Genes in prevention: Hopes and doubts

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At present almost every month there are papers reporting the discovery of new genetic variants that affect the risk of coronary artery disease and heart attacks. This is a truly exciting time for both researchers and clinicians interested in understanding the genetic basis of heart disease. The findings will undoubtedly lead to new biological insights into the mechanisms that cause heart attacks which in turn may result in the future new types of treatments. Will this new genetic information be useful in preventing heart attacks and if so how?

There are three things to know about the genetic variants that are being discovered that affect risk of heart attacks:

- There are many of them (13 have been discovered so far but the numbers probably run into several dozen)
- Each risk variant increases risk by between 10-30% (i.e. the same as smoking a few cigarettes a day)
- Risk variants are common (i.e. many people carry them)

We can consider the prevention potential of these discoveries at two levels: the population and the individual.

At the population level, the amount of risk associated with each variant and the fact that they are common, means that they could become very useful parts of prevention algorithms. For example, if one were to take

10 such risk variants, then at a population level, subjects carrying more than seven such variants may have risk more than two-fold higher than those carrying less than three variants. One can therefore envisage a situation soon where testing individuals for a panel of such risk variants could add to risk assessment and influence decisions about whether to initiate primary prevention treatments such as statins. There is an urgent need for clinical trials to examine this potential benefit.

At the individual level, however, the situation is more complex. Returning back to Mr X, knowing whether he carries a risk variant at one gene (or even a panel of genes) is not sufficient. His overall genetic risk will be determined by the proportion of risk variants he carries within ALL the genes that affect risk of heart attacks (and we do not even know them all yet). This is illustrated by imagining the genes that affect heart attack risk as individual cards in a pack of cards. Just knowing about whether you have a "bad" version of only some of the cards is not enough to judge the full quality of your hand. You need to know about all of them, before you can make an accurate individual prediction and whether you have a "good hand" or a "bad hand".

Recent progress in identifying genes that affect risk of heart attacks is revolutionising our understanding the mechanisms of heart attacks. Incorporating this new knowledge into risk prediction algorithms could help to refine targeting of primary prevention measures at a population level and make it more cost-efficient. This needs to be urgently tested in clinical trials. However, at an individual level, our current knowledge of genes for heart attacks is not sufficient to provide accurate prediction.

Source: European Society of Cardiology (news : web)