



## EDITORIAL COMMENT

## Atherothrombotic ischemic disease: The price is too high to ignore



### Doença isquémica aterotrombótica: o preço é demasiadamente elevado para ser ignorado

Marco Costa

*Cardiovascular Intervention Unit, Cardiology Department, Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal*

Atherosclerosis is a progressive disease caused by thickening and cumulative hardening of the arterial walls, mainly due to cholesterol deposits. This pathological process is associated with several risk factors, including dyslipidemia, hypertension, obesity, smoking, diabetes and some genetic abnormalities. The starting point in atherogenesis is the deposition of low-density lipoprotein cholesterol (LDL-C) and cholesterol-rich apolipoprotein B within the arterial wall, and therefore high LDL-C levels are the most important direct risk factor in atherosclerosis.<sup>1</sup> Prevention of ischemic atherothrombotic disease centers on promoting healthy lifestyles and, at the individual level, by combating unhealthy conditions and reducing the impact of direct and indirect cardiovascular risk factors.

Atherosclerosis can affect arteries in any part of the body and is the cause of important diseases such as myocardial infarction, ischemic stroke and peripheral arterial disease. Ischemic heart disease and stroke are the leading causes of death worldwide (accounting for 15 million deaths per year) and have been for the past 15 years.<sup>2</sup>

With the latest advances in invasive medicine and new drugs, more individuals survive the first ischemic event, but they are at high risk for recurrence. In patients who have had a myocardial infarction and survived, daily aspirin decreases the chance of recurrence of an atherosclerotic

event within five years by 25%, beta-blockers by 25%, angiotensin-converting enzyme inhibitors by 25% and statins by more than 40%. So, hypothetically, if a person could only take one medication after a myocardial infarction (which of course is not desirable), the most effective would be a statin.<sup>3</sup> There is strong evidence that lowering blood cholesterol levels using low-cost statins or ezetimibe is cost-effective for secondary and even primary prevention. An effective statin regimen for about five years in 10 000 patients would typically prevent major vascular events in about 1000 (10%) patients at high risk of clinical events and in 500 patients (5% absolute benefit) who are at high risk but without events (primary prevention). The evidence indicates that generic statin-based treatments are cost-effective for people at least down to 1% annual total cardiovascular risk and could be cost-effective at even lower risk.<sup>4,5</sup>

The article by Costa et al. published in this issue of the *Journal*<sup>6</sup> gives an estimate of the costs of atherosclerosis in Portugal, based on a prevalence approach, and using national epidemiological sources. These costs were estimated at 1.9 billion euros per year (11% of all health expenditure), including direct (58%) and indirect (42%) costs. Surprisingly (or perhaps not), most of the direct costs were related to primary health care (55%) rather than hospitalizations (18%), which include surgical and percutaneous procedures that are often necessary, such as angioplasty, revascularization surgery, thrombectomy and defibrillator implantation. In recent years there has been

E-mail address: [marcostacard@sapo.pt](mailto:marcostacard@sapo.pt)

wider use of new drugs, leading to longer survival of patients with atherothrombotic disease, although at the expense of increasing the number of so-called mandatory drugs, which have a clear influence on prognosis. Regarding indirect costs, it was not surprising that the largest slice (91%) was due to absenteeism in the workplace.

Estimating the costs related to atherosclerosis in a country like Portugal necessitates estimation of the costs of all these diseases and their risk factors. From a methodological point of view, this calculation is very difficult and the result will be probably less than the actual figure, as it is practically impossible to predict all the consequences of an entity such as atherosclerosis. Examples of other diseases not directly accounted for in this study and strongly associated with atherosclerotic processes are some forms of dementia and kidney failure.

Regardless of the methodology used in this and similar studies,<sup>7,8</sup> the same conclusion is always reached – variables are missing and the costs related to atherosclerosis are probably even higher than those presented. All of this leads to the main question: can these costs be reduced? Probably yes, if more money is spent on prevention measures, in order to avoid symptomatic atherosclerosis, which is more expensive. We also need to increase the use of available cost-effectiveness analyses of drugs and hospital interventions. Finally, it is still necessary to educate doctors, institutions and government decision-makers.

The value of new antiatherosclerotic drugs and hospital interventions is maximized when they are used in the right way in clinical practice. Clinical trials conducted during drug development help predict the real value of a specific therapy. Regulatory approval is an indication of value, which is complemented by an assessment of clinical value for decisions about reimbursement, using the methodology of health technology assessment. Formal cost-effectiveness studies are an important part of this methodology, to guide decisions on health care spending. For instance, incremental cost-effectiveness ratios, quality-adjusted life-years and life expectancy are valuable parameters for assessing the usefulness of a given therapeutic intervention, and so all physicians should be familiar with these tools.

According to the American Heart Association's Heart Disease and Stroke Statistics 2020 Update,<sup>9</sup> the mean annual direct and indirect cost in the USA of cardiovascular disease and stroke, caused primarily by atherosclerosis, was estimated at \$351.3 billion (\$1048 per capita). The same report estimates that by 2035, total projected costs (direct and indirect) will increase markedly for older patients.

The aging of the population, which is not only occurring in the USA, will increase this health expenditure, particularly

direct costs related to outpatient care and hospital interventions that individuals can expect throughout their adult life. Life expectancy for Portuguese adults is currently 80.8 years (77.8 for men and 83.4 for women), and this is expected to increase in the coming years.<sup>10</sup>

To deal with this situation, a new culture of education and responsibility for physicians, hospitals, universities and government entities is needed, to achieve effective reductions in costs related not only to atherosclerosis, but also to other areas of health care.

## Conflicts of interest

The author has no conflicts of interest to declare.

## References

1. Ference BA, Ginsberg HN, Graham I, et al. Low-density lipoproteins cause atherosclerotic cardiovascular disease. 1. Evidence from genetic, epidemiologic, and clinical studies. A consensus statement from the European Atherosclerosis Society Consensus Panel. *Eur Heart J.* 2017;38:2459–72.
2. Global, regional, and national age-sex specific mortality for 264 causes of death, 1980–2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet.* 2017;390:1151–210.
3. 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk: The Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS). *Eur Heart J.* 2020;41:111–88.
4. Collins R, Reith C, Emberson J, et al. Interpretation of the evidence for the efficacy and safety of statin therapy. *Lancet.* 2016;388:2532–61.
5. Pandya A, Sy S, Cho S, et al. Cost-effectiveness of 10-year risk thresholds for initiation of statin therapy for primary prevention of cardiovascular disease. *JAMA.* 2015;314:142–50.
6. Costa J, Alarcão J, Amaral-Silva A, et al. Os custos da aterosclerose em Portugal. *Rev Port Cardiol.* 2021;40.
7. Vlayen J, De Backer G, Peers J, et al. Atherosclerotic cardiovascular diseases in Belgium: a cost-of-illness analysis. *Cardiovasc Ther.* 2008;22:487–94.
8. Leal J, Luengo-Fernández R, Gray A, et al. Economic burden of cardiovascular diseases in the enlarged European Union. *Eur Heart J.* 2006;27:1610–9.
9. Virani SS, Alonso A, Benjamin EJ, et al. Heart disease and stroke statistics-2020 update: a report from the American Heart Association. *Circulation.* 2020;141:e139–596.
10. Tabuas de Mortalidade 2016-2018 - Instituto Nacional de Estatística; 2019. Available at [https://www.ine.pt/xportal/xmain?xpid=INE&xpgid=ine\\_destaquas&DESTAQUESdest\\_boui=354419871&DESTAQUESmodo=2](https://www.ine.pt/xportal/xmain?xpid=INE&xpgid=ine_destaquas&DESTAQUESdest_boui=354419871&DESTAQUESmodo=2)