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Association between migraine and cardiovascular mortality: Is there a temporal trend?

Dear Editor,

Given the increasing clinical value of the topic, we have revaluated, from a different methodological point of view, the meta-analysis published by Schürks et al. (1), which studied both all-cause mortality and cardiovascular mortality in patients with migraine compared with a control population.

Although some of the analyses done by Schürks et al. were hampered by the limited number of studies, the results on cardiovascular mortality were more robust (six studies for a total of 469,229 patients) and therefore merit further examination. In comparison with controls, Schürks et al. found a tendency towards increased cardiovascular mortality in patients with migraine which, however, remained far from statistical significance (pooled relative risk (RR) 1.09; 95% CI 0.89–1.32). On the other hand, subgroup gender-specific analyses indicated a slightly stronger association for women, with risk values at limits of statistical significance. Overall, these results were consistent with those of a meta-analysis published by the same authors in 2009, which was more specifically focused on the risk of ischaemic stroke (2).

When evidence-based information concerning a specific clinical or therapeutic issue covers several years or decades, there is an increasing interest in investigating temporal trends of outcomes or risk factors (3). For this reason, we re-examined the RR data published by Schürks et al. (1) to assess whether any such trend was apparent for the risk of cardiovascular mortality in patients with migraine in comparison with controls. From a methodological point of view, the values of RR reported by Schürks et al. were, in many cases, adjusted for the concomitant presence of other risk factors, and this adjustment increased the scientific value of the research. For this reason, our re-analysis was not based on crude event rates, but was directly focused on adjusted RR values (with their 95% CI) that were therefore the initial material for our statistics.

In our analysis, a fixed-effect meta-regression was undertaken in which the values of RR were the dependent variable and the calendar year was the covariate under examination. No random-effect model was adopted because the degree of homogeneity was acceptable (according to the ‘quick and dirty’ criterion of drawing a vertical line intercepting each of the 95% CI of the six studies). Our statistical methods were the same as those reported previously (3).

Our results are summarised in Figure 1. Meta-regression suggests a temporal trend towards an increase of cardiovascular mortality with time; this finding is at the limit of statistical significance ($p = 0.054$).

In conclusion, the association between migraine and cardiovascular mortality remains controversial and is limited because of the scarcity of studies and the conflicting nature of the results (e.g. those published by Schürks). In this framework, our meta-regression suggests that a temporal trend toward an increase of cardiovascular mortality with time seems to exist, or is in any case likely. Hence, answering the question of whether migraine can contribute to cardiovascular "

![Figure 1. Meta-regression analysis of temporal trends of cardiovascular mortality in patients with migraine compared with a control population. The graph shows the time-course of the relative risk for the referenced comparison. The regression equation is: $y = -111.520 + 0.0561 \times \text{YEAR}$ ($p = 0.054$); this result remained unchanged after applying the commonly used logarithmic transformation of values of relative risk. Symbols: each study is represented by a circle, the diameter of which is proportional to its statistical weight."
mortality seems to have, in perspective, a growing clinical relevance. New data are needed quite urgently to clarify this issue.

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**Conflict of interest**

None declared.

**References**


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