Kent DM, Ruthazer R, Weimar C, et al. An index to identify stroke-related vs incidental patent foramen ovale in cryptogenic stroke. *Neurology.* 2013;81:619–625. Paradoxical embolism via a patent foramen ovale (PFO) is a common cause of cryptogenic stroke. Because PFO is a common anatomic variant seen in 25% of the general population, clinicians are faced with the dilemma of whether a PFO is an incidental finding or stroke related. Recent clinical trials of PFO closure failed to show a benefit of closure compared with medical therapy in reducing composite primary end points. Yet, these trials may have enrolled individuals with incidental PFO.

To derive a prediction instrument to stratify patients by attributable fraction (probability that the index event was related to PFO), Kent et al performed a patient-level meta-analysis of observational cohorts of patients with cryptogenic stroke investigated for PFO by transesophageal echocardiogram or transcranial Doppler (n=3023). The patients with cryptogenic stroke with PFO were younger, less likely to have conventional risk factors or a history of transient ischemic stroke (TIA)/stroke and more likely to have large superficial infarcts than those without PFO. Multivariable logistic regression revealed that the odds of PFO presence was lower with older age, diabetes mellitus, hypertension, hypercholesterolemia, smoking, and presence of TIA. On the basis of odds ratios (ORs) of these variables, they developed the risk of paradoxical embolism (RoPE) point score, a 10-point index, assigning 1 point for each of the following: absence of diabetes mellitus, hypertension, smoking, and previous stroke/TIA, and the presence of cortical stroke. Each decade under 70 years was assigned 1 point (5 points for those <30 years). Observed PFO prevalence ranged from 12% (0–1 point) to 82% (10 points). Among 1324 individuals with PFO with follow-up data available, recurrence rates decreased as RoPE score increased, suggesting that individuals with strokes likely to be PFO attributable were least likely to experience recurrent stroke/TIA.

This study has important clinical and research implications. The RoPE score can be a useful tool for estimating the likelihood that the observed PFO is stroke related. It can aid in deciding whether hypercoagulable laboratory studies and imaging for lower extremity and pelvic deep venous thrombosis are warranted. The RoPE score can also assist in predicting risk of recurrent cerebrovascular events. Finally, it might be useful in identifying patient populations most suitable for future PFO closure trials.

Because of the study’s limitations, the results should be interpreted with caution. The component cohorts of this meta-analysis had varying methods of detecting PFO, variable definitions of cryptogenic stroke, and some had unblinded echocardiogram interpretation and adjudication of outcomes. Second, echocardiographic information (such as shunt volume, shunting at rest, and atrial septal aneurysm) and clinical data (such as venous thrombosis, Valsalva at onset of stroke, and hypercoagulability) were not available in all cohorts. Finally, the index has not been validated in other cohorts.

Imfeld P, Bodmer M, Schuerch M, et al. Risk of incident stroke in patients with Alzheimer disease or vascular dementia. *Neurology.* 2013;81:910–919. Population studies suggest that individuals with dementia have a higher risk of stroke than those without dementia; however, these studies did not distinguish between vascular dementia (VD) and Alzheimer disease (AD). To assess the risk of stroke or TIA in patients with AD and VD, Imfeld et al conducted a follow-up study with a nested case-control analysis using the UK-based General Practice Research Database. They followed 6443 individuals with AD, 2302 individuals with VD, and 9984 dementia-free matched comparison subjects for a median of 1.7 years and assessed crude incidence rates and relative risk estimates, adjusting for demographics, comorbidities, and medication use.

Compared with those without dementia, VD subjects were more likely to have an ischemic stroke (adjusted OR, 2.6; 95% confidence interval [CI], 1.7–3.9), hemorrhagic stroke (adjusted OR, 4.2; 95% CI, 2.3–7.5), and TIA (adjusted OR, 1.8; 95% CI, 1.3–2.6), and those with AD had a higher risk of hemorrhagic stroke (adjusted OR, 1.7; 95% CI, 1.1–2.7) and TIA (adjusted OR, 1.4; 95% CI, 1.1–1.8).

These findings are consistent with prior studies showing higher stroke rates among individuals with dementia. The higher stroke rate among individuals with VD is perhaps not surprising because by definition VD is associated with cerebrovascular disease. The lack of an association between AD and ischemic stroke contrasts with a population study in Taiwan1 that showed that individuals with AD had a higher risk of ischemic stroke than those without AD (adjusted hazard ratio, 1.7; 95% CI, 1.4–2.0). The disparate findings could be due to differences in methodology (such as classification of dementia, ascertainment of vascular events, and covariates in multivariable analysis) or patient population.

This study is the first to compare risk of TIA and stroke in individuals with AD versus VD. Strengths include the
use of a large and well-established primary-care database that is representative of the UK population with respect to age, sex, geographic distribution, use of a validated algorithm for identifying AD and VD, and adjustment for numerous clinical variables. Limitations include possible misclassification of AD and VD, potential errors in stroke/TIA ascertainment, lack of race/ethnicity data, and absence of information on dementia severity, radiographic characteristics, and APOE genotype. Further studies in more diverse patient populations with rigorous classification of AD, VD, and ascertainment of vascular events are necessary to better understand the association among AD, VD, and TIA/stroke risk.

Reference