Can We Stratify Cardiovascular Risk in Argentina?

¿Podemos Estratificar el Riesgo Cardiovascular en la Población Argentina?

CARLOS G. SANTOS-GALLEGO, JUAN J. BADIMÓN

Correct stratification of cardiovascular risk (CVR) is complex. In primary prevention [defined as the preventive activity performed in people without atherosclerotic evidence (most of the population > 35 years)] this is conceived as a population strategy, consisting in identifying high risk subjects to decrease levels of cardiovascular risk factors (CVRF) by means of lifestyle or medication changes, as this is a much more efficient approach than focusing on the low risk population.

The best tool to establish priorities in primary prevention is the accurate individual CVR estimation using CVR scores or functions. Cardiovascular risk scores are mathematical models based on cohort prospective studies modeling CVR as a function of different non-modifiable (as age and sex) and modifiable (smoking, hypertension, cholesterol or its fractions and diabetes mellitus) CVRF.

DO DIFFERENT CVR SCORES HAVE THE SAME EFFICACY?

There are numerous CVR scores, which means none is optimal and that all have limitations. Currently, the most important are the Framingham score in its original 1991 version, (1) in its updated 1997 version, (2) or in the most recent 2008 version, (3) the one designed by the European Society of Cardiology referred as SCORE (4) and the QRISK score (5) (developed by British NICE guidelines). However, there other less used scores, such as the PROCAM study (6) or the one derived from the NHANESI study. (7) Finally, the new 2013 ACC/AHA American guidelines (8) developed the atherosclerotic cardiovascular disease (ASCVD) tables for subjects between 40 and 75 years, based on four previous American cohorts.

Previous experience has shown that original scores can erroneously determine the true CVR by their general application to populations different (both genetically as dietary and even culturally) from the one that generated the original score. A classic example is given by the Framingham score (based on the Anglo-Saxon population and with an western diet) exhibiting almost a threefold overestimation of the true CVR (i.e. it adjusts erroneously) in the Spanish population (of different genetic origin and with a Mediterranean diet).

(9) Therefore, adaptations of the original functions to specific populations have been performed, as the function adjustment performed by REGICO for the Spanish population to compensate for the CVR overestimation obtained with the Framingham equation. (10)

The article by Masson et al work published in this issue of the Journal (11) represents a step forward within the same concept. The authors have applied different scores (Framingham, SCORE and the one developed by WHO) to a primary prevention population of the Autonomous City of Buenos Aires and Greater Buenos Aires (772 patients, age 52 ± 11 years, 66% women). Depending on whether the Framingham, the European SCORE or WHO score was applied, 76.8%, 50.9% and 91.7% of cases were respectively classified as "low risk". The most remarkable fact is the poor concordance among the three scores (kappa = 0.14), pointing out the importance of validating scores and specifically adapting them to each country, in this case Argentina. These findings are not exclusive of our country; similar results have been recently obtained in a Spanish study, (12) where the percentage of subjects at high CV risk in a primary prevention population (age 40 ± 10 years, 68% men) ranged, depending on the criterion employed, between 3.74% if the European SCORE was applied, 6.85% if the British QRISK score was used and 20.83% if the new 2013 ACC/AHA American guideline ASCVD tables were employed. A possible explanation for this great disparity refers to the different endpoints used, i.e. the probability of developing different endpoints: SCORE measures death, the QRISK assesses CV morbi-mortality due to coronary artery disease and stroke, while the new American guidelines (ASCVD) evaluate the morbidity and mortality risk due to atherosclerotic disease in general (including not only coronary disease and stroke, but also peripheral artery disease).

Masson et al. should be congratulated on their effort, as their work, (11) by identifying the poor concordance of the different scores in Argentina, generates doubt about which is the most "adequate" for application. On the other hand, the new 2013 American guidelines (8) recommend treatment if CVR is over

7.5%. However, the authors of the present study find that the optimal cut-off point (ROC curve) to detect carotid plaque in this Argentine population was nearer 5% than 7.5%, highlighting the need to calibrate the original tables in the specific populations to establish whether the cut-off points suggested by the new guidelines adjust correctly to our region.

DO DIFFERENT CVR SCORES MAKE US PRESCRIBE THE SAME MEDICATION?

The publication of the new 2013 ACC/AHA lipid guidelines (8) has involved a great international scientific debate due to the substantial changes introduced with respect to previous European and American guidelines. These new guidelines assume a change of paradigm regarding statins and recommend treating CV disease per se (and not CVRF) when CVR is > 7.5% at 10 years (according to the new calculation tool developed for ASCVD). One of the most controversial aspects is the elimination of therapeutic objectives (for example, LDL-C) both for primary and secondary prevention, and to use exclusively the CVR profile to select statin therapy intensity. In this sense, the British NICE guidelines (based on the QRISK2 score) use the same criterion that the new American guidelines. The main difference between the new 2013 ACC/AHA and European guidelines are:

1. The new 2013 ACC/AHA guidelines are exclusively based on randomized clinical trials which imply the exclusion of a significant amount of data and promote mainly a statin-centered vision.

2. The new calculation tool used in the ACC/AHA guidelines to estimate CVR in primary prevention has not been fully evaluated. In fact, a recent, methodologically very detailed article (13) shows that the "real" risk observed in a population with known CVR (belonging to the Women´s Health Study) is lower than the "estimated" CVR calculated according to the ASCVD tables proposed by the new guidelines.

3. In the new guidelines, the most important risk factor is age, far away from the rest. For example, a 65-year old woman with 175 mg/dL cholesterol, LDL 96 and HDL 54, systolic blood pressure 134 mmHg (under linisopril 5 mg daily treatment), despite having a well-controlled lipid profile, presents a CVR of 7.7% due to her age according to the new American guidelines, defining initiation of statin treatment). (14) However, most clinicians would not agree with this statin indication.

4. The reduction of statin therapy threshold in primary prevention implies that a considerable number of patients should be treated with statins, leading to an increase in economic expenditure and in the population chronically exposed to statins with the ensuing increase of secondary effects, such as myalgia or diabetes. (14)

Masson et al. (11) have performed a great work analyzing the percentage of patients that should be treated with statins according to the CVR score applied. Essentially, they found that 23.6%, 7% and 33% of cases had absolute statin indication, respectively based on the Framingham, the European score and the new 2013 ACC/AHA guidelines. This important variation in the percentage shows the great discrepancy among different guidelines.

Other recent studies confirm Masson et al.´s findings. (11) An American study (15) modeled the number of patients that would be treated with the new 2013 ACC/AHA guidelines. Based on the CVR profile of the NHANES-III study 2005-1010 cohort (3,773 participants) and extrapolating that CVR profile to all the United States population aged between 40 and 75 years (115.4 million persons), it was concluded that the number of subjects that should be treated with statins would be over 43.2 million (37.5% of the whole American population); specifically, most of this difference would correspond to subjects without CV disease. (16) Age is the most important CVRF according to the new guidelines (and regrettably not modifiable): in the subgroup of 60-75-year old patients (primary prevention), this percentage would increase statin treatment from 30.4% to 87.4% in men and from 21.2% to 53.6% in women. A similar European study analyzed a sample of 3,297 Swiss subjects with ages ranging between 50 to 75 years and also estimated that use of the new 2013 ACC/AHA guidelines would double the eligible number of persons to receive statins, (17) a difference that would be much higher in the group from 60 to 70 years. One of the most interesting results was that by extrapolating these data to the whole Swiss population, the application of the American guidelines would increase the cost of overall CV prevention in 337.8 million euros. A similar observation has been found in the Spanish population, a population more similar to that of Argentina: from a total of 258,676 workers included in the study, (12) 7.95% should be treated if the new 2013 ACC/AHA guidelines were followed, 5.15% if the British NICE (and its QRISK2 score) guideline was accepted and 1% if the European society recommendations (SCORE) were observed. In conclusion, if the 2013 ACC/AHA guidelines were followed, the daily cost of statins would be multiplied by 8.

CONCLUSION

Masson et al.´s study suggests the need of being very careful in the choice and use of any of these "universal" CVR scores until we have the specific assessment in the real population on which they will be applied.

Conflicts of interest
None declared

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