New biomarker strategy devised to screen for, diagnose deadly heart complication from cancer treatment

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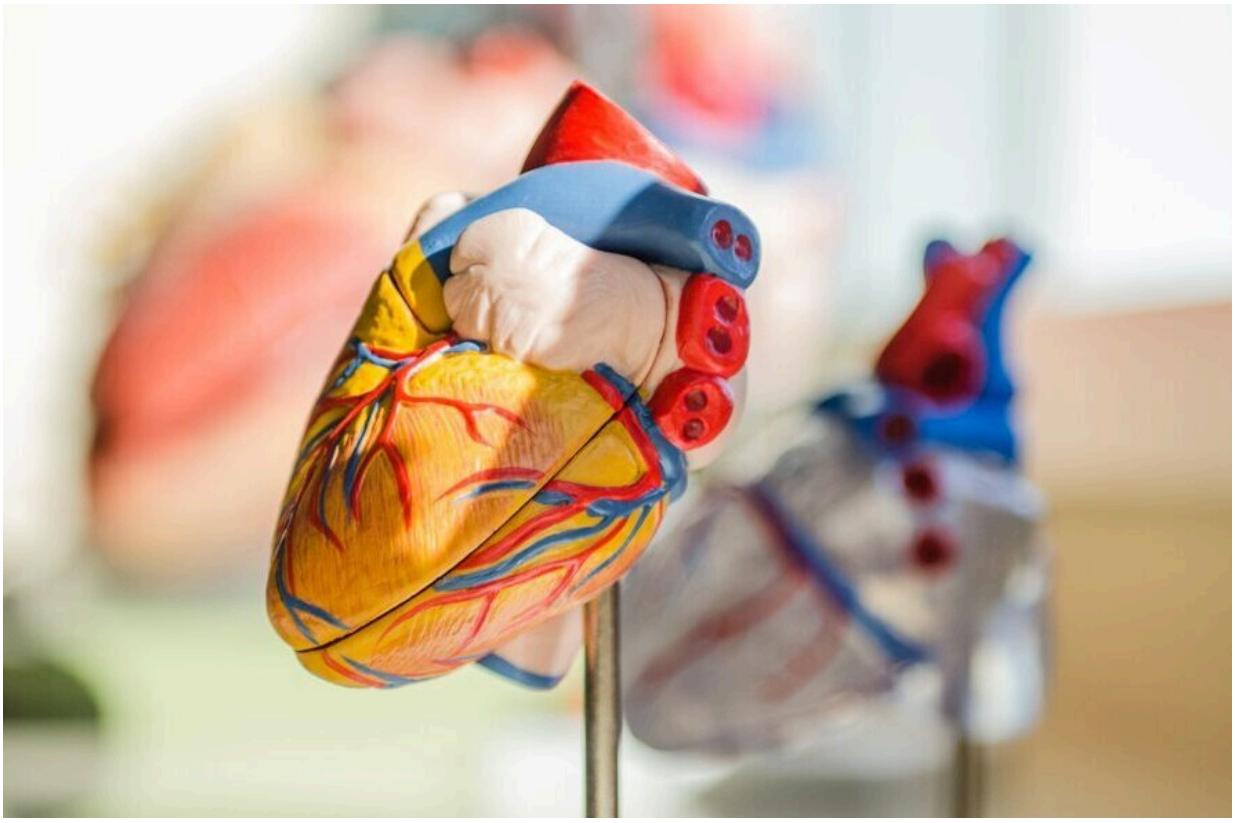

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Researchers at Michigan Medicine have devised a new biomarker-based strategy to screen for a rare and deadly complication caused by

monoclonal antibodies used to treat several cancers.

In a study published in *JACC CardioOncology*, investigators found that nearly all patients with cancer who were diagnosed with myocarditis after being treated with immune checkpoint inhibitors had early signs of muscle destruction and liver damage.

"While immune checkpoint inhibitors have revolutionized the treatment of various cancers, patients who develop the rare complication of myocarditis often present late with at least a 50% chance of death," said Salim Hayek, M.D., senior author of the study and medical director of the University of Michigan Health Frankel Cardiovascular Center Clinics.

"Diagnosing immune checkpoint inhibitor myocarditis is challenging, given that there is no one test that can differentiate it from other causes of cardiac injury. By the time patients present to the hospital, it is often too late," Hayek said. "Diagnosing patients early allows us to start immunosuppressive therapy sooner and give patients a better chance of survival."

Immune checkpoint inhibitors, or ICIs, are monoclonal antibodies that enhance the body's immune system and its response against cancerous cells. There is potential risk that the heightened immune activity from the medication can turn against the body itself, causing damage to almost any of organ system, with myocarditis being the most severe complication.

Researchers analyzed more than 2,600 patients with cancer treated with immune checkpoint inhibitors at University of Michigan Health between June 2014 and Dec. 2021. The vast majority of patients diagnosed with ICI myocarditis also had early signs of muscle injury and liver damage, even prior to hospitalization. Of these patients, 95% had at least three

elevated biomarkers, compared to just 5% of patients without myocarditis.

Among non-cardiac biomarkers, creatine phosphokinase, which signals muscle injury, was most strongly linked to the development of ICI myocarditis, as well as all-cause death.

"It makes sense that myocarditis related to immune checkpoint inhibitors does not occur in isolation, given a raging immune system is expected to affect several organs and particularly the muscles," said co-author Joe-Elie Salem, M.D. Ph.D., professor of medicine at Sorbonne Université in Paris and a leading expert in the field of ICI myocarditis.

"A large variety of antigens targeted by auto-reactive T-cells boosted by ICIs are shared between the myocardium and the peripheral muscles. Myositis, or muscle injury, is a central component of complications related to this class of drugs."

Researchers conclude that clinicians should monitor patients on ICIs regularly for biomarkers of damage elsewhere in the body, including creatine phosphokinase for muscle injury, aspartate and alanine aminotransferase for liver injury, and lactate dehydrogenase for tissue injury.

"Abnormalities in these biomarkers should prompt clinicians to test for cardiac injury using high sensitivity troponin," Hayek said. "Conversely, patient suspected of immune checkpoint myocarditis should have creatine phosphokinase levels measured. If low, or within normal limits, then the diagnosis of immune checkpoint myocarditis is highly unlikely."

More information: Salim Hayek et al, Biomarker Trends, Incidence, and Outcomes of Immune Checkpoint Inhibitor–Induced Myocarditis,

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