Of mice and men...

Carl L. Backer, MD, and Michael C. Mongé, MD

From the Division of Cardiovascular-Thoracic Surgery, Ann & Robert H. Lurie Children's Hospital of Chicago; and Department of Surgery, Northwestern University Feinberg School of Medicine, Chicago, Ill.

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Address for reprints: Carl L. Backer, MD, Division of Cardiovascular-Thoracic Surgery, Ann & Robert H. Lurie Children's Hospital of Chicago, 225 E Chicago Ave, Chicago, IL 60611 (E-mail: cbacker@luriechildrens.org).
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Krishnan and colleagues¹ have reported a novel animal model of transient left ventricle (LV) pressure overload. This model simulates repair of coarctation of the aorta (CoA) in childhood, to gain a better understanding of the late complications after coarctation repair. The authors used spontaneously hypertensive rats (SHRs) to determine how the preconditioned LV responds to late systemic hypertension after a period of "coarctation."

At age 3 weeks, an absorbable suture was used to constrict the transverse aortic arch of SHRs. This is the equivalent of sudden development of coarctation in a human at age 1.5 years.² The authors were successful in documenting a marked upper-lower body blood pressure (BP) gradient, which was relieved by gradual suture degradation, simulating coarctation repair. At 7 weeks post-constriction (5 human years), the BP gradient was gone. The banded animals' hearts demonstrated an increase in transmural thickening, mean cardiomyocyte area, and fibrosis compared with controls. The histological changes in the LV persisted following a transient period with a coarctation despite normalization of left ventricular geometry. Curiously, the authors noted no early difference in the response of the LV to the onset of systemic hypertension in these SHRs at 7 weeks postconstriction when the BP gradient was gone, but both groups were hypertensive.

The ability of this model to provide insight into the late complications after repair of CoA may be confounded by several factors. First, at 5 weeks postconstriction, or the equivalent of 4.0 human years, the pressure gradient was more than halved as the suture degraded. At 7 weeks (5 human years), the gradient was gone. Is this period with a coarctation sufficient to promote an accentuated hypertrophic response? In the study by Bocelli and associates,³ the risk of late ventricular hypertrophy was 25% for patients repaired at age 3.4 years but rose to 50% and 75% for those repaired at age 5.9 and 8.4 years, respectively. A longer period of coarctation might be useful. Second, simulating coarctation repair through an absorbable suture might not recreate the scarring, changes in aortic pressure wave propagation, and abnormally

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Central Message

An animal model using spontaneously hypertensive rats to simulate coarctation repair may provide greater understanding of late complications related to coarctation repair in childhood.

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increased aortic stiffness to which the hypertrophic stimuli have been attributed. Third, the authors' decision to use SHRs will not provide insight into the mechanisms underlying the development of left ventricular hypertrophy in normotensive patients. As noted by Lee and coworkers⁴ in their study of 82 patients following coarctation repair, there was only a weak correlation between the existence or severity of hypertension and left ventricular hypertrophy, which was present in 42% of patients with normal 24-hour blood pressure. Bocelli and colleagues³ came to a similar conclusion, noting that a considerable proportion of the patients with abnormal left ventricular geometry had no evidence of either residual or late-onset hypertension, thus supporting the evidence that mechanisms independent of persistent or recurrent hypertension were involved in affecting left ventricular mass.

Finally, banding of the rat transverse aorta at age 3 weeks is equivalent to the sudden development of a human coarctation at age 1.5 years. In the current era, a majority of coarctation repairs are performed in the neonatal period. Furthermore, a neonatal coarctation potentially may have a more profound effect on the susceptibility of the immature myocardium to an accentuated hypertrophic response, through fibrosis and/or alterations in DNA expression, than what is reproduced by this model.

Despite the aforementioned concerns, the model of temporary aortic coarctation developed by Krishnan and colleagues¹ has potential to provide insight into the late complications of

aortic coarctation repair. Different variations of timing of the coarctation creation and different durations of follow-up will add to our knowledge base of what occurs with our patients. This model may help differentiate whether the long-term complications of coarctation repair are from the hemodynamic burden or are part of a systemic process in which coarctation is just one manifestation of a systemic vasculopathy. With further investigation, the knowledge gained from this model may help improve late outcomes of aortic coarctation repair in humans.

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