ACC22
APRIL 2 - 4 | WASHINGTON, DC

1686
JACC March 8, 2022
Volume 79, Issue 9, suppl A

Valvular Heart Disease

EXTRACELLULAR GLYCOPROTEINS AND ADVANCED GLYCATION END PRODUCTS ASSOCIATE WITH CALCIFICATION DEVELOPMENT IN HUMAN AND RABBIT CALCIFIED AORTIC VALVES

Poster Contributions
For exact presentation time, refer to the online ACC.22 Program Planner at https://www.abstractsonline.com/pp8/#!/10461

Session Title: Valvular Heart Disease Flatboard Poster Selections: Basic and Translational Science
Abstract Category: 46. Valvular Heart Disease: Basic and Translational Science

Authors: *Nikolaos Anousakis-Vlachochristou, Dimitra Athanasiadou, Manolis Mavroidis, Antigoni Miliou, Manousos Makridakis, Loukas Kaklamanis, Stamatis Adamopoulos, Antonia Vlahou, Dennis V. Cokkinos, Karina Carneiro, Konstantinos P. Toutouzas, First Department of Cardiology, Medical School, National and Kapodistrian University of Athens, Athens, Greece, University of Toronto, Toronto, Canada*

Background: Aortic valve stenosis (AS) remains without pharmaceutical therapy. Infrared spectroscopy (IR) has demonstrated increased valve glycosylation, possibly by the formation of oxidation-mediated advanced glycation end products (AGEs). Here, we investigate whether AGEs are increased in non-diabetic patients and a validated AS rabbit model.

Methods: Ten AS patients with Diabetes Mellitus (DM), 10 without DM undergoing valve replacement, and 10 patients undergoing heart transplantation with healthy valves were studied. Also, 12 rabbits, randomized to normal diet vs diet supplemented with 1% cholesterol and 3500 IUs/kg Vitamin D daily for 7 weeks, were examined. Cusps were snap-frozen, homogenized, and total AGEs were measured with quantitative ELISA. Protein analysis of homogenates was performed with LC-MS/MS. Cryosections were methanol-acetone fixed and stained with calcein. Glycosylation autofluorescence and calcification were imaged with confocal microscopy (Leica SP5, 405, 488 nm lasers), and average intensity/volume was calculated. Animal valve cusps were formalin-fixed, critical point dried, and analyzed with IR (Thermo Scientific FTIR Nicolet iS20).

Results: DM patients demonstrated increased calcification compared to non-DM patients. Non-DM patients showed similar glycation autofluorescence signal compared to controls, and DM patients disclosed reduced glycation autofluorescence versus controls. Total AGEs were increased only in human DM cusps. Mass spectrometry, among 96 differentially expressed proteins, revealed 41 overexpressed glycoproteins in rabbits, of these 16 were extracellular matrix-bound, including vintronectin (ratio: x3.05), fibronectin (x4.1), fetuin-a (x6.7), and osteonectin (experimental cusps only). Spectroscopic analysis revealed peaks of increased intensity within the range 1000-1200 cm^{-1} in animal calcified vs control valves, in the same region with fetuin-a spectrum.

Conclusion: AGEs are increased in AS patients with DM and correlated with calcification, but not in non-DM patients. Extracellular matrix glycoproteins, importantly fetuin-a, are significantly increased in rabbit valves, similar to human disease.