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Statins for primary prevention: identifying low-risk individuals

Yu-li Huang, Yi Huang and Yan-xian Wu

We read the Review by Željko Reiner (Statins in the primary prevention of cardiovascular disease. *Nat. Rev. Cardiol.* doi:10.1038/nrcardio.2013.80)[1] with great interest. We are particularly interested in the role of statins in primary prevention of cardiovascular disease (CVD) in individuals at low cardiovascular risk.

As was well discussed in the Review, clear evidence exists to support the use of statins for primary prevention in high-risk individuals.[1] A risk of developing CVD >20% over 10 years, or >10% over 5 years, is widely used as the cut-off point for prescribing statins.[2] However, the use of statins in low-risk individuals is controversial. A meta-analysis from the Cholesterol Treatment Trialists' (CTT) Collaborators showed that statins reduce the risk of major cardiovascular events by about 20% across all levels of baseline risk (even in individuals with a 5-year risk of major vascular events that is <10%).[3] The CTT Collaborators suggested that the current guidelines for CVD prevention might need to be reconsidered.[3] Their study raises enthusiasm for statins in the primary prevention of CVD in individuals at low cardiovascular risk. In fact, some have advocated treating 'all comers' with statins.[4] Several issues, however, should be considered before advocating the widespread use of statins in individuals at low risk, such as the feasibility, desirability, and cost-effectiveness of such a strategy, and the quality of life for apparently healthy individuals who are prescribed lifelong drug therapy. Also important are potential adverse effects of statins.[2,5,6]

We agree that statins are likely to be beneficial to patients with low cardiovascular risk calculated using traditional risk-assessment algorithms, such as the Framingham Risk Score and the SCORE (Systematic COronary Risk Estimation) charts.[4] However, additional risk-stratification options are needed to guide the use of statins in low-risk individuals. Data from the JUPITER trial[7] showed that individuals with an elevated level of C-reactive protein measured by the high-sensitivity assay (hs-CRP) benefit from statin use, regardless of their LDL-cholesterol level. After this trial, hs-CRP is becoming accepted as a novel cardiovascular risk factor.[7]

Coronary artery calcium (CAC) scoring has been shown to predict coronary events beyond the use of the traditional Framingham Risk Score, with a high CAC burden (≥300) being associated with increased risk.[8,9] Data from comparative effectiveness studies have suggested that quantification of CAC is a superior method to measurement of the hs-CRP level for improving risk assessment.[10] Investigators in the St. Francis Heart Study[11] enrolled patients with an elevated CAC level (CAC >80th percentile) and randomly allocated them to receive 20 mg of atorvastatin daily or placebo. The overall result did not meet statistical significance (P = 0.08) because of the limited power of the trial, but showed that atorvastatin significantly reduced the composite rate of adverse events from coronary heart disease by 30%.[11]

In conclusion, the use of statins for primary prevention in low-risk individuals remains an ambiguous area. We believe that additional risk-stratification options (such as measurement of the hs-CRP level and CAC scoring) should be explored in this population. A new risk-assessment algorithm that includes the traditional risk measures, but also incorporates these novel markers should be developed to identify low-risk patients and guide the prophylactic use of statins.

*Department of Cardiology, the Affiliated Hospital at Shunde (the First People's Hospital of Shunde), Southern Medical University, Penglai Road 1, Daliang Town, Shunde District, Foshan 528300, People's Republic of China (**Y.-l. Huang, Y.-x. Wu**). The Second Clinical Medicine Institute, Guangdong Medical College, Dongguan, People's Republic of China (**Y. Huang**).*
Correspondence to: Y.-l. Huang
hyuli821@163.com

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Competing interests
The authors declare no competing interests.

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