clear haemodynamic triggered TIAs or watershed stroke** in one cerebral artery territory, **perfusion studies should be considered** to identify other haemodynamically compromised yet asymptomatic brain territories (9/9).
- **Use imaging methods most familiar and available** depending on individual institutions. (9/9)

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Expert Consensus Statement: PCA involvement and RNF213 variants

PICO 2: In patients with MMA does the assessment of involvement of posterior circulation compared with no assessment, improve the identification of patients at higher risk of unfavourable outcome ?

Expert consensus statements

- **In children, we suggest assessment of PCA** or posterior circulation involvement to identify patients at higher risk of stroke and cognitive impairment (9/9)
- **In adults, we suggest assessment of PCA** or posterior circulation involvement to identify patients at higher risk of ischaemic or haemorrhagic stroke (9/9)

PICO 3: In patients with MMA does genetic testing of the RNF213 susceptibility variants compared with no genetic test improve the identification of patients at higher risk of unfavourable outcome ?

Expert consensus statement

- Regardless of ethnicity, **we suggest against systematic screening of RNF213** p.R4810K variant (8/10)

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Expert Consensus Statement: Antiplatelet Therapy

PICO 4: In patients with MMA, does antiplatelet therapy (any possible regimen) compared with no antiplatelet therapy reduce the risk of an unfavourable clinical outcome ?

Expert consensus statement

- **In patients with non-haemorrhagic presentation**, we suggest the **use of long-term antiplatelet therapy** to reduce the risk of embolic strokes (9/9)

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Evidence-based Recommendation: Revascularization Surgery

PICO 5: In patients with MMA, does revascularization surgery compared with no surgery reduce the risk of an unfavorable clinical outcome ?

Evidence-based Recommendation

- **In adult** patients **with haemorrhagic presentation**, we recommend **revascularization surgery** (evidence only for direct STA-MCA bypass) **in case of cerebral haemodynamic impairment and** presence of **choroidal collaterals**.

Quality of evidence: Low ⨁⨁

Strength of recommendation: Weak for intervention ↑?

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PICO 5: Evidence-based Recommendation

Revascularization Surgery in MMA adult patients with haemorrhagic stroke

- Data from **one RCT**, the JAM trial
- **80 adult patients** included
- **Combined revascularization** surgery on **both sides**
- Follow-up: 4,32 years
- **Lower rate of recurrent cerebral haemorrhage in the surgical arm (11,9% vs 31,6%**, HR: 0,36 [95% CI, 0,12-1,01])
- **Low quality of evidence:** no blinded allocation of participants, optimal size not met and limit of significance

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PICO 5: Expert Consensus Statements

Revascularization Surgery in MMA patients with ischemic stroke and in asymptomatic patients

For all patients, we suggest that **surgical revascularization is performed in a referral centre** and by a neurosurgeon with significant experience in surgical revascularization techniques (9/9).

Adult patients

- In **patients with ischaemic presentation**, we suggest **revascularization surgery in case of** clinical symptoms and/or imaging **markers of haemodynamic impairment** (9/9).
- In **asymptomatic patients**, we suggest **conservative treatment** except in patients with both cerebral haemodynamic impairment and silent ischaemic lesions in the same cerebral region (9/9).

Paediatric patients

- we suggest **revascularization surgery when evidence of** ongoing ischaemic symptoms or **cerebral haemodynamic impairment**. Vote 9/9.

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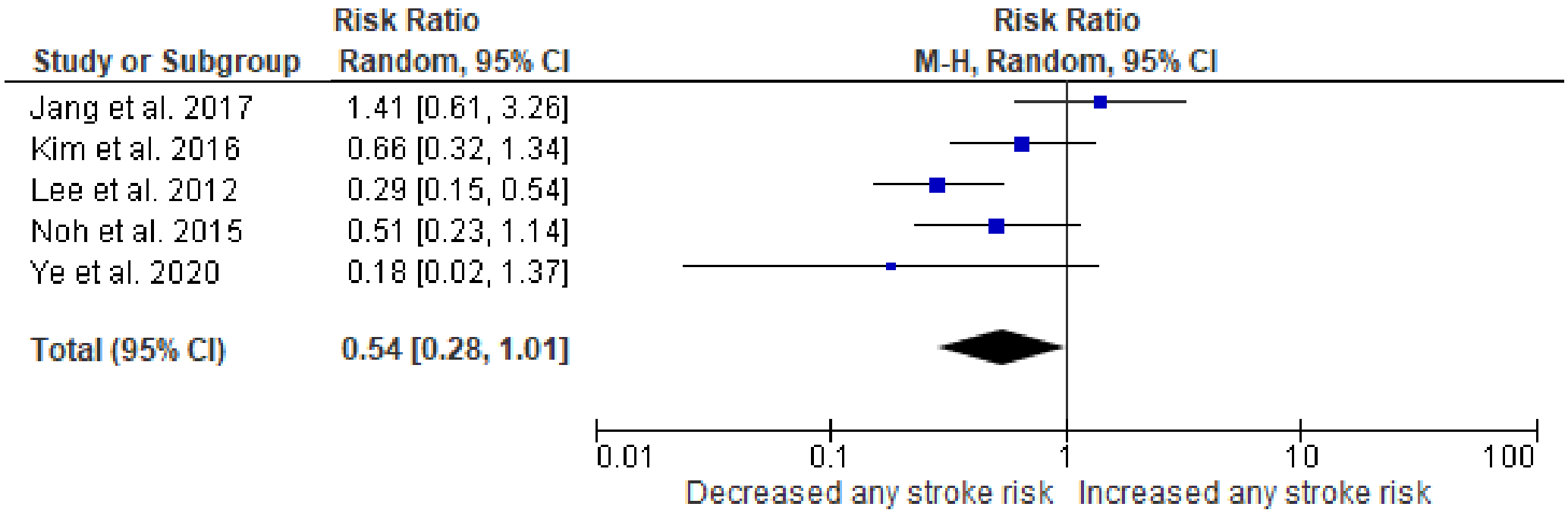
Revascularization vs conservative surgery in ischemic MMA : 5 observational studies

Meta-analysis: risk of any stroke in adult MMA patients with ischaemic presentation who underwent revascularization surgery compared to conservative care.



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Expert Consensus Statement: Revascularization Surgical Techniques

PICO 6: In patients with MMA, does direct or combined revascularization techniques compared with indirect revascularization alone reduce the risk of an unfavourable clinical outcome?

Expert Consensus Statements

Adult patients

- we suggest **direct/combined revascularization** instead of indirect strategies for reducing risk of stroke. Vote 9/9.

Paediatric patients

- we suggest **combined revascularization** instead of indirect strategies **whenever technically possible**, to decrease short term risk of stroke. Vote 9/9.

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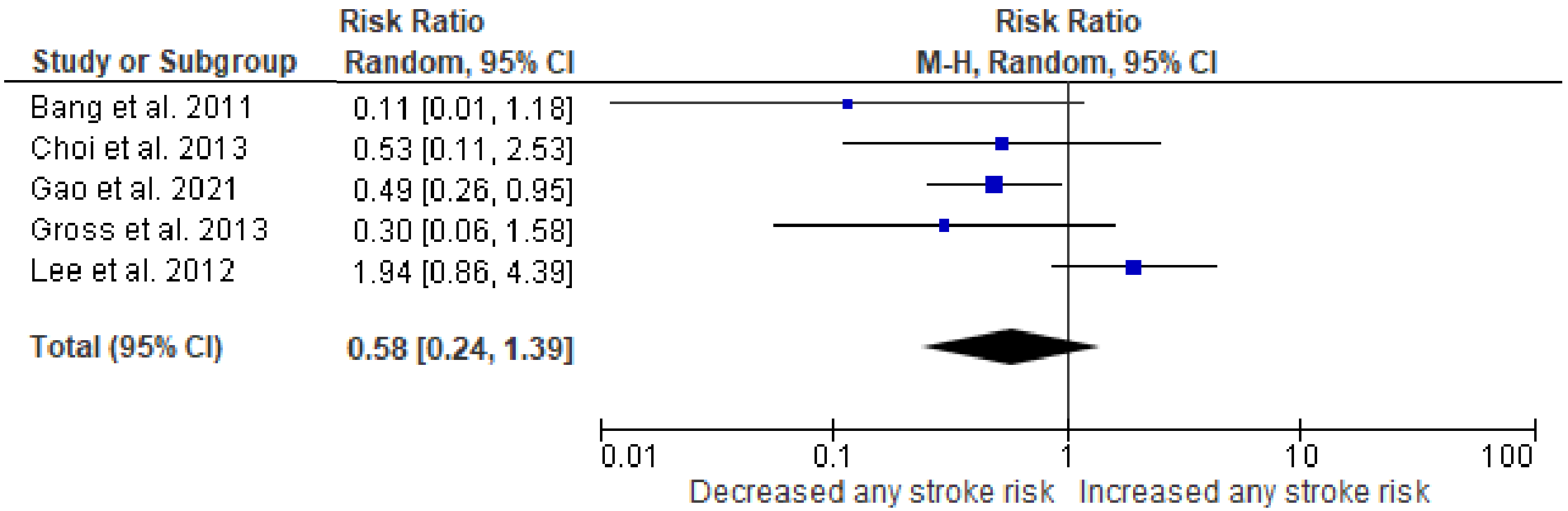
Direct/combined vs indirect revascularization in adult MMA: 5 observational studies

Meta-analysis: risk of any stroke in adult MMA patients who underwent direct or combined revascularisation surgery compared to indirect revascularization surgery



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Expert Consensus Statement: Antiplatelet continuation during surgery

PICO 7: In patients with MMA, does discontinuation compared with continuation of antiplatelet therapy during the revascularization procedure increase the risk of an unfavourable clinical outcome ?

Expert Consensus Statements

- During bypass surgery, **continuation of antiplatelet treatment as monotherapy is safe**. In case of discontinuation, we suggest restarting antiplatelet therapy 1–7 days after surgery, depending on the post-surgery CT scan (9/9)
- **In case of dual antiplatelet therapy**, we suggest **stopping the other second antiplatelet therapy**, for **7 days before surgery** (9/9)

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Expert Consensus Statement: Time interval between stroke and surgery

PICO 8: In patients with MMA, does respecting a 6- or 12-week minimum time interval from an acute cerebrovascular event to revascularization surgery compared to earlier and/or immediate surgery reduce the risk of an unfavourable clinical outcome ?

Expert Consensus Statement

- **waiting 6–12 weeks from an acute cerebrovascular event** before performing surgery to reduce the rate of postoperative complications (9/9).
- **avoid trigger factors** such as dehydration, fever, and hyperventilation as well as hypotension when waiting for surgery (9/9)
- **in children**, we suggest that **waiting for surgery** should be **balanced against the risk of further stroke** (9/9).
- **In paediatric patients**, we suggest that **early surgery** could be considered especially **for those with recurrent TIAs**, single or recurrent ischaemic **strokes with rapid and complete clinical recovery** (9/9)

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Expert Consensus Statement: Long-term follow-up

PICO 9: In patients with MMA, both after surgery and with conservative management, does long-term follow-up neuroimaging assessment compared to no follow up assessment modify the clinical practice in term of medical or surgical treatment ?

Expert Consensus Statements

- We suggest **long-term neuroimaging follow-up** to evaluate progression of angiopathy (9/9).
- In case of **unilateral MMA** and **conservatively** managed patients, **neuroimaging assessments** should be **carried out** (9/9).
- **Neuroimaging follow-up** should **include** at least **MRI-MRA** and **haemodynamic evaluation** (9/9).
- **DSA** should be performed preferentially **when** a **vascular change** is suspected and a **therapeutic decision** is to be made or when **non-invasive techniques** are **not conclusive** (9/9).
- The **timing of follow-up** assessments should be **individualized** (9/9).

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Conclusion

- **First European guideline** on the management of MMA **using GRADE methods**
- Overall **paucity of data** on diagnosis and effective treatment approach
- Mostly observational studies, **only one specific RCT was available**
- We provide:
  - **1 Evidence-based Recommendation** with ‘low quality’ of evidence on surgery
  - **9 Expert Consensus Statements**

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