Best Paper of the Year 2021

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We are excited to present a new section in JCTR that highlights the best papers of the previous year. The following articles were selected by the associate editors from those accepted during 2021 and based on their relevance, impact, and how they contribute to the Journal's aims. We believe that they showcase the quality and diversity of the papers published in JCTR.

Best Paper of the Year

- *Aged monkeys fed a high-fat/high-sugar diet recapitulate metabolic disorders and cardiac contractile dysfunction*, by Shuang Zheng and colleagues [1].

United Nations predicted that by 2050, about 16% of the world's population will be over the age of 65 [2]. Elderly people consuming high-fat or high-sugar diets have been associated with increased metabolic disturbances and all-cause mortality [3, 4], while low calorie intake was one of the features of long-living populations [5]. In this paper, a team of scientists from multiple institutes developed a model of elderly heart failure by feeding non-human primate (NHP) cynomolgus monkeys a high-fat/high-sugar (HFSD) diet [1].

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The study showed that a high-calorie diet disrupted metabolism and reduced heart function in older monkeys.

The authors measured calcium sensitivity, actomyosin ATPase activity, and myofilament phosphorylation in diet-induced failing hearts of aged monkeys. These data are critical for elucidating the underlying mechanism of the reduced systolic function identified in these animals. The authors found that a gut-derived metabolite, trimethylamine N-oxide (TMAO), was significantly increased in aged monkeys fed with a HFSD. Elevated TMAO correlated with the severity of heart failure in humans, whereas addition of TMAO caused cardiac remodelling and ventricular dysfunction in experimental animals [6, 7].

The Editorial Team acknowledged the value of this exciting animal model of elderly heart failure, especially to explore the molecular mechanisms of elderly cardiac dysfunction upon high-fat diet administration [8]. Similar to humans in anatomy, physiology, metabolism, and genetics, NHPs have been used for decades to understand the pathogenesis of cardiovascular disease. Findings suggest that the biological effects of experimental diets on NHPs resemble those on humans [9]. Long-term calorie restriction studies in rhesus monkeys initiated in parallel by three primate research centers in the 1980s further support diet as a key factor in cardiac health [10]. However, the current understanding of the mechanism of diet-induced cardiac dysfunction in the elderly is mainly derived from rodent studies. To translate rodent research findings into clinical applications, we need NHP models that are more similar to the human condition in terms of physiology, anatomy, and genetics. The best paper of 2021 addresses this issue and provides a bridge for the translation of these findings to the clinics.

Highly Commended Papers in JCTR in 2021

- *Plasmatic PCSK9 levels are associated with very fast progression of asymptomatic degenerative aortic stenosis*, by Natalia Mateos and colleagues [11].

Current guidelines suggest that asymptomatic aortic stenosis (AS) patients with fast progression may benefit from an early invasive treatment. The trick is identifying the fast-progressing patients. In this paper, the authors looked at a prospective cohort of asymptomatic AS patients and identified predictors of fast disease progression that may eventually be translatable to the management of AS patients.

- *Dickkopf 3: a Novel Target Gene of miR-25-3p in Promoting Fibrosis-Related Gene Expression in Myocardial Fibrosis*, by Ni Zeng and colleagues [12].

Fibrosis is a critical pathological feature in many heart disease. This manuscript identified the contribution of the NF- κ B/miR-25-3p/Dickkopf 3 axis to cardiac fibrosis using a mouse model. The study also demonstrated dysregulation of miR-25-3p in human cardiac samples from heart failure patients.

- *Mapping Renal Innervations by Renal Nerve Stimulation and Characterizations of Blood Pressure Response Patterns*, by Hao Zhou and colleagues [13].

The study tested a provocative mechanism and challenged current paradigms of renal nerve function. This work will be instrumental to the renal denervation field, which is soon to be approved for hypertension treatment.

- *Renal revascularization attenuates myocardial mitochondrial damage and improves diastolic function in pigs with metabolic syndrome and renovascular hypertension*, by Rahele A. Farahani and colleagues [14].

This was a well-designed and carefully executed translational study that offered important new insights into the pathophysiology of metabolic syndrome and its relationship with renovascular hypertension. Its results can be rapidly extrapolated in clinical practice by facilitating early identification of this subgroup of patients and deferring them to this non-pharmacological therapy.

- *The prognostic value of a validated and automated intravascular ultrasound-derived calcium score*, by Tara Neleman and colleagues [15].

This paper presented the first score since the introduction of the coronary artery calcium score that has been related to clinical events. The IVUS-calcium score could have the potential to improve further individual risk classification and to modify current lesion preparation algorithms.

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