Int J Cardiovasc Sci. 2023; 36:e20220193

EDITORIAL

The Influence of Primary Atherosclerotic Diseases on the Occurrence of Secondary Disease

Marcelo Chiara Bertolami[1]

Instituto Dante Pazzanese de Cardiologia,[1] Universidade de São Paulo, São Paulo, SP – Brazil

Editorial referring to the article: The Influence of the Primary Atherosclerotic Diseases on the Occurrence of the Secondary Disease

Atherosclerosis is a chronic inflammatory process in which the accumulation of cholesterol-laden plaque restricts blood flowin the arterial vasculature. The occlusion of arteries by expanding plaque or emboli from plaque rupture or erosion underlies a variety of cardiovascular diseases including myocardial infarction, ischemic cardiomyopathy, stroke, and peripheral vascular disease. Although cardiovascular disease remains a leading cause of morbidity and mortality in high-income countries, an epidemiological shift has occurred in recent decades.[1,2] Improvements in vaccination and treatment of infectious diseases have led to a notable increase in the prevalence of cardiovascular diseases in low- and middle-income nations.

The prominent and increasing burden of atherosclerotic cardiovascular disease has stimulated growing interest in the elucidation of its pathogenesis, risk factors, prevention, and treatments. There has been remarkable progress in the understanding of atherosclerosis pathophysiology,[3] and new risk factors, in addition to traditional ones, have been described to be implicated, including disturbed sleep, physical inactivity, the microbiome, the microbiota and gender-related factors.[4] Also, knowledge about the importance and possibility of its early prevention, preferably during childhood or even earlier in pregnancy, and about optimized treatment by non-pharmacological therapies,[5] pharmacotherapy,[6] and/or interventional procedures,[7] has expanded, tremendously; but even so, atherosclerotic cardiovascular disease remains the number one killer in the world.[2]

Keywords

Atherosclerosis; Cardiovascular Diseases; Myocardial Infarction; Stroke; Peripheral Vascular Disease.

A fundamental part of any preventive or therapeutic strategy proposed for atherosclerotic cardiovascular diseases is the definition of patient's cardiovascular risk. The Update of the Brazilian Guideline on Dyslipidemias and Cardiovascular Prevention, 2017, suggests a step-by-step approach to identify the risk of each patient. The first step is the identification of the very high-risk patient characterized by the presence of established atherosclerotic cardiovascular disease: coronary, cerebrovascular or peripheral vascular disease.[8]

The American guidelineon the management of blood cholesterol[9] considers very high-risk patients the ones with a history of multiple major atherosclerotic cardiovascular disease events or history of one major atherosclerotic cardiovascular disease event – acute coronary syndrome episode (within the past 12 months), myocardial infarction (other than recent acute coronary syndrome event listed above), ischemic stroke, symptomatic peripheral arterial disease (claudication with ankle-brachial index <0.85, or previous revascularization or amputation) – and multiple high-risk conditions.

Finally, the European guidelines on the management of dyslipidemias[10] considers as very high-risk patients with documented atherosclerotic cardiovascular disease, either clinical or unequivocal on imaging. Documented atherosclerotic cardiovascular disease includes previous acute coronary syndrome (myocardial infarction or unstable angina), stable angina, coronary revascularization (percutaneous coronary intervention, coronary surgery, and other arterial revascularization procedures), stroke and transient ischemic attack, and peripheral arterial disease. However, in these three guidelines, the definition of risk has been based on the different territories (heart, brain or lower extremities) involved.

Mailing Address: Marcelo Chiara Bertolami
Avenida Sabiá, 667, ap 141. Postal code: 04515-001. Moema, São Paulo, SP - Brazil.
E-mail: bertolami@uol.com.br

DOI: https://doi.org/10.36660/ijcs.20220193

In this issue of the International Journal of Cardiovascular Sciences, Picoli et al.[11] describe the role of the territory involved in the primary disease territory on the occurrence of secondary disease. The authors had the objective to calculate the statistical probability of developing myocardial infarction, ischemic stroke or peripheral arterial disease after the occurrence of a primary event and its subsequent treatment. Their data included 507,690 patients with primary atherosclerotic disease, who were in treatment during the study period and who developed or did not develop a second atherosclerotic cardiovascular disease event. After searching the literature, they found 6,840 papers that were analyzed according to the first inclusion criterion: 180 studies of patients with clinical and imaging diagnosis of acute myocardial infarction, ischemic stroke and/or peripheral arterial disease. Full text analysis led to the exclusion of 131 papers remaining 49 that were used for data extraction and statistical treatment. After calculating the probabilities, the authors found that 2.99% of patients who presented myocardial infarction as the primary atherosclerotic disease developed ischemic stroke and 2.86% developed peripheral artery disease during or after treatment. Patients diagnosed with ischemic stroke as the primary atherosclerotic disease showed a 0.95% risk for developing myocardial infarction and a 5.07% risk for developing leg ischemic event. Patients diagnosed with peripheral artery disease as the primary atherosclerotic disease showed an 8.79% risk for developing ischemic stroke and a 9.17% risk for myocardial infarction as the secondary atherosclerotic disease. They also calculated the probability of a patient who had an initial event to develop a second one. For a patient who had a myocardial infarction as the primary event, the probability of developing an ischemic stroke or leg ischemia was about 50%, similar to a patient who had peripheral artery disease as the primary event and developed myocardial infarction or ischemic stroke as the second episode. The authors called attention to patients who suffered an ischemic stroke as the primary event for whom the probability of developing peripheral arterial disease was high, about 84%, and myocardial infarction only 16%.

A possible limitation of the study was that the available data do not include the details of treatment offered to each patient. It's currently known that different medical specialties may treat patients differently, often not adequately according to guideline recommendations.[12,13] Furthermore, the papers included in this study came from different services and countries, and available evidence indicate important disparities during patients' follow-up in different centers.[14] These facts may also influence and explain the different courses of primary atherosclerotic event depending on the territory involved. Also, the paper does no relay practical clinical information about the probability of a patient presenting a recurrent event involving the same territory of the first event (e.g., a myocardial infarction after the first episode involving the heart).

Take-home messages given by the authors are:

- Patients who presented ischemic stroke or myocardial infarction as the first event possibly may have been monitored and treated to avoid a secondary event, although the probability of this is low.
- Patients with peripheral arterial disease have a higher incidence of secondary atherosclerotic diseases, highlighting the importance of careful monitoring of these patients, especially considering that they may be asymptomatic.
- If diagnosed and treated early, secondary diseases can be avoided.

References

1. Libby P. The Changing Landscape of Atherosclerosis. Nature. 2021;592(7855):524-33. doi: 10.1038/s41586-021-03392-8.
2. Dai H, Much AA, Maor E, Asher E, Younis A, Xu Y, et al. Global, Regional, and National Burden of Ischaemic Heart Disease and Its Attributable Risk Factors, 1990-2017: Results from the Global Burden of Disease Study 2017. Eur Heart J Qual Care Clin Outcomes. 2022;8(1):50-60. doi: 10.1093/ehjqcco/qcaa076.
3. Jebari-Benslaiman S, Galicia-García U, Larrea-Sebal A, Olaetxea JR, Alloza I, Vandenbroeck K, et al. Pathophysiology of Atherosclerosis. Int J Mol Sci. 2022;23(6):3346. doi: 10.3390/ijms23063346.
4. Padro T, Muñoz-Garcia N, Peña E, Badimon L. Sex Differences and Emerging New Risk Factors for Atherosclerosis and Its Thrombotic Complications. Curr Pharm Des. 2021;27(29):3186-97. doi: 10.2174/1381612826666201118094209.
5. Matei D, Buculei I, Luca C, Corciova CP, Andritoi D, Fuior R, et al. Impact of Non-Pharmacological Interventions on the Mechanisms of Atherosclerosis. Int J Mol Sci. 2022;23(16):9097. doi: 10.3390/ijms23169097.
6. Hoogeveen RM, Hanssen NMJ, Brouwer JR, Mosterd A, Tack CJ, Kroon AA, et al. The Challenge of Choosing in Cardiovascular risk Management. Neth Heart J. 2022;30(1):47-57. doi: 10.1007/s12471-021-01599-y.
7. Writing Committee Members, Lawton JS, Tamis-Holland JE, Bangalore S, Bates ER, Beckie TM, et al. 2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularization: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical

Practice Guidelines. J Am Coll Cardiol. 2022;79(2):e21-e129. doi: 10.1016/j.jacc.2021.09.006.

8. Faludi AA, Izar MCO, Saraiva JFK, Chacra APM, Bianco HT, Afiune Neto A, et al. Atualização da Diretriz Brasileira de Dislipidemias e Prevenção da Aterosclerose – 2017. Arq Bras Cardiol. 2017;109(2 Supl 1):1-76. doi: 10.5935/abc.20170121.

9. Grundy SM, Stone NJ, Bailey AL, Beam C, Birtcher KK, Blumenthal RS, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2019;73(24):3168-209. doi: 10.1016/j.jacc.2018.11.002.

10. Mach F, Baigent C, Catapano AL, Koskinas KC, Casula M, Badimon L, et al. 2019 ESC/EAS Guidelines for the Management of Dyslipidaemias: Lipid Modification to Reduce Cardiovascular Risk. Eur Heart J. 2020;41(1):111-88. doi: 10.1093/eurheartj/ehz455.

11. Picoli PMC, Amaral CST, Trovatti E. The Influence of Primary Atherosclerotic Diseases on the Occurrence of Secondary Disease. Int J Cardiovasc Sci. 2023; 36:e20210251. doi: 10.36660/ijcs.20210251.

12. Stafford RS, Blumenthal D. Specialty Differences in Cardiovascular Disease Prevention Practices. J Am Coll Cardiol. 1998;32(5):1238-43. doi: 10.1016/s0735-1097(98)00380-5.

13. Aitken SJ. Peripheral Artery Disease in the Lower Limbs: The Importance of Secondary Risk Prevention for Improved Long-Term Prognosis. Aust J Gen Pract. 2020;49(5):239-44. doi: 10.31128/AJGP-11-19-5160.

14. Steg PG, Greenlaw N, Tendera M, Tardif JC, Ferrari R, Al-Zaibag M, et al. Prevalence of Anginal Symptoms and Myocardial Ischemia and Their Effect on Clinical Outcomes in Outpatients with Stable Coronary Artery Disease: Data from the International Observational CLARIFY Registry. JAMA Intern Med. 2014;174(10):1651-9. doi: 10.1001/jamainternmed.2014.3773.