PRESS RELEASE

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Acute Febrile Illness, Influenza Vaccination and the Risk of Acute Stroke - The Interstroke Study

Is acute febrile illness associated with an increased risk of stroke and is influenza vaccination associated with a decreased risk of acute stroke?

INTERSTROKE is a large international case-control study to quantify the importance of risk factors for stroke in different parts of the world. Aim of this analysis was to evaluate the associations of recent acute febrile illness and influenza vaccination with a first-ever stroke worldwide. The study compromises 13,447 cases of acute first stroke and 13,472 community and hospital controls.

Acute febrile illness in the preceding four weeks of a stroke is more commonly reported by ischemic stroke patients than control subjects (8.7% versus 5.6%, adjusted OR 1·18; 95% CI 1·01-1·39). The association between acute febrile illness and ischemic stroke was strong in analyses with community controls but absent in those with hospital controls. Influenza vaccination was associated with lower odds of all stroke (adjusted odds ratio 0.53, 95% CI 0.46- 0.60), ischemic stroke (adjusted odds ratio 0.57, 95% CI 0·50-0·67) and intracerebral hemorrhage (adjusted odds ratio 0.34, 95% CI 0·25-0·46).

Study author C. Schwarzbach concluded that acute febrile illness is associated with increased odds of ischemic stroke in most parts of the world. Vaccination against influenza is associated with decreased odds of stroke after adjustment for a large number of covariates.

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Composition of PM 2.5 And Comorbidities Associated With Hemorrhagic Stroke Hospitalisation in Thailand

Particulate matter 2.5 (black carbon, organic carbon, sulfate, and dust) is associated with an increased risk of ischemic stroke. It is not clear if it is also associated with an increased risk of hemorrhagic stroke.

This study gathered data from the MERRA-2 satellite on pollutant concentrations and the Thailand universal health coverage system on hemorrhagic stroke incidence. 82,390 patients diagnosed with hemorrhagic stroke on admission were observed.

An increase of 1 mcg/m in black carbon and dust was associated with an increase in the risk of hemorrhagic stroke of 46.3% and 25.7%, respectively. Each 1 g/m increase in black carbon exposure increases the risk of hemorrhagic stroke hospitalisation in patients with diabetes or dyslipidemia: relative risk of 1.33 and 1.10, respectively. Each 1 g/m increase in dust exposure increases the risk of hemorrhagic stroke hospitalisation in patients with atrial fibrillation with a relative risk of 1.47.

The study author Kongbunkiat concluded that long-term exposure to black carbon and dust increases the risk of hemorrhagic stroke hospitalisation.

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Epigenetic age and stroke - Findings from the Health and Retirement Study

Epigenetic clocks are emerging as a novel way to measure biological ageing. Could this be used as a biomarker of stroke risk or target for intervention?

Chemical modifications to the genome - known as epigenetic changes - occur throughout life and influence the expression of our genes. DNA methylation is one such chemical modification and it is strongly correlated with chronological age.

A number of 'DNA methylation clocks' or 'epigenetic clocks' have been developed by supervised machine learning using DNA methylation data, trained against chronological age.

A study presented by Dr Natalia Szejko and colleagues examines the relationship between 'epigenetic clocks' and stroke. The study pursued the following questions: is older epigenetic age an independent risk factor for stroke, after accounting for chronological age? Are stroke survivors 'epigenetically' older compared to stroke-free persons, after accounting for chronological age?

The study evaluated 13 epigenetic clocks using data from the DNA samples of 4,018 participants enrolled in the Health and Retirement Study, a landmark study of ageing that has been longitudinally following study participants for 30-plus years in the United States. Of these participants, 342 (8.5%) went on to develop a stroke over a mean follow-up of 11 years.

The study found that an older epigenetic age was a risk factor for sustaining a stroke and that stroke survivors were epigenetically older when compared to stroke-free individuals. These associations were independent of age, sex and vascular risk factors.

These findings indicate that an older epigenomic age leads to a higher risk of stroke independently of the "observed" age and that the occurrence of a stroke accelerates epigenomic ageing independently of the "observed" age. As epigenomic data becomes more widely available, further research should evaluate the role of the epigenetic age for the same applications used for chronological age, including risk prediction tools and selection of patients for clinical trials.

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Circulating Interleukin-6 Predicts Carotid Plaque Severity, Vulnerability, And Progression in the Cardiovascular Health Study

Interleukin-6, a chemical secreted by cells of the immune system in inflammation, could be a reliable biomarker of carotid artery disease progression and a potential drug target.

Carotid atherosclerotic disease, a build-up of plaque in the wall of the carotid arteries that supply blood to the brain, is a major cause of ischaemic stroke. An analysis of the Cardiovascular Health Study presented today at the ESO conference added more evidence to the clinical relevance of interleukin-6 (IL-6) as a marker of plaque vulnerability and progression. The study also identified an IL-6 level cut-off that might be useful for the selection of patients who would benefit from specific anti-IL-6 treatments.

The study presented by Dr Kamtchum, from the University of Alberta, analysed data from almost 4500 patients, including their circulating IL-6 levels at baseline and the duplex ultrasound assessment of their carotid disease and plaque features at baseline and at 5-year follow-up. 29% of the patients showed plaque vulnerability at baseline, defined as irregular, ulcerated or echolucent plaques. 34% of the patients showed plaque progression at 5 years, measured using a standardised scoring system–NASCET for carotid narrowing (one or more points increase = plaque progression).

Taking into account the conventional risk factors for atherosclerosis, IL-6 level was found to be linked to plaque severity, vulnerability and progression. The authors also identified a cut-off level for IL-6, at 2.0 pg/mL, that helped to correctly classify the plaque progression status in >70% of the patients.

This study shows that assessing IL-6 levels may be useful in identifying patients at high risk of atherosclerotic disease progression. IL-6 is a cytokine released in inflammation. The results highlight inflammation as a key contributor to the risk of atherosclerosis progression independent of abnormal lipid levels and other classical cardiovascular risk factors. For decades, lowering lipid levels and controlling classical cardiovascular risk factors have been the mainstay of managing carotid atherosclerosis. This study provides evidence to support the evaluation of anti-IL-6 treatments as adjuvant stroke prevention strategies in clinical trials of patients with carotid atherosclerosis. Furthermore, the proposed cut-off IL-6 level could be used to decide which patients to include in these trials.

Anti-IL-6 drugs have the potential to offer novel treatments for patients with a high risk of stroke from carotid atherosclerosis, who are not eligible for carotid surgery e.g., patients with multiple health conditions, mild or moderate carotid artery stenosis with high-risk plaque features on imaging.

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Stroke in the Young: Cancer in Disguise?

Stroke in young people may be associated with an increased likelihood of subsequent cancer diagnosis.

The risk of being diagnosed with a new cancer in the follow-up of patients with a first-ever stroke is particularly increased in patients younger than 50 years, while this risk is similar to that of the general population in older patients, according to a study presented today at the ESO conference.

Researchers from the Radboud University Medical Centre (Netherlands) investigated the risk of receiving a cancer diagnosis in the following years after a stroke compared to the general population. They analysed the risk of incident cancer in a group of 389,398 patients with a first-ever ischaemic stroke or intracerebral haemorrhage (ICH) included in the Dutch Population Registry and national Hospital Discharge Registry from 1998 to 2019. The data were compared to matched peers from the general population. The main outcome measures were cumulative incidence of first-ever cancer after stroke, stratified by stroke subtype, age and sex, and standardised incidence rates (SIR).

The study included 27,616 patients aged 15-49 years and 362,782 patients ≥50 years old. The cumulative incidence of any cancer at ten years was 3.7% (95% CI: 3.4-4.0) in the younger and 8.5% (95% CI: 8.4-8.6%) in the older age group.

The risk of cancer was higher in the younger age group when compared to the matched general population. In this age group, the one-year risk of any new cancer was 2.6 times higher (SIR; 95% CI: 2.2-3.1) after ischaemic stroke and 5.4 times (SIR; 95% CI: 3.8-7.3) after ICH compared to matched peers from the general population. In contrast, in patients older than 50, the one-year risk of any new cancer was 1.2 times higher (SIR; 95% CI: 1.2-1.2) after ischemic stroke and 1.2 times (95% CI 1.1-1.2) after ICH.

The study highlights the increased risk of cancer after an ischaemic stroke or ICH in younger patients, which may indicate the possible relevance of stroke as the first manifestation of an already present but occult cancer.

Drs Jamie Verhoeven, who presented the results, commented: “We have proven a temporal association between a first-ever stroke and a subsequent first-ever cancer diagnosis, which is most evident in younger patients. This can be explained in two ways. First, is that the cancer diagnoses made in the first year after stroke represented cancers that were already active (occult) at the time of stroke and may very well be causally related with the stroke.”

“A second explanation is that cancer and stroke share risk factors. However, in my opinion, this does not fully explain the difference in increased risks between young and older patients. It does not fully explain why the risk of cancer is specifically higher in the first 1-2 years after the stroke diagnosis. I would think if it was just shared risk factors, the risk-increase should remain relatively stable (or even increase due to the build-up of exposure to risk factors) over the years”.

She added: “For the diagnostic work-up in young stroke patients it would be very interesting to see whether we can identify the patients who are most likely to have or develop a new cancer after stroke. We are currently working on this with a large clinical dataset of around 2000 patients. If we can identify certain characteristics of young stroke patients, the next step would be to investigate whether there would be effective screening possibilities”.

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