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ORIGINAL ARTICLE

Combined effects of hypertension, hyperlipidemia, and diabetes mellitus on the presence and severity of carotid atherosclerosis in community-dwelling elders: A community-based study

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Abstract

Background: Hypertension, hyperlipidemia, and diabetes mellitus (DM) are common cardiovascular disease (CVD) comorbidities and well-known major determinants of atherosclerosis. However, their combined effects and relative contributions have not been well explored. This study aimed to characterize the characteristics of carotid atherosclerosis and dissect the relative effects of these common CVD comorbidities on the presence and severity of carotid atherosclerosis in community-dwelling elderly individuals.

Methods: We enrolled 817 elders from communities in northern Taiwan. We evaluated their cardiovascular risk profiles and scanned their extracranial carotid arteries using high-resolution ultrasonography systems.

Results: The prevalence rates for hypertension, hyperlipidemia, and DM were 45.4%, 37.1%, and 16.8%, respectively. Sixty-two (7.6%) and 188 (23.0%) elderly had all three and two of these common CVD comorbidities, respectively. The prevalent rates of carotid plaque and moderate-to-severe atherosclerosis were 62.9% and 35.5%, respectively. The percentages of one or more common CVD comorbidities in elders with carotid plaque and moderate-to-severe atherosclerosis were 78.2% and 83.1%, respectively. Multivariate analyses showed that the number of common CVD comorbidities was the most predictive determinant. Multivariable-adjusted odds ratios (ORs) per comorbidity for the presence of carotid plaque and advanced carotid atherosclerosis were 1.52 (95% CI, 1.28-1.81) and 1.57 (95% CI, 1.28-1.93), respectively. Models containing hypertension and DM were the second most predictive. Combinatory analyses showed distinct relationship patterns between carotid atherosclerosis and hypertension, hyperlipidemia, and DM. Hypertension was significantly correlated with higher ORs for the presence of carotid plaque and advanced carotid atherosclerosis but not for hyperlipidemia.

Conclusion: Carotid plaques are highly prevalent in community-dwelling elders. The number of common CVD comorbidities was the most predictive determinant of carotid plaques and advanced carotid atherosclerosis. Our results indicate that to reduce the impact of atherosclerotic diseases, blood pressure controls precede the control of blood lipids and glucose in the community-dwelling elders.

Keywords: Association study; Carotid atherosclerosis; Diabetes mellitus; Dyslipidemia; Elderly; Hypertension; Population-based study

1. INTRODUCTION

Atherosclerosis is the progression of gradual constriction of the arteries through plaque formation within the artery walls.[1] Unstable arterial plaques that lead to thrombus formation and potentially embolism are precursors of more serious cardiovascular diseases (CVDs) such as myocardial infarction and stroke.[2–5] Atherosclerotic diseases have a great impact on global health. The deaths from CVD worldwide were estimated to be 12.3 million in 1990 and 17.3 million in 2013.[6] The global disability-adjusted life years (DALYs) increased from 314.4 million DALYs in 2007 to 366.0 million DALYs in 2017.[7] A more recent report showed that CVD cases worldwide nearly doubled from 271 million in 1990 to 523 million in 2019.[8] Significant proportions of the increases in CVD mortality and morbidity were attributable to the aging of the population.[6–8] Unfortunately, the rate of aging of the global population is accelerating more rapidly than before; the global aged population was 727.6 million in 2020 and will be 1300.5 million in 2040.[9] The impacts of atherosclerotic diseases are doubtlessly enormous and comprehensive; therefore, formulating effective prevention measures are critically relevant and prompt.

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Plaque in the extracranial carotid arteries, which can be detected non-invasively and reliably by ultrasound, is a valid indicator of atherosclerosis and is predictive of CVD risk.[10,11] Etiological studies on carotid atherosclerosis may provide critical evidence to identify target populations to prevent atherosclerotic diseases. Several studies consistently demonstrated higher risks of carotid atherosclerosis in the male sex, older age, cigarette smoking, high blood pressure, and diabetes mellitus (DM).[12–19] High blood lipids have been found to increase the risk of atherosclerosis in several studies,[12–14] but not in others.[15–17] The inconsistent findings may be due to risk determinants and correlates that varied significantly and the heterogeneities of subjects in previous studies. To the best of our knowledge, only a handful of the population- or community-based studies have contemporarily explored the effects of common CVD comorbidities, including hypertension, hyperlipidemia, and DM, on atherosclerosis. Additionally, the combined effects and relative contributions of these common CVD comorbidities to advanced atherosclerosis have not been well explored.

The prevalence of atherosclerosis increases exponentially with age, and elderly people have a higher risk of CVD. Consequently, the elderly are a reasonable target population for the prevention of atherosclerotic diseases. However, previous studies enrolled subjects with a wide range of age intervals; usually, age was treated as a correlate and only some of the study subjects were elderly.[13,14,17–19] It is unknown whether the findings of heterogeneous populations can be applied to older adults. Therefore, we conducted this population-based study in community-dwelling older adults to explore the relative and combined effects of common CVD comorbidities on the presence and severity of carotid atherosclerosis.

2. METHODS

2.1. Study subjects

In September 2010, we conducted a community-based study to explore the relationship between common health problems and modifiable risk factors in adults.[20–22] This study recruited 4102 residents aged 40 to 74 years from communities in the northern coastal area of Taiwan. The inclusion criteria were as follows: (1) aged 65 to 74 years; (2) had undergone physical examination and determination of blood pressure, lipids, and glucose; and (3) had received ultrasound scans of their extracranial carotid arteries and had good quality carotid images. A total of 817 participants met the inclusion criteria in the present study. The study was conducted following the 1975 Helsinki Declaration on Medical Research Ethics, and informed consent was obtained from all participants. The Institutional Review Board of the MacKay Medicine College (No. P990001) and MacKay Memorial Hospital (No. 14MMHIS075) reviewed and approved this study.

2.2. Measurements of common CVD comorbidities

Measurements of blood pressure, lipids, and glucose have previously been reported.[20,21] Briefly, blood pressure was measured three times, with an interval of 3 minutes, after 10 minutes of rest. For the analyses, the averages of repeated measurements of systolic blood pressure (SBP) and diastolic blood pressure (DBP) were used. A fasting blood sample was obtained from each participant to determine blood sugar and lipid levels. Total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), triglycerides, and glucose levels were determined using an autoanalyzer (Toshiba TBA c16000; Toshiba Medical System, Holliston, MA, USA) and commercial kits (Denka Seiken, Tokyo, Japan).

In this study, hypertension was defined as SBP ≥140 mmHg, DBP ≥90 mmHg, positive history of physician-diagnosed hypertension, or use of antihypertensive medications. DM was defined as a fasting glucose level ≥126 mg/dL, positive history of physician-diagnosed DM, or use of insulin or other hypoglycemic agents. Hyperlipidemia was defined as a total cholesterol level ≥240 mg/dL, LDL-C level ≥160 mg/dL, TG level ≥150 mg/dL, positive history of physician-diagnosed hyperlipidemia, or use of lipid-lowering medications.

2.3. Measurements of anthropometric attributes and health behaviors

Body weight, height, and circumference of the subject's waist and hip were measured as described previously.[20,21] In brief, we used a digital system (BW-2200; NAGATA Scale Co. Ltd., Tainan, Taiwan) to measure the body weight and height of the subjects. Waist circumference was measured mid-distance between the bottom of the rib cage and the top of the iliac crest. Hip circumference was the distance around the largest part of the subjects' hips.

In this study, we also used a structured questionnaire to collect data on the health behaviors of the participants. Cigarette smoking was defined as smoking cigarettes ≥3 days per week during the month before enrollment. Similarly, alcohol drinking was defined as consuming alcohol-containing beverages ≥3 days per week during the month before enrollment.

2.4. Determination of carotid plaque

This study determined the presence of carotid plaque, as previously described.[22] In short, high-resolution B-mode ultrasonography systems (GE Healthcare Logie E, Vivid 7, and Vivid E9; General Electric Company, Milwaukee, USA) were equipped with a multifrequency linear array transducer. Following the protocol recommended by the American Society of Echocardiography,[23] two experienced technicians operated the ultrasonographic system to obtain transverse and cross-sectional ultrasound images of the bilateral extracranial carotid arteries. A well-trained technician retrieved ultrasonographic images and measured the thickness between the lumen-intima and media-adventitia interfaces using automatic contouring software (GE Healthcare EchoPAC version 112.0.2; General Electric Vingmed, Horten, Norway). The three technicians were blinded to the clinical profiles of the subjects. In the study, the plaque was defined as a focal protrusion 50% greater than the surrounding vessel wall, an intima-media thickness ≥1.5 mm, or local thickening ≥0.5 mm.[24] In the presence of observable carotid plaque, its site, segment, size, and degree of carotid stenosis were recorded.

In this study, we used the total number of carotid plaques and maximum degree of carotid stenosis as indicators of the severity of carotid atherosclerosis. We followed the criteria proposed by the European Carotid Surgery Trial (ECST)[25] and calculated the percentage of diameter reduction in the carotid plaque segment (Fig. 1). In this study, severe carotid atherosclerosis was defined as a maximum diameter stenosis of ≥50% or multiple medium plaques (diameter stenosis 30% to 49%), and moderate carotid atherosclerosis was defined as multiple plaques with at least one medium plaque. A representative photo of carotid plaque is shown in Fig. 2.

2.5. Statistical analyses

In this study, we used Student's *t* test to compare whether there were differences in the means of continuous variables between subjects with and without observable carotid plaque or between subjects with mild and advanced carotid atherosclerosis. Differences in the proportions of categorical variables between groups were tested using Pearson's test. Factors that showed promising associations with a p-value <0.10, with the probability of having carotid plaque or advanced carotid atherosclerosis in univariate analyses were included in multivariate analyses with a stepwise selection method. The criteria for entry and stay

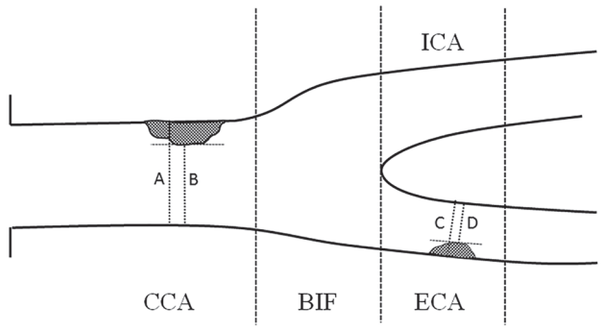

Fig. 1 The measurement of carotid stenosis by the ECST criteria. The degree of stenosis at CCA and ECA can be calculated by (A–B) × 100%/A and (C–D) × 100%/C, respectively. BIF = bifurcation; CCA = common carotid artery; ECA = external carotid artery; ICA = internal carotid artery; ECST = European Carotid Surgery Trial.

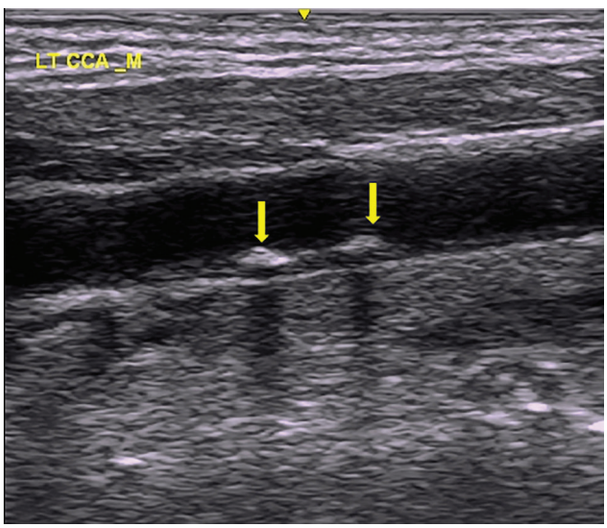

Fig. 2 Two plaques were detected at the left CCA of a middle-aged male. The lengths of the whole and remaining lumen were 0.76 and 0.52 cm (stenosis = 31.6%), respectively, for the distal plaque and were 0.75 and 0.54 cm (stenosis = 28.0%), respectively, for the proximal plaque.

in the regression model were both 0.10. Odds ratios (OR) and 95% CIs were calculated using an unconditional logistic regression model. All statistical analyses were performed with SAS 9.4 (SAS Institute Inc., Cary, NC, USA).

3. RESULTS

3.1. Baseline anthropometric and clinical characteristics of the subjects

Table 1 shows the baseline anthropometric and clinical characteristics of the participants. The mean (SD) age at enrollment was 68.6 (2.6) years, and approximately 44% of the participants were males. The prevalence rates for cigarette smoking and alcohol drinking were 6.2% and 8.0%, respectively. The percentages of hyperlipidemia, hypertension, and DM were 37.1%, 45.4%, and 16.8%, respectively. Approximately 44% of the subjects had any of these common CVD comorbidities, and ≥30% of the subjects had two or more common CVD comorbidities.

3.2. Prevalence rate for carotid atherosclerosis

The prevalence rate for carotid atherosclerosis is shown in Table 2. Approximately 63% of elderly patients had positive images of plaques in their carotid arteries. A total of 258 (31.6%) elders had multiple plaques, and 45 (5.5%) had maximum diameter stenosis of ≥50%. The prevalence rate for unilateral and bilateral carotid atherosclerosis was 27.7% and 35.3%, respectively. The prevalence rate for moderate or severe carotid atherosclerosis was 35.5%.

3.3. Comparisons between subjects with and without carotid plaques

Comparisons of baseline anthropometric and clinical characteristics between subjects with and without carotid plaques are shown in Supplementary Table 1, http://links.lww.com/JCMA/A166. The results showed that subjects with carotid plaque had a significantly higher mean age at enrollment and body height and a nonsignificant higher mean body weight and SBP, but significantly lower mean total cholesterol levels. The presence of carotid plaque was positively correlated with male sex, cigarette smoking, hyperlipidemia, hypertension, and DM. There was a significant difference in the distribution of the number of common CVD comorbidities between subjects with and without carotid plaques ($p < 0.0001$).

3.4. Univariate and multivariable analyses for the presence of carotid plaques

The results of univariate analyses for the presence of carotid plaques showed that older age, male sex, higher body height, cigarette smoking, hyperlipidemia, hypertension, and DM were correlated with significantly higher ORs of carotid plaque (Table 3). Subjects with higher body weight and SBP had nonsignificantly elevated ORs for carotid plaques. Higher total cholesterol levels were inversely correlated with the presence of carotid plaques. There was a linear trend for the number of common CVD comorbidities with the likelihood of having carotid plaques (OR, 1.55; 95% CI, 1.30-1.80).

Multivariable analyses showed that the most predictive models included age, sex, cigarette smoking, and number of common CVD comorbidities (model 1). The multivariable-adjusted OR for per 1.0 comorbidity was 1.52 (95% CI, 1.28-1.81). The second predictive model included age, sex, cigarette smoking, hypertension, and DM (model 2). The multivariable-adjusted ORs were 1.85 (95% CI, 1.38-2.48) and 1.63 (95% CI, 1.09-2.43) for hypertension and DM, respectively.

3.5. Comparisons between subjects with mild and moderate-to-severe carotid atherosclerosis

Comparisons of baseline anthropometric and clinical characteristics between subjects with mild and moderate-to-severe carotid atherosclerosis are shown in Supplementary Table 2, http://links.lww.com/JCMA/A166. Compared with subjects with mild carotid atherosclerosis, subjects with advanced carotid atherosclerosis had significantly higher mean age and fasting glucose levels and higher prevalence rates of cigarette smoking, hyperlipidemia, hypertension, and DM. The distribution of the number of common CVD comorbidities between subjects with mild and moderate-to-severe carotid atherosclerosis was significantly different ($p < 0.0001$). In contrast, participants with mild carotid atherosclerosis had higher mean total cholesterol and HDL-C levels.

3.6. Univariate and multivariable analyses for advanced carotid atherosclerosis

Univariate analyses showed that older age, male sex, higher blood glucose level, cigarette smoking, hyperlipidemia, hypertension,

Table 1

Basic clinical characteristics of 817 elders

	Mean	SD
Age at enrollment (years)	68.6	2.6
Body height (cm)	159.1	8.0
Body weight (kg)	63.1	10.7
Body mass index (BMI; kg/m^2)	24.9	3.4
Waist circumference (cm)	89.1	9.4
Hip circumference (cm)	96.8	6.9
Waist-to-hip ratio (%)	91.9	6.5
SBP (mmHg)	131.4	17.7
DBP (mmHg)	76.6	12.0
Total cholesterol (mg/dL)	199.1	37.7
HDL-C (mg/dL)	54.8	14.3
LDL-C (mg/dL)	116.7	30.6
Fasting triglycerides (mg/dL)	117.2	78.4
Fasting glucose (mg/dL)	101.1	26.7
	n	%
Male sex	355	43.5
Cigarette smoking	51	6.2
Alcohol drinking	65	8.0
Schooling years ≤12 years	575	70.4
Hyperlipidemia	303	37.1
Hypertension	371	45.4
Diabetes mellitus	137	16.8
Number of common CVD comorbidities[a]		
0	208	25.5
1	359	43.9
2	188	23.0
3	62	7.6

CVD = cardiovascular disease; DBP = diastolic blood pressure; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; SBP = systolic blood pressure.
[a]Including hypertension, hyperlipidemia, and diabetes mellitus.

Table 2

Prevalence rates of carotid atherosclerosis in 817 elders

	n	%
Right carotid arteries	399	48.8
Left carotid arteries	403	49.3
Any segment of extracranial carotid arteries	514	62.9
Number of carotid plaques		
–2	256	31.3
≥3	258	31.6
Maximum carotid stenosis (%)		
1-29	297	36.4
30-49	172	21.1
≥50	45	5.5
Site		
Unilateral	226	27.7
Bilateral	288	35.3
Severity of carotid atherosclerosis		
Mild	224	27.4
Moderate or severe	290	35.5

DM, and number of common CVD comorbidities were positively correlated with higher ORs of advanced carotid atherosclerosis (Table 4). The relationships were inversely related to total cholesterol and HDL-C levels. Multivariate analyses showed that the most predictive models included age, sex, cigarette smoking, and the number of common CVD comorbidities (Model 1). The second predictive model included age, sex, cigarette smoking, hypertension, and DM (Model 2). The multivariable-adjusted ORs for per 1.0 comorbidity were 1.57 (95% CI, 1.28-1.93) and were 1.63 (95% CI, 1.12-2.37), and 2.02 (95% CI, 1.27-3.21) for hypertension and DM, respectively.

3.7. Combined effects of hyperlipidemia, hypertension, and DM on carotid atherosclerosis

Table 5 shows the prevalent rates and adjusted ORs for the presence of carotid plaque among different combinatory groups of hyperlipidemia, hypertension, and DM. The adjusted OR was the highest for subjects who had all three common CVD comorbidities (OR, 3.78; 95% CI, 1.85-7.74), followed by subjects who had DM and HBP (OR, 3.56; 95% CI, 1.40-9.09). Hyperlipidemia and DM alone did not increase the likelihood of having carotid plaque. Table 5 also shows that subjects with two or more common CVD comorbidities had significantly higher ORs (range, 2.71 to 5.29) of having advanced carotid plaque. Adjusted OR for subjects with hyperlipidemia alone was not elevated compared to subjects with none of these common CVD comorbidities.

4. DISCUSSION

In this study, we enrolled 817 elderly individuals from communities and scanned their carotid arteries using high-resolution ultrasound systems. We found that carotid atherosclerosis was highly prevalent and concurred with the significant relationships of common CVD comorbidities (ie, hypertension, hyperlipidemia, and DM) with carotid plaque. These comorbidities were positively correlated with advanced carotid atherosclerosis. To our knowledge, only a limited number of community-based or population-based studies have assessed the effects of these common CVD comorbidities on the presence of carotid plaque, and none have assessed their combined effects and relative contribution to carotid atherosclerosis in elderly individuals.

Numerous studies have shown that older age is positively correlated with the presence of carotid atherosclerosis.[12–19] However, most previous studies have treated age as a correlate; consequently, only a few studies have reported the age-specific morbidity rate of carotid atherosclerosis. In this study, we found that carotid plaques were highly prevalent in community-dwelling elderly individuals. The prevalence rates were 65.8% and 70.0% in males aged 65 to 69 and 70 to 74 years, respectively, and 54.2% and 70.4% in females, respectively. A recent meta-analysis study in China showed that the prevalence rate of carotid plaque in males of the same age group was 53.2% and 63.8%, respectively, and 42.7% and 53.5% in females, respectively.[26] The global prevalence rate of carotid plaque in males of the same age groups was estimated to be 51.7% and 60.8%, respectively, and 36.5% and 45.0% in females, respectively.[27] The observed prevalence rates for carotid plaque in this study were significantly higher than those in the global estimates and those in China. Moreover, we found that the prevalence rate of severe carotid atherosclerosis, which was defined as a maximum carotid diameter stenosis of ≥50%, in males aged 65 to 69 and 70 to 74 years were 5.1% and 8.3%, respectively, and 4.3% and 7.8% in females, respectively. These values are higher than the upper confidence limits of global estimates in the study by Song.[27] The high prevalence rates of carotid stenosis ≥50% in this study may accountable for two possible explanations. First, there are two criteria for carotid stenosis, that is, the North American Symptomatic Endarterectomy Trial and the ECST and the degree of stenosis tends to be more severe by the ECST criteria.[28,29] The present study used the ECST criteria to define carotid stenosis but it was not described in the study by Song.[27] The second, hypertension, hyperlipidemia, and DM are the well-known determinant of atherosclerosis.[30] A previous northern Taiwan study, which enrolled subjects from the

Table 3

Multivariable logistic regression analyses for carotid plaques

	Univariable		Multivariable			
			Model 1		Model 2	
	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)
Age at enrollment (per 1 year)	1.10**	(1.04-1.17)	1.09**	(1.03-1.16)	1.09*	(1.02-1.15)
Sex (male vs female)	1.58**	(1.18-2.11)	1.34+	(0.99-1.83)	1.28+	(0.94-1.74)
Body height (per 10 cm)	1.20*	(1.00-1.44)	-		-	
Body weight (per 10 kg)	1.12+	(0.98-1.29)	-		-	
SBP (per 10 mmHg)	1.09+	(1.00-1.18)	-		-	
Total cholesterol (per 10 mg/dL)	0.96*	(0.92-0.99)	-		-	
Cigarette smoking	4.75**	(2.00-11.27)	3.92**	(1.60-9.61)	3.94**	(1.61-9.66)
Hyperlipidemia	1.37*	(1.01-1.84)	-		-	
Hypertension	1.99**	(1.49-2.66)	-		1.85**	(1.38-2.48)
Diabetes mellitus	1.76**	(1.19-2.60)	-		1.63*	(1.09-2.43)
Number of common CVD comorbidities	1.55**	(1.30-1.80)	1.52**	(1.28-1.81)	-	

-, not included; +, $0.05<p<0.10$; *, $0.005 < p < 0.05$; **, $p < 0.005$.
CVD = cardiovascular disease; SBP = systolic blood pressure.

Table 4

Multivariable logistic regression analyses for advanced carotid plaques

	Univariable		Multivariable			
			Model 1		Model 2	
	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)
Age at enrollment (per 1 year)	1.11**	(1.03-1.19)	1.11*	(1.03-1.19)	1.11*	(1.03-1.19)
Sex (male vs. female)	1.69**	(1.19-2.40)	1.51*	(1.03-2.21)	1.40+	(0.96-2.05)
Total cholesterol (per 10 mg/dL)	0.96+	(0.91-1.01)	-		-	
HDL-C (per 5 mg/dL)	0.94*	(0.88-1.00)	-		-	
Fasting glucose (per 10 mg/dL)	1.08*	(1.01-1.16)	-		-	
Cigarette smoking	2.59*	(1.28-5.24)	2.23*	(1.05-4.75)	2.16*	(1.02-4.59)
Hyperlipidemia	1.49*	(1.04-2.13)	-		-	
Hypertension	1.77*	(1.23-2.55)	-		1.63*	(1.12-2.37)
Diabetes mellitus	2.15**	(1.37-3.38)	-		2.02**	(1.27-3.21)
Number of common CVD comorbidities	1.56**	(1.27-1.91)	1.57**	(1.28-1.93)	-	

-, not included; +, $0.05 < p < 0.10$; *, $0.005 < p < 0.05$; **, $p < 0.005$.
CVD = cardiovascular disease; HDL-C = high-density lipoprotein cholesterol.

Chin-Shan Community Cardiovascular Cohort (CCCC) study, reported that the prevalence rate of carotid stenosis ≥50% was as high as 8.2% in subjects with hypertension and were 3.4% and 1.5% in subjects with borderline hypertension and normotension, respectively.[17] It is reasonable to hypothesize that an increased number of the aforementioned determinants correlate with higher morbidity of atherosclerosis. In this study, we observed a significant association between the presence of advanced carotid atherosclerosis and the number of these CVD major com-morbidities. However, due to the lack of associated information in previous studies, we are unable to validate our speculation.

This study showed that older age, male sex, cigarette smoking, hypertension, hyperlipidemia, and DM were significantly correlated with higher ORs of carotid plaque in the elderly. These findings are consistent with the results of two recent meta-analyses on carotid atherosclerosis.[27,30] Furthermore, we found that the number of common CVD comorbidities was the most significant predictor of the presence of carotid plaque, as well as the presence of advanced carotid atherosclerosis. These findings are consistent with evidence that the control of blood lipids, pressure, and glucose reduces the risk of atherosclerotic diseases.[31–34]

There have been many etiological studies on atherosclerosis, but only a limited number of studies have explored the effects of hypertension, hyperlipidemia, and DM. Observational studies in France,[12,15] Taiwan,[17] and Korea,[13] consistently showed that ORs of carotid plaque were significantly increased with hypertension and non-significantly increased with DM. However, the relationships between hyperlipidemia and carotid plaque are inconsistent.[12,13,15,17] Furthermore, none of these previous studies reported the combined effects and relative contributions of these common CVD comorbidities with advanced carotid atherosclerosis. In this study, we found that the model containing the number of common CVD comorbidities was the most predictive, and the model containing hypertension and DM was the second most predictive for the presence of carotid plaque. Similar findings were observed in relation to advanced carotid atherosclerosis. To our knowledge, this is the first study to report the relationship between these common CVD comorbidities and advanced carotid atherosclerosis in elderly individuals.

We found that the relationship between hypertension, hyperlipidemia, and DM with carotid atherosclerosis showed distinct patterns (Table 5). Subjects with hyperlipidemia alone did not have elevated ORs for carotid plaque or advanced carotid atherosclerosis. Subjects affected with DM alone had a non-significantly elevated OR for advanced carotid

Table 5

Prevalence rates and adjusted ORs of carotid atherosclerosis among different combinatory groups of common CVD comorbidities

	None	HBL alone	DM alone	HBP alone	HBL + HBP	DM + HBL	DM + HBP	All three	*p* for trend
Total no.	208	86	43	230	140	15	33	62	
Presence of carotid arteries									
n	112	43	25	146	101	9	27	51	
Prevalence rate, %	53.8	50.0	58.1	63.5	72.1	60.0	81.8	82.3	<0.0001
OR[a]	1.00	0.96	0.99	1.43[+]	2.08[**]	1.50	3.56[**]	3.78[**]	<0.0001
(95% CI)		(0.57-1.60)	(0.49-1.97)	(0.97-2.11)	(1.30-3.32)	(0.51-4.41)	(1.40-9.09)	(1.85-7.74)	
Moderate or severe atherosclerosis									
n	49	18	15	78	66	8	21	35	
Prevalence rate, %	23.6	20.9	34.9	33.9	47.1	53.3	63.6	56.5	<0.0001
OR[a]	1.00	0.99	1.35	1.56[*]	2.71[**]	4.79[**]	5.29[**]	4.07[**]	<0.0001
(95% CI)		(0.53-1.86)	(0.64-2.85)	(1.01-2.41)	(1.68-4.36)	(1.63-14.09)	(2.39-11.75)	(2.20-7.51)	

CVD = cardiovascular disease; DM = diabetes mellitus; HBL = hyperlipidemia; HBP = hypertension; OR = odds ratio.
[a]ORs were adjusted for age, sex, and cigarette smoking.

atherosclerosis but did not have an elevated OR for carotid plaque. In contrast, subjects with hypertension alone had elevated ORs for carotid plaque and advanced carotid atherosclerosis. These findings indicate that (1) hyperlipidemia alone might be insufficient to induce the pathogenesis and promote the progression of carotid atherosclerosis, (2) DM alone might be insufficient to induce the pathogenesis, but might promote the progression of carotid atherosclerosis, and (3) hypertension alone is sufficient to induce the pathogenesis and promote the progression of carotid atherosclerosis. These findings also imply that subjects affected by hyperlipidemia alone might not benefit from lipid-lowering treatment and that blood pressure control precedes blood lipid and glucose control. Prospective studies with larger sample sizes are necessary to validate our hypothesis.

There are some limitations to this study. First, the observational nature of this study means that causal inferences must be made with caution. Second, the presence of a thin or fissured fibrous cap, lipid-rich necrotic core, and intraplaque hemorrhage are emerging biomarkers of vulnerable plaques.[4,5] To increase accessibility and recruit elders in communities, ultrasound systems were used in the present study. As a result, we were unable to measure plaque vulnerability. Instead, we used the number of plaques and diameter stenosis, primarily based on the quantitative measurements of lumen and vessel wall, to reflect the severity of carotid atherosclerosis. It is indicated that quantitative measurements of lumen and vessel wall by ultrasound are highly reliable.[4,35] The last, in this study, the length of lumen and thickness of vessel wall were all measured by a single well-trained and experienced technician. To assess the intra-rater reliability of measurements, we selected a random sample of 82 subjects and re-measured it a month after. We found the intra-rater reliability of measurements was very good,[22] whereas we were unable to assess the inter-rater reliability.

In conclusion, we found that carotid plaques were highly prevalent in the elderly and that more than one-third of the subjects had moderate-to-severe carotid atherosclerosis. We found that the number of common CVD comorbidities, including hypertension, hyperlipidemia, and DM, was more predictive of the presence of carotid plaque and advanced carotid atherosclerosis. The second predictive model included hypertension and DM. Furthermore, combinatory analyses showed that subjects affected by hypertension alone had elevated ORs of carotid plaque and advanced carotid atherosclerosis, but not for subjects affected by hyperlipidemia alone. These findings imply that in the community-dwelling elder subjects, control of blood pressure precedes the control of blood lipids and glucose to reduce the impact of atherosclerotic diseases.

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APPENDIX A. SUPPLEMENTARY DATA

Supplementary data related to this article can be found at http://links.lww.com/JCMA/A166.

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