PERSPECTIVES

Point/Counterpoint: The Role of Carotid Ultrasound

POINT: USES OF CAROTID PLAQUE MEASUREMENT AS A PREDICTOR OF CARDIOVASCULAR EVENTS

J. David Spence, MD, FRCPC

Vascular prevention is most cost-effective in high-risk patients, but secondary prevention misses many opportunities. The high-risk strategy—identifying patients with high levels of risk factors—is problematic because traditional risk factors predict only half of vascular events. In multiple regression, traditional risk factors explained only half of carotid atherosclerosis. New strategies are being explored, such as electron-beam computerized tomographic measurement of coronary calcification, to identify high-risk patients. Carotid plaque is a powerful tool for identifying and managing high-risk vascular patients, as it explains twice as much of unexplained vascular risk as coronary calcium by electron beam computerized tomography, and it has significant advantages compared with intimal-medial thickness. After adjustment for risk factors, patients in the highest quartile of baseline plaque area have 3.5 times the risk of stroke, death, or myocardial infarction compared with those in the lowest quartile.

Those with regression or stable plaque have half the risk of those with progression after adjustment for the same panel of risk factors. The therapeutic target is plaque regression or stabilization, not just control of traditional risk factors. Trying to treat arteries without measuring plaque is like trying to treat hypertension without measuring the pressure, or hyperlipidemia without measuring the lipids. (Prev Cardiol. 2005;8:118–126) ©2005 Le Jacq Ltd.

Preventing vascular events is a tricky endeavor: if we wait until patients have events to initiate intensive preventive therapy (secondary prevention), we will miss many opportunities, as too often the first event is fatal or disabling. On the other hand, by prescribing intensive treatment to all patients (primary prevention), we will waste valuable resources—not only costly medications and tests, but the valuable time of both patients and physicians. Laupacis et al. described a useful tool for decision making: the Number Needed to Treat. It is clear that fewer high-risk patients need to be treated to prevent one event; therefore a more cost-effective approach to vascular prevention is the high-risk strategy, using various tools to stratify risk and thereby identify high-risk patients. High-risk patients are commonly identified by using tools such as Framingham or Systematic Coronary Risk Evaluation (SCORE) risk scores, or Sheffield Tables. However, these tools are cumbersome and seldom used, and are relatively primitive compared with future tools for individualizing therapy, such as genotypic information. Pending the availability of detailed genotypic information, we have been using fine phenotyping, based on measurement of carotid plaque, for this purpose.

An important limitation of using risk factors to identify high-risk patients, or to evaluate the response to therapy, is that these risk factors explain only a portion of vascular events. In older studies with higher cut-points for normality of cholesterol, it was estimated in Framingham that in multiple regression the traditional risk factors explained half of coronary events. More recent studies suggest that a higher proportion of vascular risk is explained by lifestyle issues: in a European study, regular exercise, a Mediterranean diet, moderate alcohol consumption, and controlled blood pressure (BP) were associated with a relative risk of only 0.35 compared with a lifestyle incorporating none of those healthy attributes. Recently the INTERHEART study showed that a new panel of risk factors, including smoking, history of hypertension, apolipoprotein B/A ratios, abdominal
obesity, exercise, psychosocial stress, and moderate alcohol intake accounted for 90% of population attributable risk. This has widely been interpreted as indicating that such risk factors “explain” 90% of coronary risk, but that interpretation fails to take into account the important difference between the prospective approach taken in Framingham, and the Bayesian issues involved in a cross-sectional case-control study. In a large twin study, coronary mortality was 57% heritable, and coronary events below age 46 were virtually entirely heritable. Patients with premature atherosclerosis, therefore, are much more likely to have unknown risk factors that are genetically determined. Defining such patients by age alone is limited; a more comprehensive approach is to quantify the extent to which atherosclerosis is not explained by a panel of traditional risk factors, in multiple regression. The residual score in the regression model (i.e., the distance off the regression line) represents the extent to which the patient has excess atherosclerosis, not explained by traditional risk factors; this quantity has been called unexplained atherosclerosis. In patients with unexplained atherosclerosis, plaque measurements can be used to look for newly identified genetic factors affecting atherosclerosis.

If we treat only the known coronary risk factors, we miss out on about half the problem, particularly in patients with unexplained atherosclerosis. In our large prevention clinics (over 16,000 patients referred; over 6000 being followed at present) we have taken a new approach to the prevention of vascular disease since 1985. We measure plaque in the carotid arteries annually, not only to stratify patients by level of risk, but also to evaluate the response to therapy. Our experience has been that approximately 37% of patients regress or remain stable in the first year, whereas 63% continue to progress despite intensive efforts at comprehensive risk reduction—including smoking cessation, a Mediterranean diet, lipid-lowering drugs, control of hypertension, use of angiotensin receptor inhibitors, exercise, and treatment of homocysteine with vitamin therapy (folate, B6, and B12). These may be thought of as therapy for the endothelium; endothelial function can be regarded as central to management of atherosclerosis.

It is common to see patients with excellent control of traditional risk factors whose carotid plaque is progressing despite all efforts. Such patients require more intensive control of traditional risk factors, but they also need investigation to determine what unknown risk factors are causing their problems. We thus use plaque measurements to identify high-risk patients, to determine whether they are responding to therapy, to measure the efficacy of new therapies, and to investigate the patient’s family for newly identified genetic causes of atherosclerosis, using linkage analysis with quantitative traits based on baseline plaque adjusted in multiple regression for traditional risk factors, and the rate of plaque progression, similarly adjusted (“unexplained progression”).

Trying to treat arteries without knowing how they are doing is like treating hypertension without measuring BP, or like treating hyperlipidemia without measuring plasma lipids. It amounts to initiating and changing therapy without measuring the response to treatment. A new approach to vascular prevention, based on carotid plaque measurements, is proposed in this review.

PLAQUE MEASUREMENT
We have described previously methods for measurement of total plaque area, which can be measured easily using any high-resolution resolution ultrasound machine. Each plaque seen in the common, internal and internal carotid arteries is centered in the longitudinal view in which it is biggest; the outline of the plaque is traced on screen with a cursor, and cross-sectional area is measured. The sum of cross-sectional areas of all plaques seen in both common, internal and external carotids is taken as total plaque area.

In our study, within-observer reliability of repeated plaque measurement was 0.95; between-observer reliability, comparing two technicians using different machines, was 0.85; the more experienced technician with the higher-resolution machine systematically detected more plaque. Figure 1 shows an example of a plaque measurement using the two-dimensional (2D) technology.

Since then we have gone on, in collaboration with Dr. Aaron Fenster and the Imaging Research Laboratories of the Robarts Research Institute, to develop three-dimensional (3D) measurement of carotid plaque volume. This technology will be far superior to 2D plaque measurement, particularly for measuring effects of therapy, as discussed below, but it requires special equipment. The 2D measurement of plaque area is simple, inexpensive compared with measurement of intimal-medial thickness (IMT) or electron-beam computerized tomography (EBCT), easily learned, and can be carried out with any standard high-resolution duplex scanner.

CAROTID PLAQUE AS A PREDICTOR OF OUTCOMES
In a study of 1686 patients from our clinic followed for up to 5 years (a mean ± SD follow-up of 2.5 ± 1.3 years), outcome was strongly predicted by baseline total plaque area. A total of 45 strokes, 94 myocardial infarctions, and 41 deaths (27 vascular, 12 cancer, and two other) occurred during follow-up. The combined 5-year risk of stroke, myocardial infarction and vascular death increased by quartile of plaque area: 5.6%, 10.7%, 13.9%, and 19.5%, respectively (p<0.001) after adjusting for all baseline patient characteristics (age, sex, systolic BP, total cholesterol, pack-years of smoking, total homocysteine, diabe-
Plaque measurement has important advantages over IMT and EBCT which have recently been reviewed.\textsuperscript{22,23,25} Plaque area is approximately twice as strong a predictor of cardiovascular events compared with EBCT, and somewhat stronger a predictor than IMT; plaque area biologically resembles atherosclerosis much more strongly than IMT, in the sense that traditional risk factors explain only 15\%–17\% of IMT in multiple regression,\textsuperscript{24} compared with 52\% of plaque area.\textsuperscript{11,25}

Plaque measurement can also be used to evaluate new therapies in much smaller sample sizes over a shorter time, compared with EBCT or IMT. Measuring plaque is much more sensitive than measuring IMT, because plaque progresses along the length of the vessel, in the axis of flow, 2.4 times faster than it thickens.\textsuperscript{26}

For maximum carotid IMT Bots et al.\textsuperscript{27} provide sample size estimates ranging from 468 per group for a parallel clinical trial with an effect size of 30\% over 2 years, to 30 per group for a 100\% effect size over 3 years. Sample sizes for mean IMT are larger. This is far inferior to measurement of plaque, for which 2D plaque area requires sample sizes of 150 per group for a 30\% effect size over 2 years,\textsuperscript{28} or 3D plaque volume, which can show significant changes in 3 months with an effect size of 100\% in 20 patients per group, and can show effect sizes of 10\% that of atorvastatin in 6 months with 78 patients per group, or in 1 year with samples of 14 per group.\textsuperscript{28}

**APPROACHES TO USING PLAQUE MEASUREMENT IN CLINICAL PRACTICE**

In our clinic, plaque measurements are routinely used to guide therapy. Patients with large plaque burdens are selected for intensive multiple risk factor intervention, and followed with annual plaque measurement. Those with regression are identified as responding to therapy, given longer follow-up intervals at our special clinic, and returned to the care of their primary care physicians. This permits us more time to spend with patients who are progressing despite good control of traditional risk factors. Such patients are investigated for more recently identified risk factors such as Lp(a), total homocysteine, and new risk factors that we are beginning to identify by studying such patients.\textsuperscript{12–15,25}

**SUMMARY**

Measurement of carotid plaque is useful for identifying high-risk patients, for determining whether patients are responding to therapy, for genetic studies to identify new causes of atherosclerosis among patients whose plaque is progressing despite effective control of traditional risk factors, and for studying new therapies for atherosclerosis. Trying to treat atherosclerosis without measuring it is like trying to treat hypertension without measuring BP.
REFERENCES
COUNTERPOINT: CAROTID ULTRASOUND—AN ESSENTIAL INVESTIGATION IN THE PREVENTION OF CORONARY ARTERY DISEASE?

C. Tissa Kappagoda, MBBS, PhD

The accompanying article asserts that measurement of carotid plaque area by ultrasonography adds a vital, new dimension to the investigation and management of patients at risk of developing coronary artery disease. The author contends also that traditional risk factors for coronary artery disease have failed to provide a basis for either predicting cardiovascular events or guiding effective therapy. Carefully acquired epidemiological data have established beyond reasonable doubt that traditional risk factors identify individuals who are likely to develop coronary artery disease. Further, effective management of these factors have been remarkably effective in preventing cardiovascular events. There is little prospective data in randomly selected populations to indicate that ultrasound examinations of the carotid arteries provides additional new information which would argue in favor of an alternative therapeutic approach for patients likely to develop coronary artery disease.

The accompanying article on the value of measurement of carotid plaque area in predicting cardiovascular events has raised several important issues relating to preventive cardiology. The author’s main contention is that traditional risk factors for coronary artery disease (CAD) have failed signally to provide a basis for either predicting cardiovascular events or guiding effective therapy. This is very distressing news for one who has labored in the trenches for several decades attempting to prevent CAD by treating traditional risk factors. Apparently, the real action is elsewhere. The British did much the same thing during WW II when they pointed their cannons at the Straits of Singapore (south) in a vain attempt to prevent the fall of that colonial outpost. The enemy came from the north and the rest is history.

Dr. Spence raises three significant issues in his paper. These are: 1) the failure of traditional risk factors to predict coronary events; 2) the need for better indices for monitoring progress of disease and targeting therapy; and 3) measurement of carotid plaque area yields information that is vital for management of patients at risk of developing CAD.

TRADITIONAL RISK FACTORS PREDICT CORONARY EVENTS

The proposition that traditional risk factors identify at best 50% of people likely to develop CAD flies in the face of available evidence. The provenance of this view is dubious and it is clearly past its “sell-by date.” The claim that the Framingham study identified half of the coronary events is based on an analysis reported in 1974. In general, the 50% proposition is based either on a selective reading of the literature, on small studies which have examined relatively few risk factors and/or consideration of long-outdated threshold values for risk factors. Recall that 250 mg/dL or greater was once considered a normal serum cholesterol. Several decades of painstaking data acquisition and analysis have established beyond reasonable doubt that traditional risk factors do identify individuals who are likely to develop CAD. In addition, the author dismisses the recently reported findings of the INTERHEART study for two reasons: 1) it is not a prospective cohort study (like Framingham) and 2) it suffers from “Bayesian issues” because of its case control nature. Excluding issues of cost, there are inherent weaknesses (and strengths) in both cohort studies and case control studies. For instance, case control studies could have a recall bias and there could also be a possible bias in the selection of controls. Alternatively, cohorts may differ at baseline, and cohort studies rely heavily on multivariate analysis to adjust for confounders. Another issue which has to be borne in mind with long-term follow-up studies is the extent to which changes in therapy could influence outcomes.

A brief recap of the aims and the rationale reported by the authors of the INTERHEART report is salutary—to wit, “...to clarify whether the effect of risk factors vary in different countries or ethnic groups, a large study undertaken in many countries and ethnic groups and using standardized methods is needed...” and “...such a study could also estimate the importance of known risk factors on the population attributable risk (PAR) for myocardial infarction.” They concluded that either a large cohort trial or case control study involving several thousand cases of myocardial infarction were required. They opted for the latter. The study was undertaken in 52 countries and...
included subjects from every inhabited continent and substantial numbers of people from eight major ethnic groups. There were 15,152 cases and 14,820 controls. Truly, it is the mother of all cohort studies. (The Framingham study, by contrast, had just over 600 patients with myocardial infarctions.) The analysis showed that nine “traditional risk factors”—abnormal lipids, smoking, hypertension, abdominal obesity, psychosocial factors, consumption of fruit, alcohol, and lack of regular physical activity—accounted for 90% of the PAR in men and 94% in women. It was recognized that the interplay of these risk factors varied in different cultures and ethnic groups. Three factors—smoking, hypertension, and diabetes—increased the odds ratio for an acute myocardial infarction to 13.01 and accounted for 53% of the PAR. Inclusion of lipid abnormalities to this triad increased the odds ratio to 42.3 and the PAR to 75.8% while the addition of abdominal obesity as a fifth factor increased the odds ratio to approximately 64 and the PAR to 80.2%. The PAR after inclusion of the additional risk factors was 90% for men and 94% for women.

This is not information which can be dismissed summarily because of undefined “Bayesian issues.” Having done so, the author advances data derived from a study on Swedish twins to suggest that 57% of the PAR resides in heritable factors. Could it be that Swedish twins are more representative of the human race than the INTERHEART study subjects? Does the Swedish study not represent a quintessential “Bayesian issue”? While it is reasonable to believe that genetic factors play a role in CAD, it is also very likely that they find phylogenic expression in the traditional risk factors.

TRADITIONAL RISK FACTORS ARE VALUABLE INDICES FOR MONITORING PROGRESS OF DISEASE AND TARGETING THERAPY

There is no question that one must have measurement of blood pressure to treat hypertension and a lipid panel to manage hyperlipidemia. Equally, it is not necessary to have a computerized tomographic scan of the head before treating all patients with headaches. The real issue is whether management of traditional risk factors prevents CAD. Multiple placebo-controlled trials have shown that the incidence of CAD and the evolution of lesions in the coronary circulation are influenced favorably by treatment of hypertension and hyperlipidemia. Observational studies have shown that smoking cessation is also beneficial. Of greater significance is that multiple intervention trials involving treatment of a range of risk factors (e.g., hypertension, physical inactivity, dietary management, hyperlipidemia, diabetes mellitus, and smoking) have shown regression of angiographically demonstrable lesions in the coronary vasculature, improvement in myocardial perfusion, and a reduction in the coronary event rate. Clearly a therapeutic approach firmly based on the effective management of traditional risk factors has much to offer clinicians. Thus one must assess what additional benefit results from carotid plaque assessment.

CAROTID ULTRASOUND HAS NOT BEEN SHOWN TO YIELD INFORMATION VITAL FOR MANAGEMENT OF MOST PATIENTS AT RISK FOR CAD

The basic proposition advanced by the author is that estimation of plaque area in the carotid artery provides essential information for the management of patients who are at risk of developing CAD. It is clearly a technically demanding procedure requiring considerable resources—beyond the scope of many institutions in the West, to say nothing of the economically challenged regions of the world. Thus, setting aside the internecine skirmishing regarding the best carotid ultrasound (US) index of atherosclerosis for the moment, certain specific questions merit answers before carotid US can be recommended for general use.

The author’s argument is based on a 5-year study of patients referred to a premature atherosclerosis clinic. A carotid US study was undertaken upon entry and a significant number had a second measurement after 1 year. The initial study yielded four quartiles of risk with the worst quartile experiencing a cumulative event rate of 19.1% over 5 years. It is of interest to apply the Third Report of the National Cholesterol Education Program (NCEP III) criteria to this group. Briefly, 67.5% were males with a mean age 68.9 years. The mean systolic pressure was 150.4 mm Hg (62.7% on therapy) and the mean serum cholesterol was 196 mg/dL (73.5% on lipid-lowering therapy). They also had a 20.1 pack-year history of smoking and 18.6% had diabetes. In such a group of patients one could estimate a 10-year event rate exceeding 30% based on NCEP III criteria. One wonders what additional information that could have modified therapy was provided by the carotid US.

Regarding the claim that repeating the carotid US measurements would identify subsets of individuals with worsening atherosclerotic disease, it is no more significant than stating that a patient’s fever has worsened because the thermometer gives a higher reading. What is important is the inference one draws from the observation. Before concluding that these patients are somehow genetically ill-favored and require unique investigations and treatment, it would be important to have evidence of effective management of risk factors. This information is not provided in the original paper or in the foregoing review paper though the estimated low-density lipoprotein concentration was approximately 110 mg/dL in the worst quartile at baseline. In the absence of unequivocal evidence that
carotid US provides a unique diagnostic dimension for assessing and managing cardiovascular risk, this investigation should be limited to either those patients who present with symptoms of CAD with no traditional risk factors or to special high risk categories as defined by NCEP III such as those with an egregious family history, evidence of peripheral vascular disease and the metabolic syndrome. Meanwhile physicians should be well advised to focus their attention on the treatment of traditional risk factors. There is no enemy action to the north.

REFERENCES
Dr. Spence Replies:
The crux of this issue is that it is entirely fallacious to use levels of risk factors within an individual to estimate the future risk in that individual from the fractions of population risk that can be attributed to those risk factors. Case-control studies such as INTERHEART—which compare individuals with coronary disease to individuals without coronary disease—contain no element of time; they ignore the future risk in those who have not yet had a coronary event, but who can be detected (and their time-dependent risk predicted) by measuring preclinical atherosclerosis. Population attributable risk (PAR) is not about predicting risk in individuals—it is about calculating what the risk would be in the population if those risk factors were eliminated. For example, PAR can be used to estimate the effect of reducing the population blood pressure by 5 mm Hg on average. The Framingham study used baseline levels of risk factors to predict risk in individuals over time in a prospective way, so Framingham risk factors can be used to estimate individual risk over time; typically the 10-year risk of events is calculated from age, sex, blood pressure, smoking, cholesterol and glucose intolerance.

Our data show that traditional risk factors explain only half of carotid plaque area in multiple regression, and that after adjusting for risk factors, patients in the top quartile of total plaque area (TPA) have 3.5 times the 5-year risk of stroke, death, or myocardial infarction vs. those in the lowest quartile of TPA. (Table). After adjustment patients with plaque progression had twice the risk of those with stable plaque or regression. This is very valuable information, as it tells us whether the patient is responding to therapy, and whether the risk has been reduced, independent of the level of risk factors.

Of course the INTERHEART study is a major, important study, but it was not a prospective cohort study about risk in individuals—it was a case-control study comparing risks across populations. It must be understood that PAR is not about individuals, it is about populations. This is obvious from the omission of age and sex, which are two of the stronger predictors in the Framingham equation. Furthermore, the authors of INTERHEART stated that the estimate of a PAR of 96% was of theoretical interest only, since that figure was based on comparing individuals with all 10 risk factors compared with those that had none; as they stated, a more realistic figure for PAR in their study is 60%, because most people have a few risk factors.

PAR is critically dependent on the level of risk in the population—exactly what Bayes’ theorem is about. In a study such as INTERHEART, comparing patients with all 10 risk factors vs. those with none, PAR will approach 100%. When the risk is lower, PAR will account for a lower fraction of events.

### Table. Risk of Highest Quartile of Plaque Area vs. Lowest Quartile

<table>
<thead>
<tr>
<th>Quartile</th>
<th>Lowest 0.00–0.11 cm²</th>
<th>Highest 1.19–6.73 cm²</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>No event in 5 years</td>
<td>398</td>
<td>337</td>
<td>735</td>
</tr>
<tr>
<td>Yes event in 5 years</td>
<td>24</td>
<td>82</td>
<td>106</td>
</tr>
<tr>
<td>Total patients</td>
<td>422</td>
<td>419</td>
<td>841</td>
</tr>
</tbody>
</table>

Event is defined as composite of stroke, myocardial infarction, and vascular death. Let $R_{LQ} = $ risk of event in the lowest quartile = 24 + 422 = 5.6%; Let $R_{UQ} = $ risk of event in the highest quartile = 82 + 419 = 19.5%; Let $P_{E} = $ proportion of patients with events in the highest quartile = 82 + 106 = 77.4%; Relative Risk (RR) of event related to highest quartile of plaque area = 19.5% + 5.6% = 3.5; Phi square = proportion of the variance explained by the relationship between carotid plaque area and occurrence of events = Chi square = N = 36.788 + 841 = 0.044 or 4.4%; Risk Difference (RD) = $R_{UQ} - R_{LQ} = 19.5% - 5.6% = 13.9%$. Population Attributable Risk = $P_{E} \times (RR – 1) ÷ RR$ = 77.4% ÷ (3.5 – 1) = 3.5 = relative proportion of total event risk in the population that would be eliminated if persons with carotid plaque area of 1.19–6.73 cm² could achieve reductions of plaque area to 0.00–0.11 cm² (cockered).

The table and notes, kindly provided by Dr. Michael Eliaziwi based on data from our study, show a comparison of patients in the lowest and highest quartiles of TPA. The relative risk is 3.5, and the PAR of TPA is 55%. The proportion of events among patients in the highest quartile of TPA was 77.4%, whereas a Framingham-style score based on age, blood pressure, smoking and cholesterol identified only 32% of events among cases with all four risk factors (data not shown).

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Since the practice of medicine is about evaluating and treating individuals, not about treating populations, it is apparent that measuring preclinical disease by measuring carotid plaque is very helpful in identifying high-risk patients who will benefit from intensive intervention, thereby reducing the number needed to treat and improving the cost-utility of therapy. Similarly, measuring progression or regression of plaque is very useful in evaluating response to therapy, and permitting both the physician and the patient to adjust their approaches to more intensive therapy in the face of progression. To mix Dr. Kappagoda’s metaphor, I am not a threat but an ally from the North—to both patients and their physicians.—J. David Spence, MD, FRCP, Stroke Prevention & Atherosclerosis Research Centre, Robarts Research Institute, London, Ontario, Canada

REFERENCE


Editor’s Note: Although INTERHEART extended the number of traditional risk factors beyond those in the Framingham Risk Score, its significance is the power of these risk factors in the prediction of first myocardial infarction and the fact that all can be assessed by traditional methods.

Dr. Kappagoda Replies: Dr. Spence makes several cogent points in his response. Since the matters raised are important, it is necessary to agree that we both understand the difference between attributable risk in a population and predicting risk in an individual. The issues in contention are: 1) whether measurement of carotid plaque area derived from carotid ultrasound (US) recordings adds another dimension to the management of patients; and 2) whether it is superior as a measure of risk of coronary artery disease (CAD) to one calculated in the conventional manner (such as the Framingham Risk Score).

There are no large prospective studies in which randomly selected individuals with carotid plaque as diagnosed by US have been followed up for an extended period to determine outcome with respect to cardiovascular events. Dr. Spence’s study population consists of individuals who have been referred to a premature atherosclerosis clinic. They either had an egregious family history of premature CAD or had evidence of CAD which was deemed excessive, based on Framingham risk factors. Dr. Spence makes two points based on findings in such a population.

The first is that individuals with the worst plaque had the worst prognosis. But judging from their risk factors they would also be classified as high risk according to National Cholesterol Education Panel III (NCEP III) criteria and would be treated as such according to current guidelines. There is nothing in the data to suggest that one should follow a different therapeutic route, based solely on carotid US findings, even in a population such as that studied by Dr. Spence.

The second relates to the “controversy” generated by the ability (or lack thereof) of the conventional risk factors to predict cardiovascular events. Dr. Spence provides information on the ability of these factors to predict the severity of carotid plaque. The figure on the preceding page, taken from his paper, shows a plot between the predicted plaque area (derived from conventional risk factors) and the observed plaque area. The distribution of points is interesting for several reasons. If one were to ignore the patients with no discernible plaque for a moment (enclosed in the rectangle), the remaining data appear likely to yield a regression line very close to the line of identity. The points falling furthest below the regression line represent people with unexplained atherosclerosis. The points located furthest above the regression line were considered to represent people with unexplained atherosclerosis. The points located within the rectangle are of interest for a different reason. These are individuals in whom no plaque was evident, yet they had significant risk factors. Could one reasonably offer no treatment for these individuals on the basis that their carotid arteries are “clean”?

If carotid US is to be a surrogate for CAD, one needs an entirely different investigative approach where carotid US is performed in randomly selected individuals who are then subjected to coronary angiography and possibly intracoronary ultrasound.—C. Tissa Kappagoda, MBBS, PhD, Division of Cardiovascular Medicine, University of California—Davis, Sacramento, CA

REFERENCES