JACC: CNIC researchers explain how high blood pressure, the most important cause of disease worldwide, accelerates atherosclerosis

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High blood pressure, the most important cause of disease worldwide, accelerates atherosclerosis but the mechanism is unknown. Using gene modified minipigs, researchers from the Centro Nacional de Investigaciones Cardiovasculares (CNIC) and Aarhus University (Denmark), demonstrate that **high blood pressure alters the structure of arteries leading to more accumulation of LDL cholesterol and faster development of atherosclerosis**. The study has been published in The Journal of the American College of Cardiology (JACC).

Blood pressure-lowering drugs are routinely used to prevent the development of atherosclerosis and

heart disease, but the mechanism of this effect is still unknown. People suffering from high blood pressure (hypertension) often have accompanying changes in the hormones that control blood pressure and it has been unclear whether the pressure itself or the hormonal changes are the driver of accelerated atherosclerosis.

To investigate this, researchers from the CNIC and Aarhus University analyzed the development of atherosclerosis in minipigs that were genetically engineered to have high blood cholesterol and develop atherosclerosis.

Minipigs have arteries that are very similar in structure to human arteries and like humans they develop atherosclerosis in the heart when exposed to high blood cholesterol, Dr. Jacob Fog Bentzon comments, coordinator of the study published in JACC. As is also the case in humans, the development of the early stages of the disease is asymptomatic and therefore experiments on atherosclerosis can be conducted in minipigs with high animal welfare.

By manipulating blood pressure in the pigs and by analyzing the effects on arteries in the heart, the researchers found that the direct forces of pressure on arteries leads to structural changes that facilitate the development of atherosclerosis. “Arteries become denser and allow less passage of molecules from the blood. This includes the LDL particles that carry blood cholesterol, which instead accumulate in the innermost layer of arteries, where they drive the development of atherosclerosis”, Dr. Jacob Fog Bentzon explains.

This finding uncovers an intimate relationship between the most important risk factors for atherosclerosis, LDL cholesterol and high blood pressure. While it has been known for decades that accumulation of LDL particles in arteries lead to atherosclerosis, the new research shows that high blood pressure accelerates the accumulation of LDL. Therefore, high blood pressure aggravates the effect of having high LDL cholesterol in the blood.

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The new insight supports the need to keep both LDL cholesterol and blood pressure low throughout life by healthy diet choices, weight control, exercise, and, when needed, by drug therapy. “It could also pave the way for the development of more effective therapies to offset the detrimental effects of hypertension on atherosclerosis”, the researchers conclude.

The research was a collaboration among the Experimental Pathology of Atherosclerosis at CNIC, the Cardiovascular Proteomics groups at CNIC, CIBER de Enfermedades Cardiovasculares, and the Atherosclerosis Research Unit at Aarhus University in Denmark.

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