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Mini Review

Fasting in Cardiovascular Disease

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In recent years, a variety of diets have emerged strongly as adjuvant therapies in the treatment of cardiovascular diseases such as gluten-reduced caloric restriction, mediterranean-style diets, vegan diets, ketone diet and intermittent fasting (IF) [1-5]. The latter can be understood as a chronic or intermittent reduction in food intake, never approaching the level of malnutrition or deprivation of essential nutrients [6]. IF diets are, therefore, personalized diets both in the duration of the fasting periods (generally 16-48 h),the periods of energy-restricted intake and the periods of normal food intake [7].

It is well stablished that IF leads to distinctive physiological adaptations which involve lower levels of glucose and insulin in the blood, an increased fatty acid mobilization and ketone body production, decreased plasma levels of leptin and insulin-like growth factor 1 (IGF-1) and stimulation of autophagy. Among the multiple cell transduction pathways that mediate all these responses, the mammalian A recent inhibition-dependent pathway of rapamycin (mTOR) and the sirtuin-mediated pathway, deserve special consideration. Also, transcription factors such as peroxisome proliferator alpha receptor (PPAR-alpha) are deeply involved in fasting-induced metabolic changes. It has been postulated that sirt1 can deacetylate the Nf-κB RelA/p65 subunit [8] by inhibiting the NF-κ B signaling pathway. This pathway is importantly involved in the induction of the expression of pro-inflammatory genes encoding for pro-inflammatory cytokines (TNF, IL-1β and IL-6), chemokines (CCL2 / MCP-1 and CXCL2 / MIP2) or adhesion molecules (E-selectin, ICAM-1 and VCAM-1) [9,10]. In addition to this, PPAR-alpha activates the so-called nuclear respiratory factor 1 and 2 (NRF-1 and NRF-2), both responsible for the activation of nuclear genes implicated in the stimulation of mitochondrial biogenesis. Indeed, NRF-2 activates mitochondrial transcription factor A (mtTFA) by inducing the replication and transcription of the mitochondrial genome [11-13]. NRF-2 also triggers the activation of transcription activating factor 4 (ATF4), which in turn promotes the expression of fibroblast growth factor 21 (FGF21).

In addition to the activation of these mitochondrial pathways, IF is known to promote antioxidant effects by lowering the production of reactive oxygen species (ROS) and by increasing antioxidant defenses [14-17]. It has been demonstrated that IF can decrease the production and release of ROS in mitochondria by increasing metabolic respiratory rate and mitochondrial efficiency. This is achieved by inducing the expression of uncoupling proteins (UCPs) such as UCP2 and UCP4 in mitochondria [17]. Both UCPs slightly uncouple the flow of protons (H+) across the inner mitochondrial membrane during oxidative phosphorylation, resulting in increased electron transport and oxygen consumption in the mitochondria [14-16,18].

All the mentioned pathways have been demonstrated to participate and their activation to be cytoprotective in cardiovascular disease (CVD) in preclinical experimental models. This has led to studies implementing these kind of dietary regimens as coadjutant therapies for CVD. A recent study published in the Cochrane Database, Allaf, et al. (2021) compared 7 studies with

intermittent fasting versus habitual feeding. They showed that three months of FI induced a greater weight loss than the usual diet, without affecting sugar levels. The authors note that these changes might no be clinically significant. They emphasize the limitations in the ways in which the studies were designed, conducted, and reported and failed to find enough evidence as whether intermittent fasting could prevent CVD [3]. Indeed, no relevant data were found on mortality, cardiovascular mortality or the risk of stroke, heart attack or heart failure.

Because published reports left unclear the benefits of IF in CVD, we decided to carry out a bibliometric review of the published articles whose topics focus on IF and cardiovascular disease. In October 4, 2022 we conducted an electronic search in the database of the web of Science of all the references that contained in the theme ["cardiovascular disease" and "Intermittent fasting"]. This search rendered 653 works of which 575 were articles. In the last 4 years a total of 276 items were published: 2022 (69 entries); 2021 (94 entries); 2020 (68 entries) and 2019 (46 entries). This represents 48.265% of the total items found, thus emphasizing the increase in the scientific community interest in the field. The oldest work dates from 1953 and focuses on the effects of IF on the tendency to atherosclerosis [19]. These references accumulated 22,604 times cited total, yielding 34.62 citation average per item, and an H-Index of 78. Being the most cited item is a review by Longo, VD and Mattson [7] with 664 citations. On the basis of the number of citations, the top original human study was conducted by Sutton, et al. (484 citations). In this study the authors demonstrated an improvement in cardiometabolic health independently of weight loss. The authors concluded that the effects of IF are not solely due to weight loss but also to an improved insulin sensitivity, beta cell responsiveness as well as lowering in blood pressure, oxidative stress and appetite [20].

Next, we focused on the most influent authors in the field as indicated by the number of published works. Top author was Mattson MP (22 articles) followed by Criqui MH, Guralnik JM, Liu K, Mcdermott MM with 12 articles. Interestingly these last three authors coauthored all the 12 works. It is worth noting that the articles by Mattson MP accumulated 4,300 citations with an average of 186.96 citation per item. Next, we determined the top research areas where these 653 items were included. These were Cardiovascular System Cardiology (436 records), Biochemistry Molecular Biology (334 records), Endocrinology Metabolism (332 records) and Nutrition Dietetics (319 records). In addition, the top 3 publication/source titles were: Nutrients (30 records), Circulation (27 records), FASEB Journal (17 records).

Conclusion

In conclusion, our bibliometric study reveals a generalized interest of the scientific community in the potential beneficial effects of IF in cardiometabolic health.

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Conflict of Interest

No conflict of interest.

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