in research that is performed in device development.[7] Is acknowledging equity ownership in the "small print" of a scientific article sufficient to eliminate reasonable concerns about data integrity and interpretation? Or should we demand that investigators who are involved in the critical analytic steps that lead to human device implantation be completely distanced from any real or perceived financial conflict of interest? Tough questions when one considers the desperate need for solutions, the paucity of options in critical settings, and limited resource opportunities. Unfortunately, it can be a slippery slope. The pressures to get devices into patients are real and compelling. When it comes to scientific evaluation of new technology for children, however, it may be best to "believe nothing, doubt everything, and demand proof."

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See Article page e201.

Commentary: "CorMatrix: If it is too good to be true, …"

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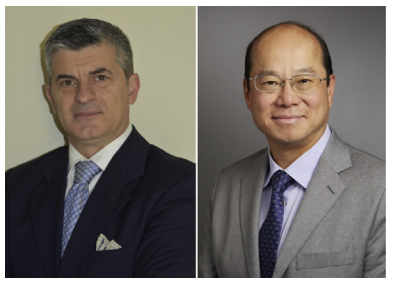

Francesco Formica, MD (*left*), Tain-Yen Hsia, MD (*right*)

CENTRAL MESSAGE

In animal studies, pulmonary valve conduit made with CorMatrix showed a high incidence of early valve failure and infection, with corresponding histologic features of inflammation and poor remodeling.

The search for a perfect substitution material in reconstructive cardiovascular surgery continues. Ideally, such material will possess these properties: freedom from calcification, traction, and retraction; fully biocompatibility; resistant to infections, inflammation, and fibrosis; easy to handle; and promotes tissue remodeling and regeneration while allowing for growth. Numerous substitute materials, either biological and synthetic, have been applied in cardiac valve repair, ventricle walls, and great vessels reconstruction. Although we have extensive experience with autologous pericardium, xenopericardium, homograft, polyethylene (Dacron) and polytetrafluoroethylene (Gore-Tex) materials, none proved to be completely satisfactory. Biological material will inevitably degenerate and calcify, and there is no growth potential in any of the synthetic options.

Since its introduction more than 20 years ago, decellularized porcine small intestinal submucosa (CorMatrix Cardiovascular, Inc, Roswell, Ga), has been tested in a variety of reconstructive cardiovascular operations. Its

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proposed ability to "repopulate" the extracellular matrix with the patient's own cells and thus be free from inflammation and degeneration sparked much enthusiasm. However, this early excitement has dimmed as preclinical and clinical studies[1] showed conflicting early and midterm outcomes. In particular, although the use of the CorMatrix for cardiac valve reconstruction/replacement in children,[2-4] in adults,[5-7] and animals[8,9] had consistently showed early acceptable results, the disappointing longevity due to inflammation and degenerative process seen with longer follow-up have raised an awareness that CorMatrix may be too good to be true.

In this issue of the *Journal*, van Rijswijk and colleagues[10] further shed light on important histologic and biochemical behavior of the CorMatrix when used as a valved-conduit construct in the pulmonary position. The authors implanted custom-made valve conduits in the right ventricular outflow tracts in 10 sheep and 10 lambs. At 6 months postimplantation, the explanted CorMatrix valve conduits showed a high incidence of chronic inflammation without evidence of constructive remodeling. More ominously, the authors reported a high rate of pulmonary valve dysfunction and increased susceptibility to infective endocarditis, observed in 20% of the explanted valves.

Although the study has important limitations, including having only 13 surviving animals, a lack of a control group, and a relatively short follow-up, the extensive biochemical analyses and scanning electron microscopy do reveal a detailed histochemical picture of what happens to CorMatrix as a pulmonary valve replacement. Unfortunately, this picture is not one that would instill confidence. If CorMatrix valve conduits exhibit such an alarming degree of failure and degeneration in the low-pressured flow domain of the right ventricular outflow tract, one must be concern of its performance and durability as valve substitution material in the aortic or mitral positions. Initially hailed as the next greatest thing in substitution material, after 20 years the jury is still out on whether CorMatrix is indeed the wunderkind discovery. With additional clinical experiences and experimental investigations, we will yet understand the potentials and limitations of CorMatrix in reconstructive cardiovascular surgery. In the meantime, as the old saying goes, "If it is too good to be true…."

CONG

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