Effectiveness of heart therapies and outcomes for patients with clonal hematopoiesis of indeterminate potential: Q&A

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Medicine, "Clonal hematopoiesis, cardiovascular events and treatment benefit in 63,700 individuals from five TIMI randomized trials."

How would you summarize your study for a lay audience?

Clonal hematopoiesis of indeterminate potential (CHIP) is a condition that promotes the multiplication of blood stem cells in the body and increases the risk of heart disease and stroke in patients. It is caused by specific gene mutations that can occur as people age, often found in patients over 60 years old.

Our team analyzed data from 63,700 patients from five different clinical trials for heart disease treatments. Over a two-year period, we observed how many patients with and without CHIP had heart-related problems, such as heart attacks, strokes and heart-related procedures.

We found that CHIP had the strongest association with first heart attack and was not associated with recurrent cardiac events. We also found that patients with CHIP benefit from a range of heart therapies to a similar degree as those without CHIP.

What knowledge gaps does your study help to fill?

There are two main knowledge gaps that are addressed in this analysis. The first is the question of which populations may benefit from knowing if they have CHIP mutations. We found that a primary prevention population, those without prior heart attacks, appear to have the strongest risk associated with CHIP.

The presence of CHIP in those who have already had a heart attack appears to provide less information on risk. The second is whether there

are any current cardiovascular therapies that could help to offset the excess risk associated with CHIP. We found that four commonly used heart medicines appear to work as well in patients with CHIP than without CHIP, with no outsized benefit seen in patients with CHIP.

How did you conduct your study?

We conducted a large-scale observational study using data from five large, randomized clinical trials from the TIMI Study Group to examine the impact of heart disease treatments on patients with CHIP. 63,700 patients with and without CHIP were included in the analysis and were followed for an average of 2.5 years.

At the conclusion of our observation, we found that 7,453 patients experienced at least one heart attack, stroke or procedure to restore blood flow to the heart. We also found patients with CHIP had a 30% higher risk of an initial heart attack, but no increased risk of repeated heart attacks.

What are the implications?

Our findings suggest that testing for CHIP may have greater utility in patients without prior heart attack than for those with a prior heart attack. In this population, the presence of CHIP identifies a 30% increased risk that can be addressed with preventive medicines. Specifically, we found that existing heart therapies such as lipid-lowering medicine, an antiplatelet therapy, and a cardiometabolic/antiglycemic agent all appear to provide benefit in these patients.

What are the next steps?

Having focused primarily on ischemic events like heart attacks and strokes in this initial CHIP analysis, we look forward to studying the relationship with other cardiovascular disease types in this large clinical trial cohort. Other diseases of interest include heart failure, atrial fibrillation, and blood clots in the legs or lungs.

More information: Marston, N.A., et al, Clonal hematopoiesis, cardiovascular events and treatment benefit in 63,700 individuals from five TIMI randomized trials. *Nature Medicine* (2024). DOI: 10.1038/s41591-024-03188-z

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