Treatin Lipids in the General Population

The Editor's Roundtable on atherosclerosis regression raises a number of interesting points. The focus of the roundtable was on low-density lipoprotein (LDL) cholesterol and the mantra "Lower is better." I have a general population database for lipids (began in 1974 and finished in 2003), and in my general population of those aged ≥80 years and/or free living in the community, only 3 of 27 men (11%) and 5 of 42 women (12%) had LDL cholesterol levels ≤100 mg/dl. Most of these patients had high-density lipoprotein (HDL) cholesterol levels ≥40 mg/dl; 17 of 27 men (63%) and 40 of 42 women (95%). This implies that HDL can compensate for moderate levels of LDL.

In the roundtable, Dr. Ballantyne pointed out the value of the LDL/HDL ratio. I have used a modification of the LDL/HDL ratio for the past 25 years. The cholesterol retention fraction (CRF, calculated as [LDL - HDL]/LDL) incorporates the atherogenic and antiatherogenic properties of LDL and HDL into a single predictor and predicts the population of patients who will eventually sustain atherothrombotic events in 5% more cases than the simple LDL/HDL ratio.

The CRF can be combined with systolic blood pressure (SBP) into a graph with the CRF on the ordinate and SBP on the abscissa (Figure 1). I have drawn a threshold line with CRF-SBP loci of (0.74, 100) and (0.49, 140) on the principle of fewest false-negative results. 85% of those in my practice who developed atherothrombotic events from 1974 to 2005 had CRF-SBP plots above this threshold line. Of the 15% who could not be predicted by CRF-SBP plot position above the threshold line, most were cigarette smokers (current or former), leaving only 6% of the entire atherothrombotic population who could not be predicted by CRF-SBP plot position and/or cigarette smoking status, and those patients sustained their atherothrombotic events, on average, in the latter eighth decade of life. Therefore, in their absence of any history of cigarette smoking, as indicative of virtual immunity to atherothrombotic events.

Any therapy that brings CRF-SBP plot position below the threshold line results in angiographic stabilization or regression of coronary artery plaque in a minimum average of 75% of patients, and had the Program on the Surgical Control of the Hyperlipidemias been structured to control SBP, the average would have approached ≥95%. Using this graph, my treated patients have sustained only 2 acute myocardial infarctions since January 1, 2000: 1 on January 10, 2000, and 1 on March 17, 2008.

I submit that putting 100 million individuals on statins is not a viable option. In my opinion, a better option is to do serial testing of young individuals. The percentage of subjects whose CRF-SBP plot positions transgress the threshold line increases linearly with age, as does the percentage of those in the same population who develop atherothrombotic events. These lines run parallel, with a 40-year gap between the lines for men and a 20-year gap for women. Serial testing affords the opportunity to determine at what age a patient transgresses the threshold line and hence becomes at risk for a future atherothrombotic event. The higher the CRF, the earlier the event. Cigarette smoking also hastens the onset of atherothrombotic events.

In conclusion, I submitted that a targeted approach makes more sense than treating everyone with an LDL level ≥100 mg/dl (2.6 mmol/L). Although statins are relatively safe, when 100 million individuals are receiving them, even rare adverse events (such as rhombomylolysis) will affect many.

William E. Feeman, Jr., MD
Bowling Green, Ohio
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