observed after coarctation repair is not a new phenomenon, but is simply the continuation of the neurosympathetic process that existed before the coarctation repair.

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 doi:10.1016/j.jtcvs.2007.11.053

Reply to the Editor:

Robicsek outlined in his letter to the Editor in response to our article¹ that arterial hypertension exists distal the coarctation even before coarctation repair. Hypertension in the long-term follow-up is simply the continuation of this neurosympathetic process.

Previously published data from our group² on blood pressure and aortic distensibility in neonates with coarctation before and after surgical repair did not show poststenotic hypertension before repair in general. However, we totally agree with Robicsek and other authors^{3,4} that inborn processes not touched by current modes of repair are also responsible for hypertension in the long-term follow-up after successful repair. We believe that the starting point of the pathophysiologic chain is the inborn alteration of the arterial wall with elastic fiber fragmentation, fibrosis, and cystic medial necrosis, which are later exaggerated by existing hypertension. This causes the increased stiffness most pronounced in the central elastic arteries, the blunted baroreceptor reflex, and the neurosympathetic activation. However, the novelty of our study was the extent of this phenomenon. Our relation to age showed that arterial hypertension has to be expected in almost all patients after coarctation repair in older ages. Close surveillance and aggressive treatment of arterial hypertension might prevent further cardiovascular disease.

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Heart valve tissue engineering: Research should proceed along validated routes

To the Editor:

In their article focusing on in vivo autologous recellularization of a tissue-engineered heart valve, Vincentelli and colleagues¹ raise 2 main questions: (1) Which are the best candidates for scaffold repopulation? (2) Does direct injection of cells into the scaffold guarantee adequate cellular recolonization?

According to the cell type chosen for scaffold seeding, the adoption of nonselected bone marrow-derived mononuclear cells was associated with early degeneration with thickening and retraction of the cusps, growth of fibrotic pannus along the suture lines, and thickening and calcification of the wall conduits. Histologically, a marked inflammatory response with extracellular matrix disarray and macrophage infiltration both in the adventitia and the media layers were observed, along with a loss of the proper collagen allocation between the

ventricularis, spongiosa, and fibrosa of the leaflets. Additionally, a significant increase of both transvalvular and distal gradients were recorded at 4-month follow-up echocardiographic analysis. On the contrary, scaffolds repopulated with mesenchymal stem cells did not evidence either degenerative notes or inflammatory reactions.

These findings might suggest “the onset of a structural deterioration of the scaffold in the [bone marrow-derived mononuclear cell] group and a protective effect of the injections of [mesenchymal stem cells].”¹ We are concerned that such conclusions seem audacious because the study suffers from a main limitation represented by the cell-seeding modality. In fact, the authors, looking for an answer to question number 2, choose to inject the cells directly into the decellularized scaffold (onto the conduit walls and valve annulus, excluding the leaflets), instead of adopting a biomimetic environment.

The adoption of this alternative technique, which has been derived from the myocardial setting,² represents an innovative concept for the valvular field and therefore requires a careful validation. Fluorescent cell tracking, which was performed on 4 of 14 animals in the first postoperative week, evidenced, on day 1, the cell persistence onto the injection site and, on day 7, a few scattered cells into the matrix, the arterial wall, and the leaflets. Moreover, nonlabeled cells of host origin were found.

Is this enough to say that “in situ injection of bone marrow cells into a porcine decellularized scaffold before implantation enhanced the in vivo recolonization and induced full re-endothelialization”?¹ First, endothelialization and scaffold repopulation do not coincide. Even bioprostheses undergo an endothelialization process of the inert components once implanted. Second, the process of repopulation implies an architectural and hierarchic cell-specific distribution along the leaflet’s ventricularis, spongiosa, and fibrosa,³ which was not observed in this experience.

In the article’s “Discussion” section, the authors themselves affirm that they had no direct evidence that cells would grow inside the matrix. According to the hypothesis that injected cells might enhance autologous recellularization, further evidence is needed to draw definite conclusions, and the provided results do not concretely support the initial hypothesis.