Recovery twice as hard for survivors of childhood acute lymphoblastic leukemia

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Nearly 90 percent of children with acute lymphoblastic leukemia (ALL) survive, yet the same treatments that save their life can adversely affect their quality of life and cardiorespiratory fitness health. In fact, the cardiorespiratory fitness of ALL survivors can be significantly worse than a sample of healthy Canadians, despite similar levels of physical activity.

Maxime Caru, an Université de Montréal doctoral student in kinesiology, demonstrates that a group of genes known as "trainability genes" are linked to cardiorespiratory fitness.

Caru's study also demonstrates that trainability genes are linked to cardiorespiratory fitness. He will present the findings of this research today at the American College of Sports Medicine's Annual Meeting in Orlando, Florida.

"Previous work by UdeM's Laboratory of physiopathology of the exercise, where I carried out my research, had suggested that ALL survivors weren't following recommendations for physical activity," said Caru, who is also a researcher at the CHU Sainte-Justine Research Centre.

"But until now no Canadian study had compared the cardiorespiratory fitness of ALL survivors against the healthy population."

Women affected more than men

In his study, which compares a cohort of 250 survivors of childhood ALL to 825 healthy Canadians, Caru found that the cardiorespiratory fitness of survivors was 22 percent worse than the healthy population, with a maximum oxygen uptake of nearly 9.2 mL.kg-1.min-1.

He also noted that moderate- to high-intensity physical activity did not improve cardiorespiratory fitness as much among survivors, and that this was particularly true among female survivors.

The reduction in cardiorespiratory fitness can only be partly attributed to ALL treatments and other environmental factors, Caru believes.

Previous studies have found links between trainability genes and changes in cardiorespiratory fitness among healthy people who perform physical activity. To better analyse those links, in the second part of the study, Caru and his colleagues ran genetic association analyses between trainability genes (238 genes, including 134 common variants and 1,225 rare variants) and the cardiorespiratory fitness of ALL survivors.

Genetically linked to 'trainability' genes

For the first time, they were able to show that poor cardiorespiratory fitness in survivors is genetically linked to trainability genes, especially the TTN gene. This gene provides cells with instructions for making a protein known as titin that is key to skeletal muscles (those used to move the body) and heart muscles. Furthermore, female survivors with poor cardiorespiratory fitness showed the strongest genetic associations with three other trainability genes: LEPR, IGFBP 1 and ENO3.

While the study's findings aren't good news, they do "provide valuable information on genetic associations with poor cardiorespiratory fitness among ALL survivors," said UdeM kinesiology professor Daniel Curnier, who directed the study.

"Although the study revealed that ALL survivors are doubly burdened by their illness and related treatments, it also provided additional evidence of the benefits of physical activity for childhood cancer treatment. In light of this, ALL survivors need better support to engage in physical activity and ensure they get the most out of it and improve their cardiorespiratory fitness."

Added Caru: "The study will help kinesiologists develop more personalized plans and effective

preventative strategies for ALL survivors to minimize long-term health effects."

Caru and his colleagues published "Identification of genetic association between cardiorespiratory fitness and the trainability genes in Childhood Acute Lymphoblastic Leukemia Survivors" in *BMC Cancer* on May 14, 2019.

More information: Maxime Caru et al. Identification of genetic association between cardiorespiratory fitness and the trainability genes in childhood acute lymphoblastic leukemia survivors, *BMC Cancer* (2019). DOI: 10.1186/s12885-019-5651-z