Fontan circulation link to changes in the genetic code may lead to new treatment for heart conditions

April 4 2024

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Patients who have had surgery to create a Fontan circulation show changes in their genetic code, which may provide a new treatment opportunity to reduce premature aging.

The procedure is used to treat children born with a range of single ventricle heart conditions and has led to most of these children surviving into during adulthood.

However, patients with a Fontan circulation are likely to develop complications affecting different organs, including the brain, with progressive functional decline, loss of muscle mass, osteoporosis, and renal impairment during their 20s and 30s, with a similar pattern to that seen in much older people. This often leads to premature death and it remains a life-limiting condition with few late treatment options.

In the first study of its kind, published in *JACC: Advances*, researchers at the University of Birmingham, in the UK, and at Zymo Research, California, found that the Fontan circulation is associated with changes in the genetic code.

These changes are suggestive of accelerated aging, or epigenetic aging, which mirrors the clinical picture of complications usually related to aging. This premature aging starts in childhood and continues during adult life.

The researchers also found that there was a greater acceleration of premature aging in men than in women.

First author Mr. Nigel Drury, Associate Clinical Professor at the University of Birmingham, commented, "The discovery of the association between the Fontan circulation and epigenetic aging may represent a new treatment opportunity to delay progression of the premature aging pattern, by reversing the effects on the genetic code and

thereby reverse the cellular effects of aging.

"However, further research, with a bigger sample of patients with a Fontan circulation is needed to assess the impact of other important factors on accelerated epigenetic aging. Our pilot study also did not evaluate whether accelerated epigenetic aging is specific to patients with a Fontan circulation or if it is present in other severe congenital heart defects."

More information: Nigel E. Drury et al, Accelerated Epigenetic Aging in Children and Adults With a Fontan Circulation, *JACC: Advances* (2024). DOI: 10.1016/j.jacadv.2024.100865

Provided by University of Birmingham