Long-Term Outcomes After Carotid Endarterectomy Can the Past Be Used to Predict the Future?

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Unless based on an immutable causal relationship, predicting the future based on past events will always entail at least some degree of uncertainty. van Lammeren et al developed a prognostic score aimed at stratifying an individual’s long-term (average 2.3 years) risk for major adverse cardiovascular events (stroke, myocardial infarction, and vascular death) after carotid endarterectomy (CEA). Both the reported results and the premises of this well-conducted analysis are worthy of careful consideration.

Risk stratification can be an important guide for the choice and intensity of primary stroke preventive interventions. One of the primary assumptions underlying the van Lammeren et al analysis is that the same would be true for patients having a CEA. Based on longitudinal follow-up of 1138 patients having a CEA between 2002 to 2009 at 2 hospitals in The Netherlands, the derived predictive score classified patients into four 3-year major adverse cardiovascular risk strata (low risk, <7%; moderate risk, 7 to <14%; high risk, 14% to <27%; very high risk, ≥27%).

The model C statistic (a measure of the capacity of the model to correctly classify patients), however, was only 0.69 (95% CI, 0.64–0.73), reflecting limited discrimination (by convention, a predictive model with a C statistic >0.8 is considered to have excellent discrimination and adequate for clinical use). The limited predictive capacity of the model is, at least in part, a result of the widespread systemic nature of atherosclerotic disease.

It has long been recognized that carotid atherosclerosis is a marker for similar involvement in other vascular territories. For example, >3 decades ago, both the Evans County, Georgia, Study and the Framingham Study noted that persons with an asymptomatic cervical artery bruit were at high risk for myocardial infarction. Adult Treatment Panel III lipid management guidelines consider symptomatic carotid artery atherosclerosis to be a coronary heart disease (CHD) risk equivalent, carrying a 10-year CHD risk of >20%, similar to those with established CHD. Consistent with these observations, exploratory analysis of data from the Stroke Prevention with Aggressive Reduction in Cholesterol Levels (SPARCL) trial found that treatment of patients who had a stroke or transient ischemic attack and carotid artery stenosis with a statin led to a 43% (95% CI, 0.32–1.00; P = 0.05) reduction in the risk of major coronary events, although study subjects could have no known CHD at the time of enrollment. It is, therefore, not surprising that van Lammeren et al found that 95% of patients undergoing CEA were at moderate to very high risk of having a major adverse cardiovascular event. The model, therefore, did not achieve the goal of identifying a high-risk subgroup of patients undergoing CEA in which more intense secondary preventive treatment is warranted; the authors appropriately conclude that all patients having CEA should be considered at high risk and receive maximal secondary preventive interventions.

Although internally validated using bootstrapping techniques, the study cohort was relatively homogenous, and as the authors point out, external validation in a more diverse population is necessary. Another listed study limitation is that data on postendarterectomy medical management were lacking. Observational studies suggest that there has been a dramatic decline in the rate of stroke in patients with an asymptomatic carotid stenosis treated with medical therapy over the last decade. Similar reductions are observed in secondary stroke prevention trials. In the present cohort, the cumulative incidence of stroke, myocardial infarction, or vascular death over a mean of 2.3 years was 13%. This is approximately twice the rate reported in the Carotid Revascularization Endarterectomy versus Stenting Trial (CREST) for patients undergoing endarterectomy (the rate of stroke, myocardial infarction, or vascular death over a median of 2.5 years was 6.8%). Whether this discrepancy is due to differences in the use of medical therapy, a “clinical trial effect” in the CREST population, or other factors cannot be determined. The issue, however, is relevant for even otherwise optimal predictive schemes and underscores that all statistical models aimed at predicting the risk of future events need to be continuously re-evaluated to assess their accuracy over time.

Another premise underlying the analysis was that “high-risk patients need to be motivated for lifestyle adjustments and stringent compliance with medication regimens,” implying an important, independent role of risk stratification. Data showing that an individual’s knowledge of their level of risk influences their activities or compliance, however, remains scant. A systematic review of global CHD risk estimation identified a single randomized trial showing a nonsignificant increase in adherence to statin medications among those given a risk assessment score in addition to education as compared with education alone. It was concluded that, “current data precludes definitive conclusions on the effects of global CHD risk information on adherence, BP reduction,
smoking cessation, diet [or] exercise." Clearly, more work needs to be done to determine the degree to which a person’s knowledge of his or her level of risk affects their health-related behaviors.

Predicting the future for an individual patient has never been easy. Despite this, risk stratification models remain an important tool for guiding primary preventive interventions. The report by van Lammeren et al underscores that having significant carotid atherosclerosis, in and of itself, identifies persons at high risk of vascular events thereby justifying tailored, intensive preventive interventions.

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References

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