Novel tests for early detection and prevention of cardiovascular disease

Professor Jay Cohn, University of Minnesota Medical School, has successfully shown that disease score, calculated from 10 non-invasive and non-radiological tests, can be used to detect cardiovascular disease in its early stages. This has the potential to prevent the progression of cardiovascular disease and suggests that a combined approach, using disease score and cardiovascular risk factors, may be the most effective strategy to identify high-risk individuals for intervention with preventive therapy.

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Cardiovascular disease (CVD), or heart disease, is the leading cause of death in the United States. In the pre-COVID days, CVD caused about one in every three deaths in Americans, with one person dying every 36 seconds. CVD is characterised by changes in the arteries and heart that eventually lead to cardiovascular events, such as heart attacks, heart failure or strokes. Some of these illnesses are caused by a build-up of fatty deposits in the arteries which narrow or block them and increase the risk of blood clots and disrupted blood flow through these vessels. As changes to the arteries and heart progress, there is an increased risk of these acute illnesses, often referred to as cardiovascular morbid events (CVMEs).

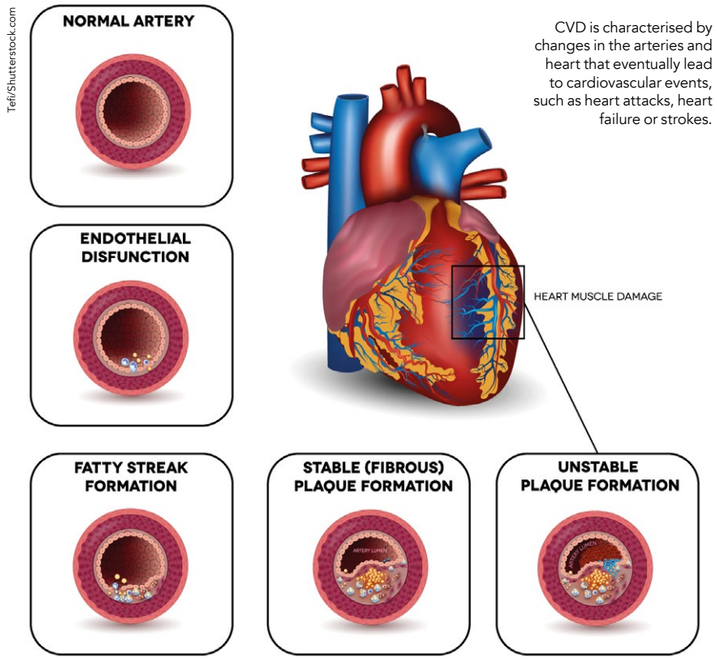
Diet and lifestyle changes are often recommended to prevent CVMEs but only smoking cessation in smokers has proved to be effective. Diet and exercise are often promoted, but no well-designed and well-conducted prospective studies have been able to document or quantitate effectiveness. What has worked to prevent CVME are drugs aimed at lowering an elevated blood pressure or reducing a high cholesterol level, markers that are called risk factors. But most CVME occur in individuals who do not have elevated risk factor levels. These at-risk individuals go untreated and continue to have CVME that shorten their life expectancy. In order to use these and other potential therapies more effectively, it is vital to identify individuals at risk of developing CVD long before it becomes symptomatic. Abnormalities of the arteries and heart can be detected long before the CVME. These abnormalities are a powerful target for therapy whether the individual has elevated risk factors or not.

Most studies of therapy involve people with advanced cardiovascular disease rather than focusing on asymptomatic individuals with early vascular and cardiac abnormalities. This approach excludes the possibility that there may be more benefit to the cardiovascular system if the biological processes behind CVD are evaluated, not just more general risk factors. Indeed, screening processes for early detection of other diseases, such as cancer, are already commonplace.

RISK FACTORS FOR CARDIOVASCULAR DISEASE

There are already existing guidelines that advocate the identification and treatment of risk factors linked to CVD, including high blood pressure, high cholesterol, obesity, smoking and sedentary behaviour. On the other hand, many individuals who develop CVD do not meet these criteria and have no pre-existing risk factors.

The aim of Prof Jay Cohn's work at the University of Minnesota Medical School is to develop ways in which early CVD changes in the heart and arteries could be identified and treated in order to intervene early and prevent progression into more advanced CVD. This represents a paradigm shift away from identification of risk factors and towards treatment of early disease to prevent disease progression to CVMEs. Instigating preventative therapies in early disease may be effective in delaying CVMEs until much later in life.



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SLOWING PROGRESSION OF CARDIOVASCULAR DISEASE

Prof Cohn and his colleagues were able to utilise ten existing simple, non-invasive and non-radiological tests. These tests can be used to assess the structure and function of large and small arteries, as well as the heart itself. Their studies of asymptomatic individuals with an average age of less than 50 years showed that the level of abnormalities seen through these tests was directly related to the risk of experiencing future episodes of disease.

Testing someone at regular intervals, for example every year or even every 5 years, provides the opportunity to monitor disease progression, to quantify the efficacy of existing drugs and to potentially monitor the effects of new, emerging drugs. This personalised approach can more accurately identify and monitor early changes to the cardiovascular system. Thus, CVD is detected and treated earlier, thereby reducing disease progression and the chance of developing future complications.

ASSESSMENT OF RISK OF CARDIOVASCULAR DISEASE

Prof Cohn's most recent work focused on the predictive value of non-invasive tests – tests that do not require entry below the skin. The study utilised the tests done by the M Health Fairview Rasmussen Center for Cardiovascular Disease Prevention, who routinely carry out an assessment that lasts 60 minutes and includes a non-radiological assessment of the function and structure of arteries and the heart. This provides a guide to the level of disease present, if any, and therefore the likelihood of experiencing a CVME.

Preliminary work had already shown a relationship between the disease score and future CVMEs, but this only equated to 35 CVMEs over an average follow-up of three years. Prof Cohn's study expanded on this by exploring the same relationship in a larger population, over a longer time period.

The study recruited 1,900 participants who had no symptoms of CVD or prior CVMEs and had been conducted between 2000 and 2013. Three target organs – large arteries, small microscopic branches of these arteries, and the pumping chamber of the heart – were assessed for signs of disease, as changes in these areas were assumed to be the cause of most CVMEs Although there was no formal follow-up

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The researchers utilise ten non-invasive tests on asymptomatic individuals with an average age below 50.

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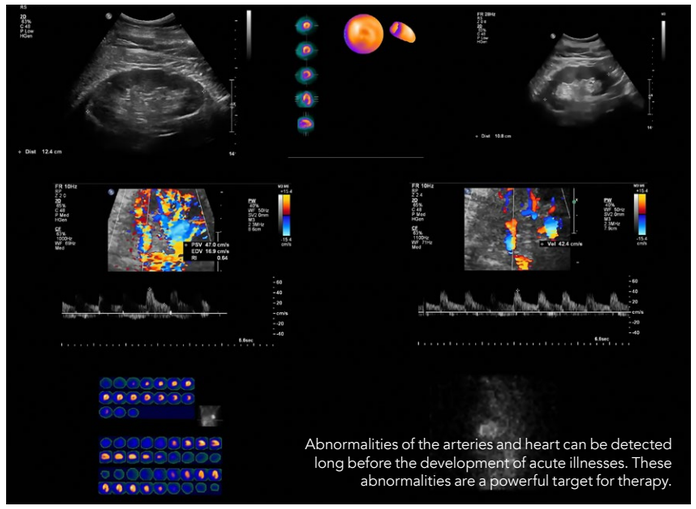

Abnormalities of the arteries and heart can be detected long before the development of acute illnesses. These abnormalities are a powerful target for therapy.

This represents a paradigm shift away from identification of risk factors and towards treatment of early disease to prevent disease progression to CVMEs.

protocol, participants were encouraged to return for repeat testing at 1- to 5-year intervals. Of the 1,900 subjects, the researchers were able to calculate CVMEs for over 75% of participants.

The ten tests include a range of blood pressure measurements, an assessment of stiffness of the arteries, a urine test to detect protein leaking from the kidney, an ultrasound scan of the arteries and heart, an electrocardiogram to detect abnormalities of the heart and a blood test to detect stress on the heart muscle. The major advantages of this combination of tests is that (apart from a single blood test), they are non-invasive, do not use radiation and can be undertaken by a single healthcare professional in the space of an hour.

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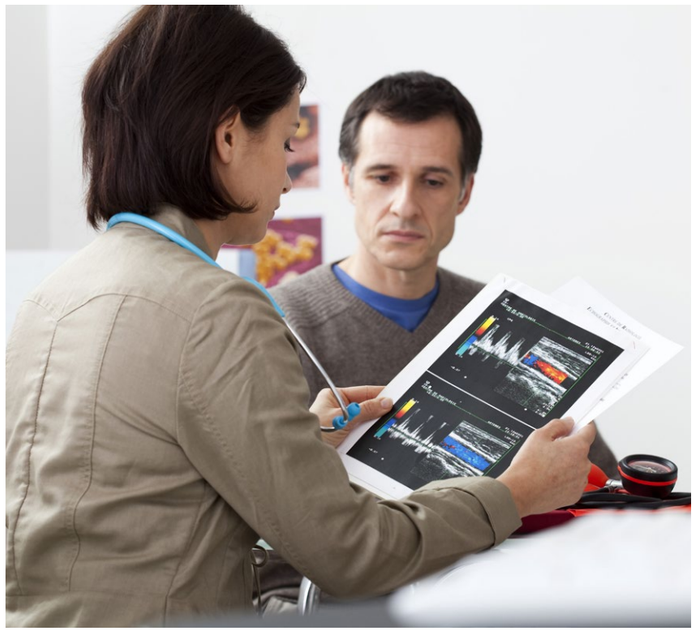

Participants of the study were encouraged to return for repeat testing at 1- to 5-year intervals.

For each individual, a disease score was calculated based on the results of the ten tests. The results showed that those with the lowest disease scores experienced 0.16 cardiovascular events per 100 patient-years (the number of events divided by the number of years the patients were in the study), whereas this increased to 1.3 events in those with the highest disease scores, suggesting that early identification of disease and effective treatment to slow its progression could translate into fewer cardiovascular events in the future.

Interestingly, when the researchers used statistical analyses to determine which components of the disease score were most powerfully associated with CVMEs, rest and exercise blood pressure and small artery stiffness were the most reliable predictors. Sex and cholesterol levels were not related to the disease score, in contrast to existing assumption that men and those with high cholesterol levels are at higher risk.

There were some limitations to the study. Participants chose to opt into the study, biasing recruitment to those who are concerned about their health. Therefore, Prof Cohn aims to replicate the findings of this study in a more diverse population.

PREVENTION OF CARDIOVASCULAR DISEASE

Prof Cohn also recommends that larger and longer studies are required to further investigate the best approach to reducing death from CVD, whether this be the identification of risk factors, signs of early-onset disease, or a combination of both. For example, this could include the disease score in addition to the Framingham risk score. The Framingham risk score is the chance of experiencing a CVD event over the next 10 years and is based on CVD risk factors rather than tests of organ structure and function.

Behind the Research

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Research Objectives

Prof Cohn has developed ten non-invasive and non-radiological tests for early cardiovascular disease detection.

Detail

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Bio

Jay N. Cohn, M.D. is Professor Emeritus of Medicine and former Director of the Cardiovascular Division and Director of the M Health Fairview Rasmussen Center for Cardiovascular Disease Prevention.

Funding

University of Minnesota Medical School

Collaborators

Colleagues who provide patient care and research services to the M Health Fairview Rasmussen Center

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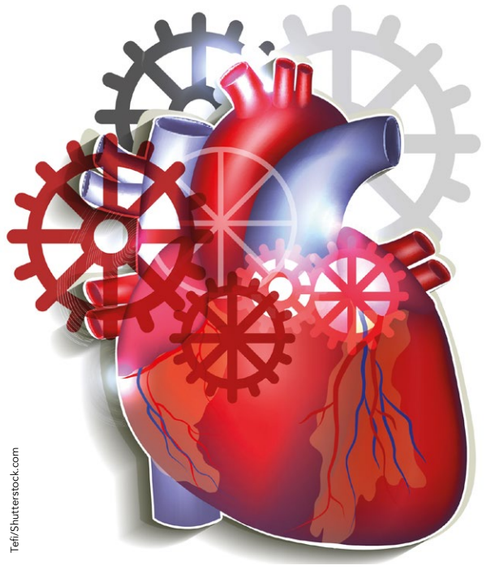

References

Duprez, D.A., Duval, S., Hoke, L., Florea, N., Grandits, G., Carlson, C., Lee, J., & Cohn, J.N. (2020). Early cardiovascular structural and functional abnormalities as a guide to future morbid events. *European journal of preventive cardiology,* 2047487320901416. Advance online publication.

Personal Response

Are the ten tests more cost effective than the existing approach based on identification of CVD risk factors?

"Drugs that lower blood pressure and LDL cholesterol are currently the most effective interventions we have to prevent cardiovascular morbid events. The problem is that we usually confine prescriptions for these drugs to those with levels of blood pressure and cholesterol above some arbitrary threshold, even though most morbid events occur in individuals with values below those thresholds. Finding early disease in the arteries and heart appears to be a more effective way to identify those at risk and provides the opportunity to track the effectiveness of therapy. The cost-effectiveness of this approach to prolonging symptom-free life expectancy needs to be established in larger populations."

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