Socioeconomic Status and Progression of Carotid Atherosclerosis

Prospective Evidence From the Kuopio Ischemic Heart Disease Risk Factor Study

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Abstract Socioeconomic status (SES) is importantly associated with cardiovascular morbidity and mortality, but no information exists on the relationship between SES and progression of atherosclerotic vascular disease. We investigated the association between education and income and the 4-year progression of carotid atherosclerosis in a population-based sample of Finnish men. Data from the Kuopio Ischemic Heart Disease Risk Factor Study were used to estimate changes in maximum and mean intima-media thickness (IMT) and maximum plaque height across levels of SES in 1022 men. Associations between SES and atherosclerotic progression were examined in relation to risk factors and stratified by baseline levels of atherosclerosis and prevalent ischemic heart disease (IHD). There were significant, inverse, graded relationships between levels of education and income for all three progression measures, which were largely unaffected by risk factor adjustment. For education, the age- and baseline IMT–adjusted maximum progression for those with primary schooling or less was 0.28 mm and for those who graduated from high school, 0.24 mm ($P=.05$). Compared with the lowest SES group, men with the highest SES had 14% to 29% less atherosclerotic progression, depending on the measure used. Associations of the same magnitude were evident in subgroups without advanced baseline IMT and in men who were free of IHD. These results show that men with poor education and low income have significantly greater progression of carotid atherosclerosis than men with more advantages. The findings strengthen the contention that SES plays a significant role early in the atherosclerotic disease process and that reducing the burden of atherosclerotic vascular disease associated with lower SES will require approaches that focus on all stages of the life course. (*Arterioscler Thromb Vasc Biol.* 1997;17:513-519.)

Key Words • socioeconomic status • atherosclerotic progression • B-mode ultrasound

The inverse association between SES and CVD morbidity and mortality has been well established. Regardless of which measures of SES were used, many studies have shown an inversely graded relationship, with increased SES associated with lower rates of disease or death.[1-5] However, it remains unclear whether this association is limited to the clinical presentations of CVD, such as myocardial infarction, that occur late in the natural history of the disease and are a combination of underlying atherosclerotic disease and various triggering or precipitating factors, such as plaque instability or left ventricular electrical disturbances.[6] Greater understanding of how SES is related to CVD might be gained by examining earlier stages of the disease process, when the clinical presentations of disease can be separated from the process of atherosclerosis itself.[7]

Recent advances in ultrasonographic assessment of the carotid arteries have provided opportunities to study noninvasively the prevalence and development of atherosclerosis within unselected human populations.[8-10] B-mode imaging–based measurement of IMT in the carotid arteries has been shown to be reliable, to relate to the extent of disease in the coronary arteries, and to have predictive validity with regard to risk of coronary events.[9,11-15] In an earlier study, we reported the inverse associations of education, income, and occupation with ultrasonographically assessed IMT.[7] One limitation of this cross-sectional investigation was its inability to examine whether SES was related to the progression as well as the prevalence of atherosclerosis. The present study, to the best of our knowledge, is the first to examine prospectively the association between education and income and the 4-year progression of carotid atherosclerosis using three indicators of the atherosclerotic process: maximum IMT, plaque height, and mean IMT. Extensive information on baseline levels of atherosclerotic risk factors and prevalent disease enabled us to examine the association between SES and atherosclerotic progression with adjustment for known risk factors and stratified by both prevalent disease and the extent of atherosclerosis at baseline.

Methods

Subjects

Subjects were participants in the Kuopio Ischemic Heart Disease Risk Factor Study, which was designed to investigate previously unestablished risk factors for IHD and carotid atherosclerosis in a population-based sample of eastern Finnish men.[16] Of the 3235 eligible men 42, 48, 54, or 60 years old who resided in the town of Kuopio or its surrounding rural communities, 198 were excluded because of death, serious disease, or

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Selected Abbreviations and Acronyms

CCA = common carotid artery
CVD = cardiovascular disease
IHD = ischemic heart disease
IMT = intima-media thickness
SES = socioeconomic status
VCR = videocassette recorder

migration away from the area, and of the remainder, 2682 (82.9%) agreed to participate in the study. Baseline examinations were conducted between March 1984 and December 1989. No marked sociodemographic differences have been found between participants and nonparticipants.[17]

At baseline, subjects were recruited in two waves. The first group comprised 1166 men 54 years old, and the second comprised an age-stratified sample of 1516 men 42, 48, 54, or 60 years old. Ultrasonographic assessment of carotid atherosclerosis at baseline was conducted between February 1987 and December 1989 on the second wave of participants only. There were no systematic differences between the two waves of recruitment for the study other than the differences in age distribution. A 4-year follow-up examination was conducted between March 1991 and December 1993 on those men who had undergone ultrasonographic examination of the carotid arteries at baseline.

Follow-up examinations were conducted at the same time of day and principally during the same month as the baseline examination. Mean follow-up time was 4.2 years (range, 3.9 to 5.2 years). Of the 1229 participants who were eligible for the follow-up examinations, 52 either had died, were suffering severe illness, or had migrated away from the area. Of the remainder, 139 could not be contacted or refused to participate. Information on progression of carotid atherosclerosis, covariates, and education was available for 1012 men and on income for 994 men. There were 233, 237, 281, and 261 men in the 42-, 48-, 54-, and 60-year-old age groups, respectively. In this sample, 73 men acted as control subjects and 73 men were participants in the treatment group of an unrelated clinical trial of pravastatin.[18]

Evaluation of Carotid Atherosclerotic Progression

Atherosclerotic progression was assessed with high-resolution B-mode ultrasonographic examination of a 1.0- to 1.5-cm section of the left and right CCAs below the carotid bulb. Images were focused on the posterior (far) wall with the subject supine. At baseline, ultrasonographic scanning was conducted with the ATL UM4 duplex ultrasound system with a 10-MHz sector transducer (Advanced Technology Laboratories). The Biosound Phase 2 equipped with a 10-MHz annular array probe was used at the 4-year follow-up examinations. Wedge phantom studies of this system, calibrated against an RMI 414B tissue phantom, have demonstrated measurement precision of ±0.03 mm.[19] A total of five technicians, each trained for at least 6 months, conducted both the baseline and 4-year follow-up scannings, which were also recorded by VCR.

Video frames of the B-mode scanning were digitized with the Data Translation DT2861 video frame grabber installed on an 80486 PC and a Panasonic AG7355 VCR. IMT was assessed with Prosound software, which incorporates an edge-detection algorithm specifically designed for use with ultrasound scanning and enables automatic detection, tracking, and recording of the lumen/intima and media/adventitia interfaces (University of Southern California).[20] On average, 100 estimates of the distance between these interfaces were recorded over the 1.0- to 1.5-cm section of each CCA. The IMT of the posterior wall was measured as the distance from the leading edge of the first echogenic line to the leading edge of the second echogenic line, as explained earlier in detail.[9] Measurements of the near wall were not made because of greater measurement variability.[21]

The present study uses three measures of IMT: (1) maximum IMT (defined as the average of the maximum IMT in the right and left CCAs), (2) plaque height (defined as the difference between the maximum and minimum IMT recordings averaged over the right and left CCAs), and (3) mean IMT (defined as the mean of the ≈100 IMT readings from each CCA). These measures were conceptualized to represent potentially different aspects of atherosclerotic progression. Maximum IMT was thought to provide an assessment of how deeply intima-media thickening intruded into the lumen in this segment of the CCA. The measurement of plaque height was conceptualized to be sensitive to the roughness of the arterial wall by representing the range of IMT and thus assessing how steeply atherosclerotic lesions protruded into the lumen. Mean IMT was seen as an overall measure of the process of atherosclerosis. Progression of carotid atherosclerosis was calculated as the arithmetic difference between the baseline and 4-year follow-up values for each of the three measures: maximum IMT, plaque height, and mean IMT.

Baseline IMT recordings were also classified by one physician into four categories: (1) no atherosclerotic lesion; (2) intima-media thickening; (3) nonstenotic plaque; and (4) large, stenotic plaque. Intima-media thickening (category 2) was defined as >1.0 mm between the lumen/intima interface and the media/adventitia interface in the CCAs below the carotid bulb. Nonstenotic plaque (category 3) was defined as a distinct area of mineralization or focal protrusion into the lumen. A plaque was defined as stenotic (category 4) if it obstructed >20% of the lumen diameter.[9]

Evaluation of Education and Income

Various measures of socioeconomic status were available from questionnaires completed as part of the baseline examination, including education, occupation, income, housing tenure, and ownership of material goods.[22] The present study reports results by highest educational attainment and current income. The highest level of education was classified into three categories: "primary school or less" (included those who had only part of or who had completed primary school, n=321), "some high school" (included those who had some high school or other vocational training beyond primary, n=490), and "completed high school or better" (included those who finished high school or who had tertiary education, n=201). The distribution of the respondents' current income was divided into approximate quartiles.

Evaluation of Covariates

Lipoproteins were separated from unfrozen plasma within 3 days of sampling. HDL and LDL fractions were separated from fresh plasma by both ultracentrifugation and precipitation. The cholesterol content of all lipoprotein fractions was measured enzymatically (CHOD-PAP cholesterol method, Boehringer Mannheim) on the day after the last spin.[23] Blood pressure was measured with a random-zero sphygmomanometer with the subject both supine and sitting, after 5-minute rests in each position. Three systolic and diastolic pressures were taken and averaged. Average systolic pressure was used in this analysis. Body mass index was calculated by dividing the subject's weight by the square of his height (kg/m^2). Alcohol consumption was assessed by instructed dietary recording for a 4-day period, and also for the previous 12 months, by self-administered questionnaire.[24] Smoking was measured by questionnaire and classified for this analysis as "never smoked," "former smoker," and "current smoker" (measured in pack-years). Treatment for hypertension or hyperlipidemia was assessed by a review of medications.

Evaluation of Prevalent IHD

Subjects were considered to have prevalent IHD at baseline if they (1) had any history of prior myocardial infarction or angina pectoris, (2) currently used antiangina medication, or

TABLE 1. Mean (SD) or Prevalence (%) of Covariates by Level of Highest Educational Attainment and Quartiles of Income at Baseline

	Highest Education			Income Quartiles			
	Primary (n=321)	Some High School (n=490)	High School (n=201)	Lowest (n=176)	Second (n=284)	Third (n=280)	Highest (n=254)
Age, y	55.2 (5.7)	50.0 (6.3)	48.6 (6.2)	54.3 (6.5)	52.4 (6.5)	49.9 (6.5)	49.7 (6.1)
Maximum IMT, mm	1.03 (0.25)	0.94 (0.24)	0.86 (0.16)	1.02 (0.26)	0.98 (0.26)	0.95 (0.23)	0.88 (0.18)
Plaque height, mm	0.42 (0.19)	0.38 (0.18)	0.34 (0.13)	0.41 (0.19)	0.39 (0.20)	0.38 (0.17)	0.35 (0.14)
Mean IMT, mm	0.82 (0.18)	0.76 (0.17)	0.70 (0.12)	0.81 (0.18)	0.78 (0.18)	0.75 (0.18)	0.72 (0.13)
LDL, mmol/L	3.97 (0.89)	3.80 (0.96)	3.75 (0.96)	3.88 (1.0)	4.0 (0.91)	3.87 (0.94)	3.71 (0.93)
HDL, mmol/L	1.31 (0.31)	1.30 (0.29)	1.28 (0.30)	1.29 (0.31)	1.29 (0.30)	1.29 (0.27)	1.32 (0.31)
Body mass index, kg/m^2	26.9 (3.3)	26.5 (3.3)	26.8 (3.7)	26.5 (3.7)	26.8 (3.2)	26.7 (3.3)	26.7 (3.3)
Systolic blood pressure, mm Hg	132.5 (16.2)	132.0 (15.9)	130.56 (15.7)	132.4(17.4)	132.5 (17.0)	131.9 (15.2)	131.2 (14.5)
Alcohol consumption, %							
Abstainers	13.7	12.7	7.5	18.8	11.7	11.4	8.3
Lowest 25%	26.8	20.0	18.4	25.0	25.1	19.6	17.7
2nd quartile	23.4	21.3	22.4	22.2	19.4	22.5	25.2
3rd quartile	19.6	21.7	27.4	16.5	19.1	23.6	27.6
Highest 25%	16.5	24.3	24.4	17.6	24.7	29.2	21.3
Smoking, %							
Never	20.5	30.9	32.1	23.7	22.0	27.7	37.3
Former	42.0	40.9	39.1	36.1	42.8	42.3	41.1
1st tertile, pack-y	11.0	11.1	14.7	12.4	12.7	12.4	8.9
2nd tertile	13.7	11.0	16.3	18.9	10.8	10.2	8.1
3rd tertile	12.7	6.0	6.0	8.9	11.6	7.3	4.7
Treatment for							
Hyperlipidemia, %	11.8	5.5	9.0	8.5	9.2	9.3	6.3
Hypertension, %	27.7	18.8	14.4	30.1	22.9	18.9	13.8
Prevalent IHD, %	32.7	20.8	11.0	38.6	27.1	19.6	9.5
*Advanced atherosclerosis, % at baseline	45.5	28.6	14.4	48.2	30.3	27.1	22.0

*Advanced atherosclerosis is defined as stenotic plaque >20% lumen diameter or nonstenotic plaque=distinct mineralization or focal protrusion.

(3) had positive findings of angina from the London School of Hygiene Cardiovascular Questionnaire.[25]

Statistical Methods

The association between SES and the progression of IMT was assessed by estimating the mean change in each measure of IMT (maximum thickness, mean thickness, and plaque height) for each level of education and income. The analyses were conducted with the GLM procedure in SAS version 6.09 on a Sun Sparc Station II.[26] This procedure allows for age-adjusted least-squares mean values of IMT to be estimated and contrasted for each level of SES while baseline IMT and other covariates are simultaneously controlled for.

We were interested in comparing differences in mean IMT progression between the highest income or education group (reference category) and each lower category. The pairwise contrasts between the reference group (highest education or income) were adjusted for multiple comparisons to maintain an overall type 1 error of $P<.05$ by use of Holm's procedure as described by Aickin and Gensler.[27] In addition to age, baseline levels of IMT, and covariates, all estimates were adjusted for participation in the clinical trial of pravastatin, the zooming depth of the ultrasound scan, and separate indicator variables for the individual technicians who conducted the scans.[9]

Results

Table 1 provides means (SD) and prevalence (%) for baseline levels of IMT and other covariates distributed across categories of education and income. Tables 2, 3, and 4 present the estimated mean changes in maximum thickness, plaque height, and mean thickness of the

TABLE 2. Education, Income, and Progression of Average Maximum IMT in 1012 Finnish Men

	Model 1, Adjusted for Age and Baseline IMT			Model 2, Additional Adjustment for Covariates†		
	Mean	SEM	P*	Mean	SEM	P*
Education						
Primary or less, n=321	0.28	0.012	.05	0.28	0.012	.09
Some high school, n=490	0.26	0.009	.11	0.26	0.009	.12
Completed high school or better, n=201	0.24	0.014	Reference	0.24	0.014	Reference
Income						
Lowest 25%, n=176	0.30	0.015	.05	0.29	0.015	.15
2nd quartile, n=284	0.26	0.012	>0.5	0.26	0.012	>0.5
3rd quartile, n=280	0.27	0.012	.31	0.27	0.012	.41
Highest 25%, n=254	0.25	0.012	Reference	0.25	0.012	Reference

*P refers to pair-wise contrast with reference category (adjusted for multiple comparisons).
†Adjusted for HDL, LDL, smoking, alcohol, body mass index, systolic blood pressure, treatment for hypertension, and hyperlipidemia.

TABLE 3. Education, Income, and Progression of Mean Plaque Height in 1012 Finnish Men

	Model 1, Adjusted for Age and Baseline IMT			Model 2, Additional Adjustment for Covariates†		
	Mean	SEM	P*	Mean	SEM	P*
Education						
Primary, n=321	0.29	0.011	.01	0.29	0.011	.06
Some high school, n=490	0.27	0.008	.07	0.27	0.008	.11
Completed high school or better, n=201	0.24	0.013	Reference	0.24	0.013	Reference
Income						
Lowest 25%, n=176	0.29	0.014	.12	0.29	0.014	>.5
2nd quartile, n=284	0.27	0.011	.40	0.27	0.011	>.5
3rd quartile, n=280	0.27	0.011	>.5	0.27	0.011	>.5
Highest 25%, n=254	0.25	0.012	Reference	0.26	0.012	Reference

*P refers to pairwise contrast with reference category (adjusted for multiple comparisons).
†Adjusted for HDL, LDL, smoking, alcohol, body mass index, systolic blood pressure, treatment for hypertension, and hyperlipidemia.

intima-media complex by SES with adjustment for age and baseline levels of IMT (model 1) and with additional adjustment for covariates (HDL, LDL, systolic blood pressure, smoking, body mass index, alcohol consumption, and treatment for hyperlipidemia and hypertension) in model 2.

SES and IMT Progression in the Whole Sample

Progression of maximum IMT, mean IMT, and plaque height all demonstrated similarly graded relationships with education and income. In Table 2, the age- and baseline IMT–adjusted 4-year average maximum progression within categories of education was 0.28 mm for those who had only primary education, 0.26 mm for those with some high school, and 0.24 mm for those who had completed high school or continued with tertiary studies (F=2.55, P=.08). Men who had completed high school had 14% less maximum atherosclerotic progression in 4 years than those with only primary education (P=.05). Adjustment for covariates did not alter the magnitude of the differences between the education categories. When income was used as the measure of SES, men in the highest income quartile had 17% less maximum progression than the highest income earners (P=.05). This difference was not substantially altered by adjustment for covariates.

The pattern of results for progression of plaque height was very similar to that for maximum IMT progression. In Table 3, the age- and baseline IMT–adjusted 4-year mean progression of plaque height within categories of education was 0.29 mm for those who had only primary education, 0.27 mm for those with some high school, and 0.24 mm for those who had completed high school or continued with tertiary studies (F=3.74, P=.02). Men who had completed high school had 17% lower 4-year progression in plaque height than those with only primary education (P=.01). Adjustment for covariates did not alter the magnitude of the differences between the education categories. Similarly, graded, significant associations were seen for quartiles of income in model 1, with the lowest income group having 14% less progression of plaque height than the highest income group.

Overall, a consistent pattern of results emerged when progression of mean IMT was used as the outcome, although somewhat stronger gradients were found for income as opposed to education (Table 4.) The age- and baseline IMT–adjusted 4-year progression of mean IMT within income quartiles was 0.14, 0.11, 0.12, and 0.10 mm for the lowest to highest income quartiles, respectively (F=3.1, P=.03). Men in the highest income quartile experienced 29% less progression in mean IMT than men in the lowest income group (P=.02). The magnitude of this difference was not affected by adjustment for atherosclerosis risk factors.

SES and IMT Progression in Men Without Stenosis or Nonstenotic Plaque at Baseline

Table 5 shows the relationship between education and progression of maximum IMT, plaque height, and mean

TABLE 4. Education, Income, and Progression of Mean IMT in 1012 Finnish Men

	Model 1, Adjusted for Age and Baseline IMT			Model 2, Additional Adjustment for Covariates†		
	Mean	SEM	P*	Mean	SEM	P*
Education						
Primary, n=321	0.12	0.008	.23	0.12	0.008	.37
Some high school, n=490	0.12	0.006	.16	0.12	0.006	.15
Completed high school, n=201	0.10	0.010	Reference	0.10	0.010	Reference
Income						
Lowest 25%, n=176	0.14	0.011	.02	0.14	0.011	.06
2nd quartile, n=284	0.11	0.008	>.5	0.11	0.008	>.5
3rd quartile, n=280	0.12	0.008	.10	0.12	0.009	.12
Highest 25%, n=254	0.10	0.009	Reference	0.10	0.009	Reference

*P refers to pairwise contrast with reference category (adjusted for multiple comparisons).
†Adjusted for HDL, LDL, smoking, alcohol, body mass index, systolic blood pressure, treatment for hypertension, and hyperlipidemia.

TABLE 5. Education and the Progression of Maximum IMT, Plaque Height, and Mean IMT in 697 Finnish Men Without Carotid Stenosis or Plaque at Baseline

	Model 1, Adjusted for Age and Baseline IMT			Model 2, Additional Adjustment for Covariates†		
	Mean	SEM	*P**	Mean	SEM	*P**
Maximum IMT progression						
Primary or less, n=175	0.29	0.012	.02	0.28	0.012	.06
Some high school, n=350	0.26	0.009	.34	0.26	0.009	.35
Completed high school or better, n=172	0.24	0.012	Reference	0.24	0.012	Reference
Plaque height progression						
Primary or less, n=175	0.29	0.011	.04	0.28	0.011	.21
Some high school, n=350	0.26	0.008	.39	0.26	0.008	.42
Completed high school or better, n=172	0.25	0.012	Reference	0.25	0.011	Reference
Mean IMT Progression						
Primary or less, n=175	0.13	0.008	.12	0.12	0.008	.16
Some high school, n=350	0.11	0.006	.25	0.11	0.006	.22
Completed high school or better, n=172	0.10	0.009	Reference	0.10	0.008	Reference

*P refers to pairwise contrast with reference category (adjusted for multiple comparisons).
†Adjusted for HDL, LDL, smoking, alcohol, body mass index, systolic blood pressure, treatment for hypertension, and hyperlipidemia.

IMT in a subgroup that excluded 315 men with ultrasonographic evidence of ≥20% carotid stenosis or nonstenotic atherosclerotic plaque (categories 3 and 4). Each measure of IMT progression showed strong, significant, inverse gradients with higher levels of education. Men without carotid stenosis or nonstenotic plaque at baseline who had completed a high school education had 17% (P=.02), 14% (P=.04), and 23% (P=.12) less progression of maximum IMT, plaque height, and mean IMT, respectively, than men with primary schooling or less. The magnitude of these differences was not greatly affected by adjustment for atherosclerosis risk factors.

SES and IMT Progression in Men With No Prevalent IHD at Baseline

Table 6 shows the relationship between education and progression of maximum IMT, plaque height, and mean IMT in a subgroup that included only those men who were free of IHD at baseline (n=783). Both progression of maximum IMT and plaque height showed strong, significant, inverse gradients with higher levels of education. Although the magnitude of the differences for mean IMT progression between educational groups conformed to the overall pattern of results, the differences were not statistically significant. Men with no prevalent IHD at baseline who had completed a high school education had 14% (P=.08), 14% (P=.04), and 17% (P=.28) less progression of maximum IMT, plaque height, and mean IMT, respectively, than men with primary schooling or less. Adjustment for atherosclerosis risk factors did not greatly affect the magnitude of the educational differences. A similar pattern of findings was obtained when income was used as the SES measure. The Figure shows the age- and baseline IMT–adjusted associations between levels of education and progression of maximum IMT in the whole sample, in men with no prevalent IHD, and in men without carotid stenosis or nonstenotic plaque.

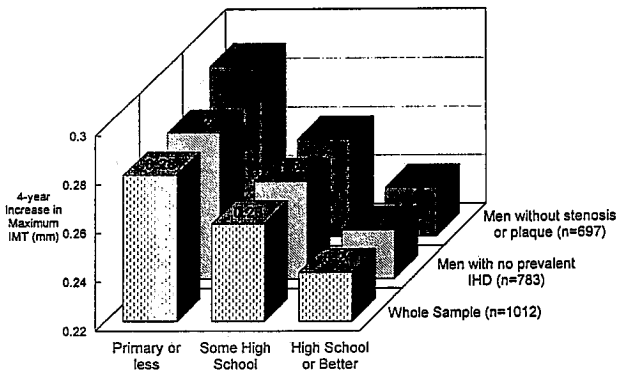
Discussion

These results show that men with low education and low incomes had significantly greater 4-year progression of carotid atherosclerosis than men with more advantages. All the measures of carotid atherosclerotic progression demonstrated similarly graded, inverse relationships across levels of SES. The magnitude of these relationships was largely unaffected by adjustment for known atherosclerosis risk factors. However, SES is

TABLE 6. Education and Progression of Maximum IMT, Plaque Height, and Mean IMT in 783 Finnish Men With No Prevalent IHD at Baseline

	Model 1, Adjusted for Age and Baseline IMT			Model 2, Additional Adjustment for Covariates†		
	Mean	SEM	*P**	Mean	SEM	*P**
Maximum IMT progression						
Primary or less, n=216	0.28	0.012	.08	0.27	0.012	.08
Some high school, n=388	0.26	0.009	.16	0.26	0.009	.14
Completed high school or better, n=179	0.24	0.013	Reference	0.24	0.013	Reference
Plaque height progression						
Primary or less, n=216	0.29	0.012	.04	0.28	0.012	.06
Some high school, n=388	0.26	0.009	.21	0.26	0.009	.20
Completed high school or better, n=179	0.24	0.013	Reference	0.25	0.013	Reference
Mean IMT Progression						
Primary or less, n=216	0.12	0.009	.28	0.12	0.009	.34
Some high school, n=388	0.11	0.006	.13	0.12	0.006	.11
Completed high school or better, n=179	0.10	0.009	Reference	0.10	0.009	Reference

*P refers to pairwise contrast with reference category (adjusted for multiple comparisons).
†Adjusted for HDL, LDL, smoking, alcohol, body mass index, systolic blood pressure, treatment for hypertension, and hyperlipidemia.



Association between progression of maximum IMT and education in the whole sample (n=1012), in 697 men without stenosis or nonstenotic plaque at baseline, and in 783 men without prevalent IHD at baseline.

associated with both baseline levels of atherogenesis risk factors and changes in those risk factors over time. Because of this, the analytic strategy of examining the association of SES with changes in carotid atherosclerosis by adjusting for baseline levels of atherogenesis risk factors is somewhat problematic. Thus, the lack of confounding from these risk factors should not necessarily be interpreted as evidence that the association between SES and progression of carotid atherosclerosis is "independent" of these risk factors. In fact, we reported earlier that the cross-sectional association between SES and carotid atherosclerosis in the same population was largely mediated by a similar group of known atherosclerosis risk factors.[7] It is also possible that temporal variations in risk factor levels were not captured by single measurements at baseline and so reduce their ability to act as confounders. Furthermore, there are other potential risk factors for atherosclerosis progression, such as hemostatic variables, that were not included in these analyses.

Although these results implicated SES in the progression of IMT, we conducted a more stringent examination of the role of SES in its relation to the early stages of atherosclerosis by excluding men who at baseline showed any evidence of stenosis or nonstenotic plaque. The same magnitude of associations between SES and progression was revealed in this group of men who did not have advanced thickening at baseline and suggests that SES is influential early in the natural history of carotid atherosclerotic progression. This finding is even more compelling in light of the fact that low-SES men had much higher prevalence of advanced atherosclerosis at baseline and so were disproportionately excluded from these analyses. Table 1 shows that 45.5% of the least educated group compared with 14.4% of the most educated group had advanced atherosclerosis at baseline.

To examine whether the association between levels of SES and progression of IMT was a reflection of the fact that those who had less education or lower incomes were more likely to have higher prevalent IHD, we repeated the analysis in a healthy subsample. All men who had any indication of prevalent IHD at baseline were excluded from the analysis. In this healthy subsample, the same graded, inverse relationship between SES and progression of maximum IMT, plaque height, and mean IMT was observed. The magnitude of the differences between the most extreme categories of SES was similar to those obtained within the whole sample.

Our results are important for a number of reasons. This study is the first in a large, unselected sample to show strong relationships between SES and the early signs of atherosclerotic vascular disease progression. These findings strengthen the contention that SES plays a significant role early in the atherosclerotic disease process in addition to its more well-established associations with the clinically relevant and distal manifestations of CVD.[28] Although this sample is limited to middle-aged men, our findings are consistent with a recent cross-sectional study by Diez-Rouz et al[10] in the United States that found similar relationships between measures of SES and IMT in men and women and in blacks and whites.

Second, the results are consistent across different measures of atherosclerosis progression, with education and income showing similar associations with progression of maximum IMT, plaque height, and mean IMT. Although the differential pathological importance of changes in these measures remains to be clearly established, it seems reasonable to suggest that SES is associated with progression of the overall atherosclerotic burden as well as in the development of focal lesions that protrude into the lumen and increase the surface roughness of the CCA. The development of roughened arterial walls with steep-sided projections into the lumen is likely to subject the lesion to increased shear stress and flow turbulence, thus raising the potential for plaque fissuring and possible rupture.

Third, the differences in IMT progression between extreme categories of SES observed in these data have potentially important clinical and public health interpretations. Although there is little information on the relationship between carotid atherosclerotic progression and clinical events, Salonen and Salonen[9] demonstrated cross-sectionally that a 0.1-mm difference in maximum IMT raised the risk of acute myocardial infarction significantly, by 11% (95% confidence interval, 6% to 16%; $P<.001$).

Finally, these findings provide some of the strongest evidence to date against the "drift" or "selection" hypothesis, which has been proposed as a potential explanation for the observed inverse associations between SES and health.[29] According to this notion, any association between SES and health may occur because sick individuals "drift down" the social hierarchy, so that lower socioeconomic position is a consequence of the disease process. Although this no doubt occurs to some extent, it is unlikely to explain the overwhelming burden of disease borne by those with lower SES.[30] Demonstrating the same significant, graded differences in carotid atherosclerosis progression across categories of SES in the whole population as well as in a healthy subgroup who were free of prevalent IHD provides cogent evidence that lower SES is importantly involved in greater atherosclerotic vascular disease before any clinical evidence of illness occurs.

In summary, the evidence presented here indicates that the impact of SES is apparent early in the natural history of atherosclerotic vascular disease and is impor-

tantly related to disease progression. It seems entirely plausible that lower SES should be related to the early phases of atherosclerotic progression, at least in part because of its well-reported associations with higher levels of smoking, blood pressure, lipids, and other CVD risk factors.[31-35] Moreover, recent evidence from the Kuopio Ischemic Heart Disease Risk Factor study also shows that lower SES during childhood is an important predictor of adult smoking, physical activity, diet, and a number of adult psychosocial characteristics.[36] Although adjustment for some of these atherosclerotic risk factors did not greatly affect the magnitude of the associations reported here, it is likely that lower SES is important in influencing the complex accumulation of biological, behavioral, and psychosocial risk factors that influence the progression of atherosclerosis.[37] If this is true, reducing the atherosclerotic vascular disease burden associated with lower SES will require approaches that focus on all stages of the life course.

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