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Decline in the Severity of Carotid Atherosclerosis and Associated Risk Factors From 2002 to 2014

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Background and Purpose—Several recent studies suggest declining rates of carotid revascularization for patients with carotid stenosis. We investigated whether carotid atherosclerosis severity has declined in recent years.

Methods—We used carotid ultrasound to evaluate stenosis and plaque area in 6039 patients presenting to vascular medicine clinics in 3 eras: 2002 to 2005, 2006 to 2009, and 2010 to 2014.

Results—The total plaque area at the time of referral to the clinics declined by 24% between 2002 and 2014; the percentage of patients presenting with carotid stenosis >60% declined by 29.9%, and the number presenting with >80% stenosis declined by 36.4%. There were significant reductions in plasma lipids and blood pressure during the same interval.

Conclusions—Atherosclerosis severity seems to be declining over time. Better treatment of risk factors in the community may be responsible. (*Stroke*. 2018;49:2786-2788. DOI: 10.1161/STROKEAHA.118.021445.)

Key Words: atherosclerosis ■ carotid artery diseases ■ carotid stenosis ■ humans ■ risk factors

A recent analysis in the Medicare population found large decreases in the rates of carotid endarterectomy and carotid stenting during a recent 15-year period (1999–2014). The national carotid endarterectomy rate in the United States decreased from 298 per 100 000 beneficiary-years in 1999 to 2000 to 128 per 100 000 beneficiary-years in 2013 to 2014.¹ A smaller decline in carotid interventions occurred in Canada; the combination of endarterectomy and stenting in persons aged >40 years declined from 6.0 procedures per 100 000 individuals in April 2002 to 4.3 per 100 000 in the first quarter of 2014 (a 29% decrease).² The strikingly different rate of interventions and the greater decline in the United States may reflect a decline in inappropriate interventions in the United States,³ where most interventions were for asymptomatic carotid stenosis (approximately twice the proportion in Canada) and perhaps capacity issues in Canadian health care.

The authors speculate that better management of cardiovascular risk factors may have reduced the population-level prevalence of carotid stenosis that typically warrants revascularization. In other words, over time, patients may be presenting with less severe atherosclerosis.

To test this hypothesis, we analyzed data from a vascular prevention cohort drawn from mixed secondary and primary prevention patients. All patients underwent carotid ultrasonography with quantification of stenosis (if any) and total plaque area. To account for our results, we also analyzed changes in risk factor burdens over time.

Methods

The authors declare that all supporting data are available within the article (and its [online-only Data Supplement](#)). This is a retrospective

analysis of prospectively collected data from a clinical database, comparing consecutive patients according to era of accrual.

Data Sources

This study was conducted at the Stroke Prevention and Atherosclerosis Research Center of the Robarts Research Institute, London, Ontario, Canada. The study was approved by the Western University Health Science Research Ethics Board, protocol No. 107051. Requirement for written informed consent was waived by the board.

Study Population

Patients in the database were referred to J.D.S. and D.G.H. for prevention of cardiovascular events, to the Stroke Prevention Clinic, Urgent Transient Ischemic Attack Clinic, or the Premature Atherosclerosis Clinic at University Hospital, London, Canada. Most of the patients were referred to the Urgent Transient Ischemic Attack Clinic, where J.D.S. is the only neurologist who follows patients for stroke prevention; the other neurologists attending in that clinic usually refer patients to D.G.H. for that purpose. Routine measurement of carotid plaque area for monitoring of therapy began at the Stroke Prevention and Atherosclerosis Research Center in 1996. This article presents data at baseline.

Stenosis and Plaque Area Measurement

Carotid plaque area was measured as described previously⁴ with the use of a high-resolution duplex ultrasound scanner. Plaque was defined as a local thickening of the intima ≥ 1 mm in thickness.

Measurements were made in magnified longitudinal views of each plaque seen in the right and left common, internal, and external carotid arteries. The plane in which the measurement of each plaque was made was chosen by panning around the artery until the view showing the largest extent of that plaque was obtained. The sum of cross-sectional areas of all plaques seen between the clavicle and the angle of the jaw was taken as total plaque area. We performed a study of interobserver reliability, in which plaque area measurements in 25 patients were repeated 1 week apart by 2 technicians using 2 different

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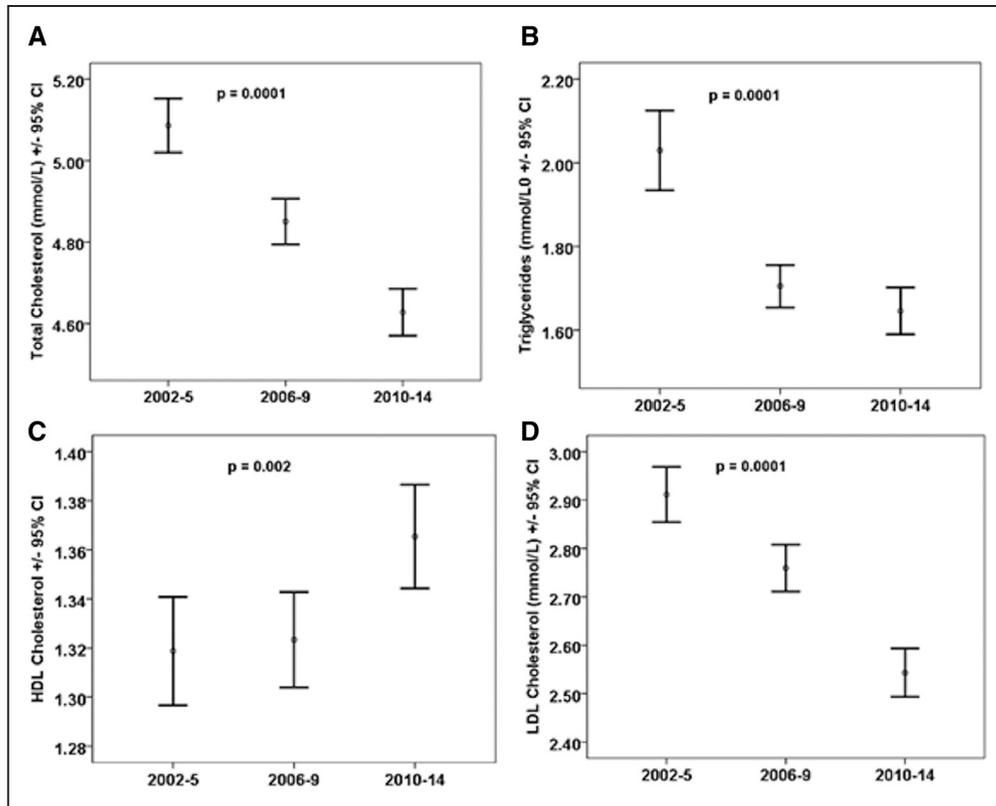


Figure 1. Plasma lipids at the time of referral by era. **A**, Total cholesterol, **(B)** triglycerides, **(C)** HDL (high-density lipoprotein) cholesterol, **(D)** LDL (low-density lipoprotein) cholesterol, all in mmol/L. Total cholesterol, triglycerides, and LDL cholesterol declined significantly (all $P=0.0001$), and HDL cholesterol ($P=0.002$) increased significantly.

machines. The intraclass correlation for within-technologist repeat measurements was 0.94. Stenosis was measured by Doppler peak frequency measurements, calibrated against angiography in 100 patients (212 arteries) measured in NASCET (North American Symptomatic Carotid Endarterectomy Trial). The R^2 for the correlation between stenosis measured by the 2 methods was 0.88.

Statistical Analyses

Patient characteristics are presented using mean±SD for continuous variables and percentage for categorical variables. Carotid stenosis and plaque area were compared using a χ^2 test across 3 different accrual eras (approximately tertiles of patients): 2002 to 2005, 2006 to 2009, and 2010 to 2014. We assessed the mean total plaque area and mean of the maximum stenosis, the percentage of patients presenting with carotid stenosis >60% and >80%, and the levels of vascular risk factors for each era. We also assessed the proportion of patients presenting with a total plaque area ≥ 119 mm² (the threshold of the top quartile of plaque area, which in our 2002 report⁵ predicted a 19.5% 5-year risk of stroke/myocardial infarction/vascular death, after adjustment for coronary risk factors). We tested the hypothesis that atherosclerosis severity is changing over time using a backward stepwise linear regression. Total plaque area (normalized by a cube root transformation) was the dependent variable. We entered the following predictor variables into the database: age, sex, systolic and diastolic blood pressure, diabetes mellitus (yes/no), serum cholesterol, triglycerides, LDL (low-density lipoprotein) cholesterol, HDL (high-density lipoprotein) cholesterol, smoking status (never, quit, and still smoking), and date of entry (year of the baseline carotid ultrasound). Variables were excluded with $P > 0.10$.

Results

In total, there were 6039 patients in the 3 eras: 1807 in 2002 to 2005, 2262 in 2006 to 2009, and 1970 in 2010 to 2014. Table I

in the [online-only Data Supplement](#) shows the characteristics of the patients. The carotid plaque burden (total plaque area) at the time of referral to the clinics declined by 24% between 2002 and 2014; the percentage of patients presenting with stenosis >60% declined by 29.9%, the number presenting with >80% stenosis

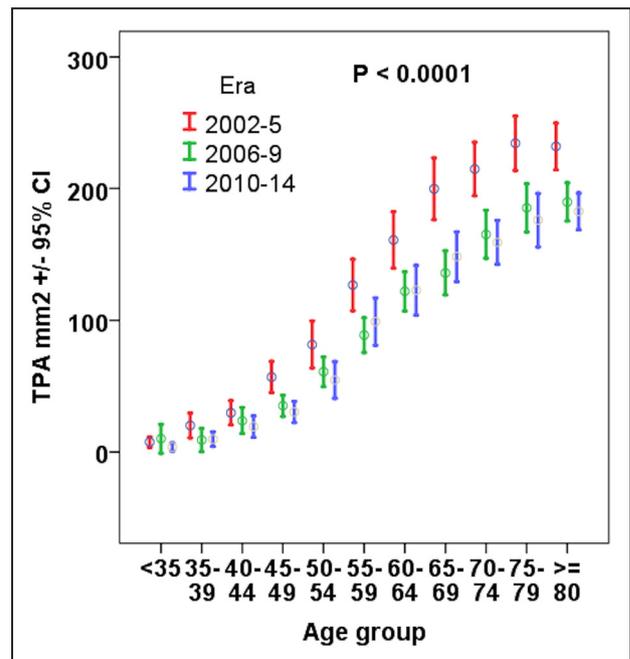


Figure 2. Total plaque area (TPA) by age group and era. TPA was significantly greater in all age groups in the first era.

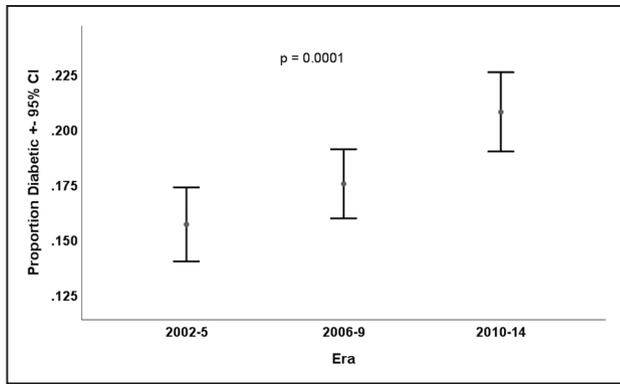


Figure 3. Prevalence of diabetes mellitus at the time of referral by era.

declined by 36.4%, and the number presenting with total plaque area ≥ 119 mm² by 22.5% (Table II in the [online-only Data Supplement](#)). Although age and sex did not change, and diabetes mellitus increased significantly over time (Table II in the [online-only Data Supplement](#)), levels of blood pressure (Figure I in the [online-only Data Supplement](#)) and plasma lipids (Figure 1A through 1D) improved significantly. This reflected community practice because the risk factors were assessed at the time of referral, before we began treating them more intensively.⁶

A multivariable regression analysis found that the year of entry into the cohort was a strong negative predictor of plaque area (standardized β -coefficient, -0.065 ; $P < 0.001$). Other predictors in the model included age, sex, systolic and diastolic blood pressure, diabetes mellitus, and HDL cholesterol. As shown in Figure 2, total plaque area was significantly higher at all age groups in the first era. Diabetes mellitus increased across the 3 eras (Figure 3).

Discussion

We found decreasing severity of carotid atherosclerosis presenting to vascular medicine clinics during a recent 12-year interval. This is supported by ongoing decline in the age-adjusted US stroke rate, from 54.6 per 100 000 in 2003 to 39.1 per 100 000 in 2010.⁷ Accordingly, there have also been reductions in carotid revascularization procedures during recent years.^{1,2} The reason for reduced atherosclerosis severity is probably a reduction in vascular risk factors, including blood pressure and lipids. In the Steno-2 trial, intensive multifactorial treatment of cardiovascular risk factors in patients with type 2 diabetes mellitus and microalbuminuria increased median time before first cardiovascular event after randomization by 8.1 years longer in the intensive-therapy group ($P = 0.001$).⁸

Our results have implications for clinical care. First, carotid procedures should be restricted to patients with severe, symptomatic carotid artery stenosis. Medical therapy is effective for managing most (90%) of the patients with asymptomatic carotid disease (the few, $\approx 10\%$ of patients, who could benefit from intervention can be identified by a number of methods, among which transcranial Doppler embolus detection is the best validated⁹). Second, the increase in the proportion of patients with diabetes mellitus is worrisome because diabetes mellitus was a predictor of total plaque area. Lifestyle modification in the community aimed at preventing diabetes mellitus is paramount, or reversals in the downward trend in atherosclerosis severity may occur. Between 2006 to 2009 and 2010 to 2014, there was a smaller decline in atherosclerosis severity, and this may be because of increasing rates of diabetes mellitus among referred patients.

Disclosures

None.

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