Trends in Cardiovascular Medicine 29 (2019) 148–149

Contents lists available at ScienceDirect

Trends in Cardiovascular Medicine

journal homepage: www.elsevier.com/locate/tcm

Editorial commentary: Cardiometabolic diseases and gut microbiota–removing the veil☆

Jaime A. Riquelme, PhD[a], Catterina Ferreccio, MSc[b], Sergio Lavandero, PhD[a,c,*]

[a] Advanced Center for Chronic Diseases (ACCDiS), Faculty of Chemical and Pharmaceutical Sciences & Faculty of Medicine, Universidad de Chile, Santiago, Chile
[b] Advanced Center for Chronic Diseases (ACCDiS), Faculty of Medicine, Pontificia Universidad Catolica de Chile, Santiago, Chile
[c] Cardiology Division, Department of Internal Medicine, University of Texas Southwestern Medical Center, Dallas, TX, United States

ARTICLE INFO

Keywords:
Cardiovascular diseases
Metabolic diseases
Inflammation
Microbiome
Diet
Non-caloric artificial sweeteners

Over the past few years, extensive research has been performed to find novel treatments for cardiac dysfunction. Nonetheless, while gene and cell therapies offer promising solutions for reducing cardiovascular mortality, translation from bench to bedside has proven difficult [1,2] and cardiovascular diseases remain the leading cause of mortality around the world [3]. Indeed, the more we know about cardiovascular pathology, the more complex the landscape becomes. To add insult to injury, metabolic diseases, which are known to affect the cardiovascular system, are increasingly prevalent in the global population [4]. Thus, the spotlight has been put on the complexity of these diseases, with investigators searching for: a) better understanding of cardiometabolic pathophysiology and b) novel therapies to treat cardiometabolic illnesses.

Twenty years ago, a link between cardiometabolic diseases and gut microbiota would have been considered implausible. Today, an emerging field of research is focused on the potential relationship between these conditions [5]. Thus, it is important to monitor, update, critically discuss and organize the new knowledge surrounding this topic.

The review article presented by Schiattarella et al. [6] provides a fresh look at the association between cardiometabolic diseases and gut microbiota. Enterotypes can be compared with the continuum or gradient of species functionality as an approach for classifying gut microbiota [7,8]. This concept reminds us that a consensus on how to accurately characterize a patient's microbiome would be useful in translation to clinical practice. Moreover, the authors highlight the fact that the relationship between diet and gut microbiota is a two-way street. On the one hand, microorganisms can metabolize macronutrients to produce smaller molecules, such as short-chain fatty acids. On the other, the type of food ingested affects the gut microbiota composition of the host [6]. Thus, the take-home message is that a thorough diet profile contributes to a more accurate characterization of the interplay between a patient's microbiome and potential cardiometabolic disorders.

Regarding cardiovascular diseases, this review suggests that the association between gut microbiota and hypertension observed in pre-clinical studies requires more robust evidence in humans to establish a cause-effect relationship [9,10]. Animal models suggest that trimethylamine N-oxide (TMAO)—a metabolite produced by gut microbes—may wield pro-atherogenic properties [11,12]. In addition, increased circulating levels of TMAO have been shown to correlate with increased cardiovascular risk and mortality in humans [13]. As TMAO may be a promising biomarker for cardiovascular diseases, it is interesting to speculate whether other metabolites produced by gut microbiota may have similar diagnostic value.

The role of gut microbiota in metabolic diseases is also addressed by Schiattarella et al. [6]. The authors report that changes in the microbiome affect weight gain and metabolism in animal models [14–16]. Similarly, the authors discuss the use of non-caloric artificial sweeteners and their potential association with type II diabetes [17]. Interestingly, intake of non-caloric artificial sweeteners has been observed to induce glucose intolerance via dysbiosis [18]. However, the potential link between gut microbiota

☆ Disclosures: The authors have no disclosures to report.

* Corresponding author at: Advanced Center for Chronic Diseases (ACCDiS), Faculty of Chemical and Pharmaceutical Sciences & Faculty of Medicine, Universidad de Chile, Santiago, Chile.
E-mail address: slavander@uchile.cl (S. Lavandero).

https://doi.org/10.1016/j.tcm.2018.08.009

and non-caloric artificial sweetener-induced type II diabetes requires further exploration.

The authors also discuss the role of gut microbiota in inflammation and modulation of the immune system. Indeed, given that chronic inflammation is a common finding in cardiovascular disease [19], it stands to reason that the microbiome and immune system may have a bidirectional relationship, which could be a therapeutic target.

The state of the art presented by Schiattarella et al. [6] reveals that the mechanisms involved in the interplay between gut microbiota and cardiometabolic diseases is poorly understood. Therefore, future research should focus on unraveling the complex signaling pathways mediating this interaction in order to fully harness its power to diagnose and treat cardiometabolic disorders.

From a clinical perspective, treatment with pre-, pro- and antibiotics, as well as diet modifications are easy and practical approaches to modulate the composition of gut microbiota. Thus, careful evaluation and regulation of the microbiome profile of patients with cardiometabolic diseases is an achievable goal and may constitute a substantial leap towards precision medicine.

Acknowledgments

This work was supported by FONDECYT (1161156 to S.L), FONDAP(15130011 to C.F. and S.L.) and Postdoctoral FONDECYT (3160298 to J.A.R.).

References

[1] Banerjee MN, Bolli R, Hare JM. Clinical studies of cell therapy in cardiovascular medicine: recent developments and future directions. Circ Res 2018;123:266–87.
[2] Gorabi AM, Hajighasemi S, Tafti HA, Soleimani M, Panahi Y, Ganjali S, Sahebkar A. Gene therapy in cardiovascular diseases: a review of recent updates. J Cell Biochem 2018 [Epub ahead of print]. doi:10.1002/jcb.27303.
[3] Roth GA, Huffman MD, Moran AE, Feigin V, Mensah GA, Naghavi M, et al. Global and regional patterns in cardiovascular mortality from 1990 to 2013. Circulation 2015;132:1667–78.
[4] Reilly JJ, El-Hamdouchi A, Diouf A, Monyeki A, Somda SA. Determining the worldwide prevalence of obesity. Lancet 2018;391:1773–4.
[5] Tang WH, Kitai T, Hazen SL. Gut microbiota in cardiovascular health and disease. Circ Res 2017;120:1183–96.
[6] Schiattarella GG, Sandino A, Esposito G, Perrino C. Diagnostics and therapeutic implications of gut microbiota alterations in cardiometabolic diseases. Trends Cardiovasc Med 2018 pii: S1050-1738(18)30155-5.
[7] Arumugam M, Raes J, Pelletier E, Le Paslier D, Yamada T, Mende DR, et al. Enterotypes of the human gut microbiome. Nature 2011;473:174–80.
[8] Jeffery IB, Claesson MJ, O'Toole PW, Shanahan F. Categorization of the gut microbiota: enterotypes or gradients? Nat Rev Microbiol 2012;10:591–2.
[9] Yang T, Santisteban MM, Rodriguez V, Li E, Ahmari N, Carvajal JM, et al. Gut dysbiosis is linked to hypertension. Hypertension 2015;65:1331–40.
[10] Adnan S, Nelson JW, Ajami NJ, Venna VR, Petrosino JF, Bryan RM Jr, et al. Alterations in the gut microbiota can elicit hypertension in rats. Physiol Genom 2017;49:96–104.
[11] Wang Z, Tang WH, Buffa JA, Fu X, Britt EB, Koeth RA, et al. Prognostic value of choline and betaine depends on intestinal microbiota-generated metabolite trimethylamine-N oxide. Eur Heart J 2014;35:904–10.
[12] Gregory JC, Buffa JA, Org E, Wang Z, Levison BS, Zhu W, et al. Transmission of atherosclerosis susceptibility with gut microbial transplantation. J Biol Chem 2015;290:5647–60.
[13] Schiattarella GG, Sannino A, Toscano E, Giugliano G, Gargiulo G, Franzone A, et al. Gut microbe-generated metabolite trimethylamine-N-oxide as cardiovascular risk biomarker: a systematic review and dose-response meta-analysis. Eur Heart J 2017;38:2948–56.
[14] Turnbaugh PJ, Backhed F, Fulton L, Gordon JI. Diet-induced obesity is linked to marked but reversible alterations in the mouse distal gut microbiome. Cell Host Microbe 2008;3:213–23.
[15] Turnbaugh PJ, Ley RE, Mahowald MA, Magrini V, Mardis ER, Gordon JI. An obesity associated gut microbiome with increased capacity for energy harvest. Nature 2006;444:1027–31.
[16] Ridaura VK, Faith JJ, Rey FE, Cheng J, Duncan AE, Kau AL, et al. Gut microbiota from twins discordant for obesity modulate metabolism in mice. Science 2013;341:1241214.
[17] Fagherazzi G, Vilier A, Saes Sartorelli D, Lajous M, Balkau B, Clavel-Chapelon F. Consumption of artificially and sugar-sweetened beverages and incident type 2 diabetes in the Etude Epidemiologique aupres des femmes de la Mutuelle Generale de l'Education Nationale–European Prospective Investigation into Cancer and Nutrition cohort. Am J Clin Nutr 2013;97:517–23.
[18] Suez J, Korem T, Zeevi D, Zilberman-Schapira G, Thaiss CA, Maza O, et al. Artificial sweeteners induce glucose intolerance by altering the gut microbiota. Nature 2014;514:181–6.
[19] Golia E, Limongelli G, Natale F, Fimiani F, Maddaloni V, Pariggiano I, et al. Inflammation and cardiovascular disease: from pathogenesis to therapeutic target. Curr Atheroscler Rep 2014;16:435.