JACC: BASIC TO TRANSLATIONAL SCIENCE VOL. 2, NO. 5, 2017

ISSN 2452-302X

Letter

TO THE EDITOR

Aortic Valve Disease Is Not a Monogenetic Disorder

The recent publication in *JACC: Basic to Translational Science* by Torzewski et al. (1) highlights a rapidly evolving mechanism in the development of calcific aortic valve disease (CAVD), which includes the role of lysophosphatidic acid (LPA) and the effect of autotaxin on the signaling pathway activating ecto-nucleotidase pyrophosphate (ENPP) in cardiovascular calcification.

Over the past 25 years, studies in the field of aortic valve disease have identified several complex mechanisms in the initiation, progression, and cellular differentiation of osteogenesis in the aortic valve (2). A disease which was thought to be degenerative at the turn of the century is now well known to express an osteogenic bone phenotype secondary to traditional risk factors and several complex genetic associations (2). The genetic associations in the field are rapidly increasing which include Notch1, estrogen, lipoproteins, low-density lipoprotein receptor (LDLR), and LPA (3). In this article, the authors describe calcific aortic valve disease as a monogenic disorder secondary to LPA. Although the evidence is strong for the role of LPA in the progression of this disease, there are several other genetic associations identified in patients with CAVD. These genetic abnormalities have played critical roles in the teasing out of the mechanisms which activate of the osteogenic phenotype in patients with CAVD.

Is there still a role for traditional risk factors in the progression of CAVD? Is there potential for targeted medical therapy to slow progression of disease?

Although the randomized studies in the field of statin therapy in CAVD have been negative, there is 1 open label study entitled RAAVE (Rosuvastatin Affecting Aortic Valve Endothelium) wherein the patients who received rosuvastatin according to the Adult Treatment Panel guidelines for lowering low-density lipoprotein did slow progression of disease after 16 months (4). In the future, studies evaluating LPA, autotaxin, Lrp5, low-density lipoprotein receptor, oxidized phospholipids (5), which activate the osteogenic cascade in the aortic valve, will be critical for the future development of randomized clinical trials.

*Nalini M. Rajamannan, MD

*Most Sacred Heart of Jesus Cardiology and Valvular Institute
703 North 8th Street, Suite 303
Sheboygan, Wisconsin 53081
E-mail: nrajamannan@gmail.com

https://doi.org/10.1016/j.jacbts.2017.09.003

Please note: Dr. Rajamannan is the inventor on a patent for the treatment of calcific aortic valve disease with statins. The patent is owned by the Mayo Clinic and she does not receive any royalties.

REFERENCES

1. Torzewski J, Ravandi A, Yeang C, et al. Lipoprotein(a)-associated molecules are prominent components in plasma and valve leaflets in calcific aortic valve stenosis. J Am Coll Cardiol Basic Trans Science 2017;2:229–40.

2. Rajamannan NM, Evans FJ, Aikawa E, et al. Calcific aortic valve disease: not simply a degenerative process: a review and agenda for research from the National Heart and Lung and Blood Institute Aortic Stenosis Working Group. Executive summary: calcific aortic valve disease-2011 update. Circulation 2011; 124:1783–91.

3. Rajamannan NM. Calcific aortic stenosis: lessons learned from experimental and clinical studies. Arterioscler Thromb Vasc Biol 2009;29:162–8.

4. Moura LM, Ramos SF, Zamorano JL, et al. Rosuvastatin affecting aortic valve endothelium to slow the progression of aortic stenosis. J Am Coll Cardiol 2007;49:554–61.

5. Best PJM, Rajamannan NM. OxPL: elusive risk factor in calcific aortic valve disease or another piece of the puzzle? Arterioscler Thromb Vasc Biol 2017;37: 1425–7.