Excessive increase in heart rate before exercise doubles risk of sudden cardiac death in later life

April 29 2009

French researchers have discovered a simple and cheap method of predicting who is at greater risk of dying suddenly and unexpectedly from a heart attack.

In a study of 7746 French male civil servants, published in Europe's leading cardiology journal, the *European Heart Journal* today (Wednesday 29 April), the researchers found that men whose heart rate increased the most during mild mental stress just before an exercise test had twice the risk of dying of a sudden heart attack in later life than men whose heart rate did not increase as much. The study is the first to discover this association and since taking a patient's pulse is an easy and inexpensive procedure, it suggests a way of identifying people who may be at increased risk.

Professor Xavier Jouven, of the Hopital Européen Georges Pompidou (Paris, France), who led the research, said the findings have significant clinical implications. "People who showed a higher heart rate increase with mild mental stress could be considered for additional investigations and for tailored preventive strategies, aimed in the first place at reducing the probability of heart disease," he said.

Sudden death from heart attack is a major public health problem, accounting for between 200,000-400,000 deaths each year in the USA alone (population of about 306 million). In the 27 EU countries it

accounts for about 486,000 deaths in a population of 497 million. Less than five per cent of people suffering a heart attack are successfully resuscitated, and so being able to identify early on those who are at greatest risk in a general and apparently healthy population would be a big step forward in preventing some of these deaths.

Prof Jouven and his colleagues examined data from the Paris Prospective Study 1 of 7746 Frenchmen, aged 42-53, employed by the Paris Civil Service as policemen. The men were given health examinations between 1967-1972, including electrocardiograms and physical examinations. Their resting heart rate was measured, and then it was measured in the few minutes just before they took part in a bicycle exercise test, while they were sitting on the bike; this was the time when the researchers considered the men to be under mild mental stress in preparation for the exercise stress test. Their heart rate was measured during the exercise and afterwards during the recovery period.

During an average 23 years of follow-up there were 1516 deaths including 81 sudden deaths as a result of a heart attack. The risk of sudden death from a heart attack increased with an increase in heart rate during mild mental stress. After adjusting for confounding factors such as smoking, age, weight, physical exercise, cholesterol levels and diabetes, the researchers found that men who had the highest increase in heart rate during mild mental stress (increasing by more than 12 beats a minute) had twice the risk of death compared to men who had the lowest increase in heart rate (an increase of less than four beats a minute).

Conversely, men who had the highest increase in heart rate during the exercise test itself, had less than half the risk of sudden death compared with the men whose heart rate increased the least during the exercise test.

Further analysis showed that, in fact, there were no sudden deaths from

heart attack amongst the 440 men who increased their heart rate the least during mild mental stress and the most during the exercise test. On the other hand, the highest proportion of sudden deaths were among the men who increased their heart rate the most during mild mental stress and the least during exercise - 14 out of 471 men. In addition, the researchers found that the risk of dying suddenly from a heart attack was influenced strongly by genetic predisposition: the risk of sudden death increased nearly three-fold in men whose mothers had died suddenly, and nearly ten-fold when both parents had died suddenly, compared to men with parents who had not died in this way.

Prof Jouven said: "This study shows that the heart rate increase during a mild mental stress in preparation for exercise is a strong predictor of sudden death. These findings may carry significant clinical implications. Few measurements in medicine are as inexpensive and as easy to obtain in large general populations as to measure the heart rate difference between resting and being ready to perform an exercise test. Taking a person's pulse has been part of clinical examinations for thousands of years - the Chinese carried it out, for instance - and now our study shows it can be used as a prognostic marker. The results will contribute towards a better understanding of the mechanisms of cardiac death."

Prof Jouven and his colleagues believe that the mechanism behind this effect has to do with interaction between the vagus nerves (which are an important part of the autonomic nervous system that controls the body's unconscious functions such as the heart beat) and sympathetic activation (activation of the sympathetic nervous system, which is one half of the autonomic nervous system and is responsible for increasing the heart rate, widening blood vessels in the muscles and constricting them in the skin and intestines).

"There is a balance between the accelerator (sympathetic activation) and the brake (vagal activation). If vagal withdrawal occurs it is like

releasing the brake. During an ischaemic episode, when blood flow to the heart is reduced, sympathetic activation occurs to counteract it. However, if there is no protection by the vagal tone (the brake), the activation can become uncontrolled and then it becomes dangerous. Our underlying assumption, which this study appears to have proved correct, is that the faster the vagal withdrawal in response to mental stress, the greater will be - during an ischaemic episode - the damaging effect of sympathetic activation unopposed by vagal activity," he explained.

The researchers say that, as the study was carried out in men only, it is possible that findings in women may be different and this should be the subject of future research.

More information: "Excessive heart rate increase during mild mental stress in preparation for exercise predicts sudden death in the general population". *European Heart Journa*l. doi:10.1093/eurheartj/ehp160.

Source: European Society of Cardiology (news : web)