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Untreated clinical course of cerebral cavernous malformations: a prospective, population-based cohort study

Dr Rustam Al-Shahi Salman FRCP ^a ... for the Scottish Audit of Intracranial Vascular Malformations (SAIVMs) collaborators ^{â€}

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Summary

Background

Cerebral cavernous malformations (CCMs) are prone to bleeding but the risk of intracranial haemorrhage and focal neurological deficits, and the factors that might predict their occurrence, are unclear. We aimed to quantify these risks and investigate whether they are affected by sex and CCM location.

Methods

We undertook a population-based study using multiple overlapping sources of case ascertainment (including a Scotland-wide collaboration of neurologists, neurosurgeons, stroke physicians, radiologists, and pathologists, as well as searches of registers of hospital discharges and death certificates) to identify definite CCM diagnoses first made in Scottish residents between 1999 and 2003, which study neuroradiologists independently validated. We used multiple sources of prospective follow-up both to identify outcome events (which were assessed by use of brain imaging, by investigators masked to potential predictive factors) and to assess adults' dependence. The primary outcome was a composite of intracranial haemorrhage or focal neurological deficits (not including epileptic seizure) that were definitely or possibly related to CCM.

Findings

139 adults had at least one definite CCM and 134 were alive at initial presentation. During 1177 person-years of follow-up (completeness 97%), for intracranial haemorrhage alone the 5-year risk of a first haemorrhage was lower than the risk of recurrent haemorrhage (2.4%, 95% CI 0.0–5.7 vs 29.5%, 4.1–55.0; $p < 0.0001$). For the primary outcome, the 5-year risk of a first event was lower than the risk of recurrence (9.3%, 3.1–15.4 vs 42.4%, 26.8–58.0; $p < 0.0001$). The annual risk of recurrence of the primary outcome declined from 19.8% (95% CI 6.1–33.4) in year 1 to 5.0% (0.0–14.8) in year 5 and was higher for women than men ($p = 0.01$) but not for adults with brainstem CCMs versus CCMs in other locations ($p = 0.17$).

Interpretation

The risk of recurrent intracranial haemorrhage or focal neurological deficit from a CCM is greater than the risk of a first event, is greater for women than for men, and declines over 5 years. This information can be used in clinical practice, but further work is needed to quantify risks precisely in the long term and to understand why women are at greater risk of recurrence than men.

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