Regulation of RNA expression and biomarkers in sinus node dysfunction induced atrial fibrillation in vivo.

Seung-Young Roh
Kwang-No Lee
Jaemin Shim
Jong-II Choi
Young-Hoon Kim

Introduction: The sinus node (SN) is located at the apex of the cardiac conduction system. SN dysfunction (SND), characterized by electrical remodeling, has usually been attributed to idiopathic fibrosis or ischemic injuries in the SN. SND is associated with increased risk of cardiovascular disorders, including syncope, heart failure, and atrial arrhythmias, particularly atrial fibrillation (AF). One of the histological hallmarks of SND is degenerative atrial remodeling linked with conduction abnormalities and increased right atrial refractoriness. Although SND is frequently accompanied by increased fibrosis in the right atrium (RA), molecular basis thereof remains elusive. Therefore, we aimed to examine whether SND evokes significant molecular changes in the RA that account for structural remodeling.

Methods: For this purpose, we induced cardiac dysfunctions such as bradycardia and atrial fibrosis in a rabbit model of experimental SND, and found that ablation of the SN leads to adverse fibrotic remodeling of the RA regardless of AF. Transcriptome analysis identified differentially expressed gene transcripts in the RA in response to impaired SN function, and accompanying gene enrichment analysis suggested extensive pro-fibrotic changes including activation of transforming growth factor-β (TGF-β) signaling, and alterations in components of the extracellular matrix and their regulators.

Result: Of particular importance, our findings suggested that periostin, a matricellular factor controlling cardiac tissue development, might have a key role in mediating TGF-β-signaling–induced aberrant atrial remodeling.

Conclusion: In conclusion, the present study provides valuable information on the molecular signatures underlying the SND-related atrial remodeling and implies a diagnostic potential of periostin in fibroproliferative cardiac dysfunctions.