Genetic testing for stroke will soon be clinically relevant

No; Hugh Markus, UK.

There are a number of rare causes of stroke resulting from single gene disorders. The most common of these is Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy (CADASIL). In such cases a diagnosis can be made reliably from genetic testing, and most individuals with a NOTCH3 mutation causing, for example, will develop features of the disease during their lifetime. In such cases genetic testing is very important both to make a diagnosis, and also to offer presymptomatic testing to family members. This may be particularly relevant if family members are planning to have children and would like to consider prenatal testing.

However these causes are rare and genetic factors are much more important, on a population basis, for multifactorial stroke. Epidemiological studies, and more recently techniques estimating heritability from genome-wide association study (GWAS) data, have shown that genetic factors are important in common stroke. GWAS analyses have identified a number of genetic associations for stroke and strikingly almost all of these are associated with specific stroke subtypes (i.e. for ischaemic stroke, large artery disease or cadioembolic stroke).

It has been suggested that genotyping for these variants could be useful in predicting stroke risk in individuals. Indeed a few years ago some commercial companies were offering risk prediction using genotyping for patients with a variety of complex diseases including cardiovascular disease.

However currently this is not useful to the individual patient, and indeed this led to the FDA stopping companies from advertising these services. The reason it is not useful is that each genetic variant accounts for only a small amount of increased risk. The odds ratios are usually between 1.1 and 1.2, i.e. they cause an extra 10% or 20% increase in risk. By studying sibling relative risk (an epidemiological measure of how genetic stroke is) one can work out how many variants with an odds ratio of about 1.1 to 1.2 account for the observed heritability of stroke. This comes to about 100-200. Currently we have only described only about 8 risk variants for ischaemic stroke. This means that even if we genotype these 8 variants we are only accounting for a very small proportion of overall stroke risk. Essentially the amount we can account for is so small that it does not serve any useful predictive use. Indeed it could be misleading in giving patients a full sense of reassurance.

There are other issues which include whether patients would really want this information, and whether giving patients this information would have a useful effect on lifestyle measures to reduce stroke risk.