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EDITORIAL

Update and validation of cardiovascular risk

Actualización y validación del riesgo cardiovascular

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Cardiovascular diseases are the most prevalent diseases and are currently the leading cause of death, so identifying those who are at greatest cardiovascular risk is a priority for epidemiological, healthcare and economic reasons. For this reason, the first section of the cardiovascular prevention guidelines provides some guidance on how to assess the cardiovascular risk of our patients.[1]

To calculate cardiovascular risk based on its risk factors there are both quantitative and qualitative systems, the quantitative ones being the most widespread, such as the systems derived from the Framingham study[2] or the European SCORE[3] (Systematic Coronary Risk Estimation). However, in clinical practice we use a mixed approach, as what interests us is risk stratification: i.e., recognising the risk stratum that each patient fits within: low, intermediate or moderate, high, or very high risk.[1] A new risk category recently introduced is extreme risk, with LDL-cholesterol targets lower than those set for very high risk subjects.[1,4] For this stratification we use a number of conditions that defines the stratum or level of risk (qualitative calculation). We also use a cardiovascular risk quantification system that gives us a numerical value that we then convert into the previously mentioned levels.

Once the risk level is known, treatment targets can be set for these risk factors, especially as regards lipids. By knowing the treatment targets, a treatment strategy can be devised to achieve these. Risk stratification is therefore an essential tool in patient management.

Although patients who have already suffered a cardiovascular event (myocardial infarction, stroke, peripheral arterial disease, etc.) are those most at risk of having another event, at population level, the greatest number of events occur in subjects in a position of primary prevention. It is therefore important to have valid risk quantification systems in primary prevention.

At the European level, cardiovascular prevention guidelines[1] recommend the SCORE2 system to calculate cardiovascular risk in primary prevention. In addition, the usual age range for risk quantification has been extended from a maximum age of 65 or 70 years to approximately 90 years, thanks to the SCORE2-OP[5] (older people) system, which is based on different studies to those of SCORE2 but uses the same calculation methodology. The guidelines themselves recognise the limitations of these 10-year absolute risk calculation systems.

The main limitation is the extremely wide age range. It is common for young subjects to record extremely heightened risk factors but not high cardiovascular risk. At the other extreme, older subjects, even if they do not have any risk factors - or have them under control - their risk is high. This can lead to under-treatment of the young, with the obvious risk of cardiovascular events, and over-treatment of the elderly, with the consequent unnecessary financial expense or the possibility of side effects that could have been avoided.

This fact has led to the search for alternatives to the calculation of absolute 10-year risk over the last two decades. Concepts such as relative risk, risk percentiles, vascular age, vascular ageing rate and long-term (e.g., lifetime) risk are alternatives,[6] some of which are recommended in cardio-

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vascular prevention guidelines.[1] These alternatives can be used in conjunction with the 10-year risk calculation.

The article by C. Brotons et al.[7] published in this issue of *Clínica e Investigación en Arteriosclerosis* fits into this context by providing an update and validation of a lifetime cardiovascular risk function: IBERLIFERISK.[2] This is the update of the previous IBERLIFERISK model. It uses data from Spain, from a sample working population of 762,058 workers who underwent an occupational health examination between 2004 and 2007 and were assessed for cardiovascular events up to 2017, taken from the Ibermutua Prevention Society data. With the large sample size and taking Cox's proportional hazard model, they constructed a model that extends the usual age range from 18 to 75 years. Seventy percent of the cohort was used to build the model and 30% to assess calibration and discrimination.

Although the new model does not improve the calibration of the previous model, it does improve discrimination with areas under the Receiver Operating Curve (ROC) curve of 0.88 in men and 0.77 in women. This improvement is important as, when compared with the SCORE equation, widely used in our environment, this recorded an AUC between 0.71 and 0.84 in different cohorts in low-risk countries such as ours.[8] When the SCORE equation was validated in the Spanish cohort of the FRESCO study, an AUC of 0.68 was obtained in men and 0.69 in women.[9] An AUC of 1, as we recall, indicates perfect discrimination and an AUC of 0.5 is equivalent to flipping a coin.

Other long-term risk functions have been published such as the prediction of lifetime risk of cardiovascular disease by risk factor burden at age 50 and the LIFEtime-perspective CardioVascular Disease (LIFE-CVD) model.[10] Neither model has been developed or validated in Spain. In our field, we are therefore up against a pioneering study of lifetime risk estimation. However, work still remains to be done, as IBERLIFERISK[2] was validated with part of the study cohort and should be validated externally. This is work that the authors themselves acknowledge as having begun.

Although the cardiovascular prevention guidelines indicate the cut-off points in the 10-year absolute risk models, defining the different risk categories (low, intermediate, high and very high) with SCORE2 and SCORE2-OP, no equivalent cut-off points were provided in the other alternative risk assessment systems and no treatment instructions have therefore been given. If this situation does not change, we can use the alternative systems only to supplement the risk assessment and to inform the patient of his or her risk status and motivate them to better adhere to hygiene-based, dietary and pharmacological measures.

Cardiovascular risk assessment is one of the initial steps in the care of patients with cardiovascular risk factors. There are still gaps in knowledge, however, and new avenues are opening up to better assess patients. Undoubtedly, the work presented in this issue of *Clínica e Investigación en Arteriosclerosis* is a very useful tool for improvement in patient care.

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