Assessing and Treating Cardiovascular Risk: Traditional Moderation is the Way to Go

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The 2013 American College of Cardiology/American Heart Association (ACC/AHA) guidelines on cholesterol treatment did away with target lipid levels to aim for, instead emphasizing the need to treat the correct group of patients at high risk of future cardiovascular events1. Similarly, the 2013 European hypertension guidelines made the point that treatment depends not just on blood pressure (BP) levels, but on the patient’s risk for adverse cardiovascular events, which is affected by other cardiovascular risk factors, target organ damage and the presence of established disease2. Clinicians are increasingly being called upon to stratify patients and to treat the patient at highest risk of clinical events rather than to aim for some arbitrary measured parameter.

To more accurately calculate the 10-year risk of clinical cardiovascular disease, defined as the occurrence of nonfatal myocardial infarction (MI), coronary death as well as fatal and nonfatal stroke, the ACC/AHA has drawn up a new Pooled Cohort Equation (available electronically at http://tools.cardiosource.org/ASCVD-Risk-Estimator/) to replace the previous Framingham risk scores3. Nevertheless, this stratification methodology is still based on the traditional risk factors of sex, age, race, total and HDL cholesterol, presence of diabetes or treated hypertension, smoking status and systolic BP level. High sensitivity C-reactive protein (hsCRP) and carotid intima-media thickness (CIMT) are not included in the Pooled Cohort Equation although they have been consistently shown to be able to pick up patients at high risk of subsequent cardiovascular events4. This issue of the MJM sees a report on measurement of CIMT and hsCRP in 123 urban Sarawakians with at least 2 cardiovascular risk factors; these subjects are also participants in a larger study recruiting 2726 patients from 8 Asian countries5. Since most studies on hsCRP and CIMT are not from Asia, the publication of these Malaysian, and Asian, data is certainly to be welcomed and lauded. In fact, the ACC/AHA guideline notes that in the absence of adequate data, Asian-Americans can be considered similar to the nonHispanic Whites but are probably at lower cardiovascular risk6.

CRP is a marker of inflammation and was initially used as an indicator of inflammatory disease, infection or malignancy when it rises above 10mg/L. CRP levels in the normal non-inflammatory range has also been found to be a useful indicator of cardiovascular risk and the commercial availability of sensitive assay techniques that can accurately quantify CRP in these normal levels has led to hsCRP becoming a useful tool for cardiovascular risk stratification7. Patients with CRP levels less than 1.0 mg/L are at low cardiovascular risk, levels between 1.0 to 3.0 mg/L indicate average risk while high risk patients have CRP levels above 3.0 mg/L. Recent guidelines now advise that cardiovascular risk is elevated with hsCRP levels at and above 2mg/L. Statin therapy lowers CRP levels and the cardiovascular protective effect of statins may in fact be from an anti-inflammatory impact8. Elevation of hsCRP has even been postulated as a therapeutic objective. Treatment of the healthy patient with essentially normal lipids but high hsCRP using a potent statin in the JUPITER trial produced highly significant reduction of myocardial infarction (HR 0.46; 95% CI, 0.30-0.70; P=0.0002), stroke (HR 0.52; 95% CI, 0.34-0.79; P=0.002) and total death (HR 0.80; 95% CI, 0.67-0.97; P=0.02)9.

B-mode ultrasound of the carotid circulation and calculation of CIMT is a marker of atherosclerotic load and is a reliable predictor of future cardiovascular events10. Statin therapy has been shown in numerous trials either to slow CIMT progression or even induce regression11. Interestingly, compared to simvastatin alone, the addition of ezetimibe to simvastatin further lowers lipid levels, but did not produce any change to CIMT progression over a 24 month period suggesting that ezetimibe may reduce lipid levels without affecting the atherosclerotic process12. On the other hand, metoprolol has been shown to retard progression of CIMT thereby raising a possible pathophysiological basis for its beneficial effect of reducing mortality after MI11.

The ACC/AHA Pooled Cohort Equation uses traditional parameters to stratify patients into a high risk group with 10-year risk of clinical events at and above 7.5% and the low risk group with a ≤ 7.5% risk. The low risk group comprised of first degree relatives, male <55, female <65 or coronary calcium ≥ 300 or ankle-brachial index <0.9 - elevates a patient into the high risk group. Measurement of CIMT is not recommended for clinical risk stratification because it does not significantly add to the risk information from the Pooled Cohort Equation and its performance is still associated with measurement and standardization issues13,14. Since expensive...
specialized equipment and personnel is required, measuring CIMT cannot be cost-effective as a primary screening tool for large populations.

It should be remembered that treatment of cardiovascular risk factors is treatment of the asymptomatic patient to protect against future adverse clinical cardiovascular outcomes. Since risk factor therapy is a lifelong endeavor, it is important for the patient to understand the aim of treatment and to undertake lifestyle changes before embarking on drug therapy. All drugs have side effects, and the more intensive the treatment, the more the side effects experienced. Drug induced disease or adverse clinical outcome is possible. Diabetes is increased with statin therapy in JUPITER and in BP levels had equivalent cardiovascular events but possibly a higher mortality compared to the less intensively treated group on prolonged follow-up. Some patients even get into a hyper-anxious state constantly monitoring their BP or lipid levels when in fact cardiovascular risk factor management, first with lifestyle change and then with drugs, is actually a part of the modern aging process.

In 2014 risk of adverse cardiovascular outcome is still accurately predicted by the traditional risk factors of sex, age, race, total and HDL cholesterol, presence of diabetes or treated hypertension, smoking status and systolic BP level. hsCRP is useful for further classifying those whose overall risk appear intermediate. The more expensive, time consuming and elaborate investigation of CIMT measurement should be reserved for research purposes in tertiary centres. All patients at high risk should be advised on lifestyle modification measures. In primary prevention amongst patients who are yet to manifest clinical disease, if drug therapy is needed, moderate but not intensive drug therapy is appropriate.

REFERENCES