

High testosterone levels could play a role in serious heart conditions

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Ball-and-stick model of the testosterone molecule, $C_{19}H_{28}O_2$, as found in the crystal structure of testosterone monohydrate. Credit: Ben Mills/Wikipedia

Having a genetic predisposition to high testosterone levels could play a role in the development of major heart problems in men, such as blood clots and heart failure, finds a study published by *The BMJ* today.



The findings may also have implications for men who take testosterone supplements to boost energy levels and sex drive.

Some evidence suggests that genetically predicted ("endogenous") testosterone is positively associated with heart disease and stroke, especially in men. It is not clear whether testosterone has a causal role in the development of <u>heart disease</u>, but this is an important question for <u>public health</u> and regulators.

So an international research team, led by Professor Mary Schooling at the City University of New York's Graduate School of Public Health & Health Policy and the University of Hong Kong, set out to assess the effect of endogenous testosterone on major blood clots, <u>heart failure</u>, and heart attacks.

Using a technique called mendelian randomisation, they analysed genetic variants that predict testosterone levels and their associations with blood clots (thromboembolism), heart failure and <u>heart attack</u> (<u>myocardial</u> <u>infarction</u>) in almost 400,000 men and women from a large genome study and the UK Biobank database.

Participants were aged 40 to 75 years and most were of British or European ancestry. Heart conditions were identified from self-reports, hospital and death records, and results were validated using data from another large genome study.

Analysing genetic information in this way avoids some of the problems that afflict traditional observational studies, making the results less prone to unmeasured (confounding) factors, and therefore more likely to be reliable.

An association that is observed using mendelian randomisation therefore strengthens the inference of a causal relationship.



The researchers found that in men, endogenous testosterone was associated with a higher risk of <u>blood clots</u> and heart failure, but not heart attack. In the validation study, endogenous testosterone was also associated with a higher risk of heart attack. Associations were less obvious in women.

The researchers point to some study limitations. For example, UK Biobank participants tend to be more highly educated and have healthier lifestyles compared with the general population, which may have affected the results.

Nevertheless, they say these findings extend and complement previous findings, and suggest that endogenous testosterone "is detrimental for thromboembolism, heart failure, and myocardial infarction, especially in men."

They say further evidence is needed to clarify whether these findings are relevant to the higher rates of these diseases in men than in women, and suggest it might be worth considering whether existing treatments that lower testosterone could help protect against these conditions.

More information: Association of genetically predicted testosterone with thromboembolism, heart failure, and myocardial infarction: mendelian randomisation study in UK Biobank *BMJ* (2019). DOI: 10.1136/bmj.l476, www.bmj.com/content/364/bmj.l476

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