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Letter to the Editor

Association between Parity, Carotid Plaques, and Intima Media Thickness in Northern Chinese Women*

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Pregnancy is always associated with several important physiological changes in women, including sex hormone levels, glycolipid metabolism, and oxidative stress. These changes may have short-term and long-term effects on their cardiovascular system. Parity is the number of times a woman has given birth. Several studies have investigated the association between parity and risk of cardiovascular diseases in women. Prospective studies have shown a fairly low incidence of cardiovascular endpoints for parous women[1]. Therefore, it would be meaningful to assess the relationship between parity and other surrogate markers.

Carotid atherosclerosis is widely recognized as a good marker of systemic atherosclerotic burden, including the presence of carotid plaques and the measurement of carotid intima-media thickness (IMT). It is well known that carotid atherosclerosis is a significant predictor of subsequent cardiovascular diseases such as myocardial infarction and ischemic stroke. Although the association between parity and carotid atherosclerosis has been assessed in various ethnic populations, the results are conflicting. A progressive increasing tendency was found in elderly women from the Netherlands[2], a U-shaped association was found in women from Germany[3], and a J-shaped association was observed in British women[4]. However, no significant association was found between parity and either IMT or presence of plaques in women from Finland and southern Germany[5,6]. To the best of our knowledge, the findings related to this topic have not been reported in Chinese population. Therefore, we performed a cohort study of women aged ≥ 40 years in Northern China with an aim to assess the association between parity and carotid atherosclerosis in this cross-sectional analysis.

Participants were recruited from Jidong and Kailuan communities (Tangshan City, Hebei, Northern China) in 2010 to 2014. A total of 3,386 participants remained in the statistical analysis after excluding 8,025 males, 2,002 females aged < 40 years, and 1,082 females with missing information on parity and carotid plaques. Twenty-three nulliparous women were also excluded from the current analysis because of small sample size. The study was conducted according to the guidelines of Helsinki Declaration and was approved by the Ethics Committee of Jidong Oilfield Inc. Medical Center and Kailuan General Hospital. Written informed consent was obtained from all the participants.

A standardized, structured questionnaire was administered to collect information on subjects' demographic characteristics, socioeconomic status, cardiovascular risk factors, and medical history by well-trained interviewers. Parity was classified into four categories: one, two, three, and four or more (Supplementary Table S1 available in www.besjournal.com).

The carotid artery was assessed by certified sonographers blinded to participants' clinical characteristics. High-resolution B-mode ultrasound (Philips iU22 ultrasound system, Philips Medical Systems, Bothell, WA, USA) with a 5–12 MHz linear array transducer was used to detect plaques bilaterally on three segments: the common carotid artery, the carotid artery bifurcation, and the internal carotid artery. IMT was defined as the

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distance from the leading edge of the lumen-intima interface to the leading edge of the media-adventitia interface on a longitudinal image of each carotid artery. Carotid plaque was defined as a focal structure encroaching into the arterial lumen of at least 0.5 mm or 50% of the surrounding IMT value or a thickness > 1.5 mm as measured from the media-adventitia interface to the intima-lumen interface. Carotid atherosclerosis was considered as the presence of plaques at one or more sites. IMTs of the bilateral common carotid artery and the internal carotid artery were then averaged to obtain a mean IMT value for each subject. IMTs were measured twice by the same technician for subsequent assessment of interpreter reproducibility. The results were reviewed by two independent sonographers. Discrepancies between their evaluations were resolved by consensus.

Comparisons between the parity groups were tested using one-way ANOVA for continuous variables or chi-square test for categorical variables. Ordinal variables and continuous variables with skewed distribution were compared using the nonparametric Kruskal-Wallis test. The association between parity and carotid artery plaques was examined by logistic regression models, while the association of parity with carotid artery IMT was analyzed by multivariate linear regression models. Results of logistic regression models are presented as odds ratio (*OR*) with 95% confidence interval (*CI*), and results of linear regression models are presented as unstandardized β-coefficient and standard error (SE). Potential confounders, including age, hypertension, diabetes mellitus, dyslipidemia, education level, income, current smoking, alcohol use, body mass index (BMI), physical activity, antihypertensive medication, use of insulin or oral hypoglycemic drugs, use of antilipidemic agents, and oral contraceptives, were adjusted in these models. The parity of one was considered as the reference in all models. A *P* value of < 0.05 was considered to be statistically significant. All statistical analyses were performed with SAS 9.4 (SAS Institute Inc., Cary, NC, USA).

Parity in this population ranged from one to a maximum of seven births (Supplementary Table S1). Women with one birth (2,498 participants) constituted the majority (73.8%) of the population. Table 1 shows the baseline characteristics of the participants according to the parity status. Both age and age at menopause increased with increasing parity. The incidence of current smoking increased with increasing parity, while alcohol usage decreased with increasing parity. Physical activity showed a significant difference across the parity groups. Higher prevalence of hypertension, diabetes mellitus, and dyslipidemia was associated with increasing parity (all with *P* < 0.001). There was also a significant trend toward the usage of more antihypertensive, antidiabetic, antihyperlipidemic, and contraceptive drugs with parity (all with *P* < 0.001), except estrogen replacement therapy (*P* = 0.36). Socioeconomic status, measured by education level and mean equivalent household income, showed a statistical difference among the parity groups (all with *P* < 0.001). In Supplementary Table S2 (available in www.besjournal.com), it adds the parity group of zero.

Figure 1 shows the association between parity and carotid artery plaques. Women with more births tended to have higher risk of carotid artery plaques than those with only one birth. Logistic regression analysis yielded an age-adjusted *OR* of 1.61 (95% *CI* 1.41 to 1.84) per birth. Additional adjustment for hypertension, diabetes mellitus, and dyslipidemia did not alter the association (*OR* 1.55, 95% *CI* 1.35 to 1.77). In the multivariate adjusted model, the risk of carotid artery plaques increased by 49% (95% *CI* 29% to 72%) per birth after full adjustment for age, hypertension, diabetes mellitus, dyslipidemia, education level, income, current smoking, alcohol use, BMI, physical activity, antihypertensive medication, use of insulin or oral hypoglycemic drugs, use of antilipidemic agents, and oral contraceptives. Supplementary Figure S1 (available in www.besjournal.com) shows the results of parity group of zero.

As shown in Table 2, a positive association was found between parity and mean carotid artery IMT. Linear regression analysis showed an age-adjusted β of 0.024 (SE = 0.004) for common carotid IMT and 0.017 (SE = 0.003) for internal carotid IMT. In the fully adjusted model, this association remained statistically significant between parity and common carotid IMT [β (SE) = 0.016 (0.004)] and between parity and internal carotid IMT [β (SE) = 0.011 (0.003)]. Interestingly, higher parity was associated with greater IMT values for both the common carotid artery and the internal carotid artery in all the adjusted models, although this association appeared to be weaker with internal carotid IMT than with common carotid IMT for women with the same parity. If added the parity group of zero, it seemed no influences on these associations (Supplementary Table S3 available in www. besjournal.com).

We assessed for the first time the association between parity and carotid atherosclerosis in Chinese women. We found that women with more births had increased risk of carotid plaques. A positive association was observed between parity and carotid artery IMT, and increased parity was associated with higher IMT values for both the common carotid artery and the internal carotid artery.

Several previous studies have reported inconsistent relationships between parity and carotid atherosclerosis. Humphries et al. found a progressive increase between parity and risk of carotid artery plaques in Dutch women aged ≥ 55 years[2]. Skilton et al observed a linear association between parity and risk of carotid artery plaques in French women aged > 45 years[7]. Wolff et al. found a U-shaped association between parity and mean and maximum common carotid IMT among women aged 45–79 years in northeast Germany[3]. Sanghavi et al. reported a U-shaped relationship between parity and the risk of subclinical coronary and aortic

Table 1. Baseline characteristics of participants stratified by parity

Characteristics	Overall	Parity group				*P* value
		1	2	3	≥ 4	
Number, *n* (%)	3,386	2,498	633	186	69	
Age, year	52.5 ± 8.9	49.2 ± 6.3	59.4 ± 7.3	66.5 ± 6.9	71.9 ± 6.9	< 0.001
Age at menopause, year	58.4 ± 7.4	54.5 ± 5.4	61.4 ± 5.6	66.3 ± 5.9	72.3 ± 6.2	< 0.001
BMI, kg/m^2	24.5 ± 3.4	24.2 ± 3.3	25.2 ± 3.5	25.3 ± 3.7	25.2 ± 3.4	< 0.001
Current smoking, *n* (%)	92 (2.7)	57 (2.3)	20 (3.2)	10 (5.4)	5 (7.3)	0.006
Alcohol use, *n* (%)	84 (2.5)	71 (2.8)	13 (2.1)	0	0	0.025
Physical activity, *n* (%)						< 0.001
Inactive	1,106 (32.7)	831 (33.3)	196 (31.0)	62 (33.3)	17 (24.6)	
Moderate active	650 (19.2)	535 (21.4)	74 (11.7)	29 (15.6)	12 (17.4)	
Active	1,630 (48.1)	1,132 (45.3)	363 (57.4)	95 (51.1)	40 (58.0)	
Hypertension, *n* (%)	1,210 (35.7)	720 (28.8)	331 (52.3)	115 (61.8)	44 (63.8)	< 0.001
Diabetes mellitus, *n* (%)	304 (9.0)	168 (6.7)	92 (14.5)	32 (17.2)	12 (17.4)	< 0.001
Dyslipidemia, *n* (%)	1434 (42.4)	960 (38.4)	320 (50.6)	115 (61.8)	39 (56.5)	< 0.001
Antihypertensive medication, *n* (%)	592 (27.8)	301 (21.1)	189 (37.1)	69 (48.3)	33 (67.4)	< 0.001
Insulin or oral hypoglycemic drug, *n* (%)	178 (9.5)	91 (7.1)	61 (13.4)	17 (16.0)	9 (31.0)	< 0.001
Antilipemic agent, *n* (%)	72 (2.1)	41 (1.6)	17 (2.7)	12 (6.5)	2 (2.9)	< 0.001
Oral contraceptives, *n* (%)	119 (7.4)	67 (5.3)	32 (15.2)	11 (12.1)	9 (17.3)	< 0.001
Estrogen replacement therapy, *n* (%)	33 (1.7)	26 (2.2)	5 (1.0)	2 (1.2)	0	0.361
Education level, *n* (%)						< 0.001
Illiteracy/primary school	280 (8.3)	76 (3.0)	129 (20.4)	46 (24.7)	29 (42.0)	
Middle/high school	2,187 (64.6)	1,588 (63.6)	444 (70.1)	121 (65.1)	34 (49.3)	
College or above	919 (27.1)	834 (33.4)	60 (9.5)	19 (10.2)	6 (8.7)	
Income, ¥/month, *n* (%)						< 0.001
≤ ¥3,000	2,444 (72.2)	1721 (68.9)	511 (80.7)	155 (83.3)	57 (82.6)	
¥3,001–5,000	813 (24.0)	670 (26.8)	105 (16.6)	27 (14.5)	11 (15.9)	
> ¥5,000	129 (3.8)	107 (4.3)	17 (2.7)	4 (2.2)	1 (1.5)	
Plaques, *n* (%)	853 (25.2)	484 (19.4)	215 (34.0)	103 (55.4)	51 (73.9)	< 0.001
Mean common carotid IMT, mm	0.72 ± 0.13	0.70 ± 0.11	0.76 ± 0.13	0.84 ± 0.14	0.86 ± 0.13	< 0.001
Mean internal carotid IMT, mm	0.65 ± 0.09	0.63 ± 0.08	0.67 ± 0.10	0.69 ± 0.10	0.73 ± 0.10	< 0.001

atherosclerosis in US women aged 30–65 years[8]. In British women aged 60–79 years, a J-shaped association was found between parity and the risk of coronary heart disease[4]. However, in Finnish women aged 45–74 years and in women aged 50–81 years from southern Germany, no significant associations were observed between parity and carotid plaques or IMT[5,6]. In the present study, we found positive associations between parity and carotid artery plaques and between parity and carotid IMT. Women with more births tended to have higher risk of carotid artery plaques than those with only one birth. Higher parity was associated with greater IMT values for both the common carotid artery and the internal carotid artery. Our results agreed with the findings of Humphries in women from the Netherlands[2].

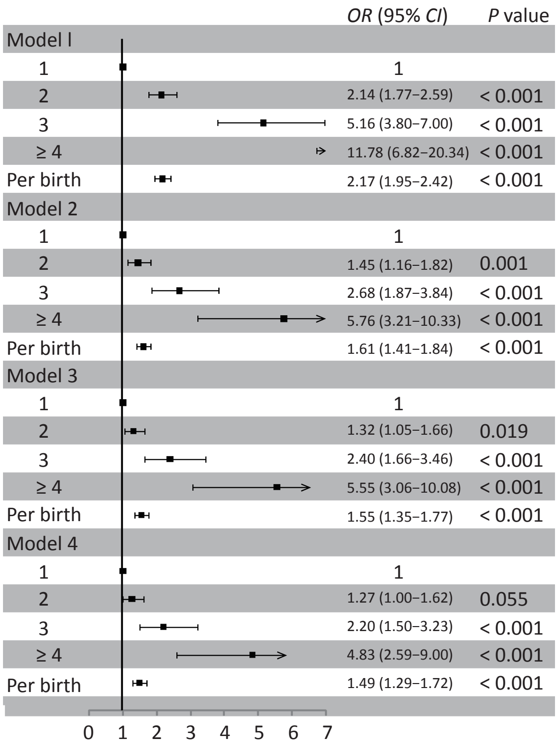

Figure 1. Association between parity and carotid artery plaques. Model 1: unadjusted; Model 2: adjusted for age; Model 3: adjusted for age, hypertension, diabetes mellitus and dyslipidemia; Model 4: adjusted for age, hypertension, diabetes mellitus, dyslipidemia, education level, income, current smoking, alcohol use, BMI, physical activity, antihypertensive medication, insulin or oral hypoglycemic drug, antilipemic agent, and oral contraceptives.

Several reasons might explain the inconsistencies among these studies. First, the study populations were from different countries with different ethnicities, and consequently, they had specific sociodemographic characteristics, which might lead to confounding results related to the associations[9]. Second, women were enrolled at different age groups. Several studies included only elderly women, whereas some other studies included both young and old women. In addition, the composition of study population was distinct from each other. Nulliparous women constituted 21.5% of the population in the Netherlands[2], but there were 8.5% and 18.0% nulliparous women in cohorts of Germany and France[3,7], respectively. In our cohort, the majority were women with parity of one (73.8%), which might be because of specific one-child birth control policies in China.

The present study has several limitations. First, the study participants comprised women from northern China and had specific sociodemographic characteristics; hence, the findings might not be generalized to other districts and countries. Second, there were particular family planning policies in China during the study period, such as one-child policy; therefore, the composition of study population was different from other cohorts, which might cause unavoidable bias. In addition, reproductive factors, including miscarriage, abortions, breastfeeding, pre-eclampsia, and gestational hypertension, were not assessed in the present study. Finally, the cross-sectional study design might overlook some ongoing changes in carotid IMT.

In conclusion, we found there were positive associations between parity and carotid atherosclerosis in Chinese women. Increased parity conferred more risk of developing carotid plaques and higher values of carotid IMT, suggesting that multiparous women may experience more atherosclerotic burden.

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Table 2. Association between parity and carotid artery IMT

Parity	Model 1		Model 2		Model 3		Model 4	
	β (SE)	*P* value	*β* (SE)	*P* value	*β* (SE)	*P* value	*β* (SE)	*P* value
Common carotid IMT								
1	0		0		0		0	
2	0.062 (0.005)	< 0.001	0.017 (0.006)	0.003	0.010 (0.006)	0.086	0.005 (0.006)	0.393
3	0.136 (0.009)	< 0.001	0.056 (0.010)	< 0.001	0.046 (0.010)	< 0.001	0.039 (0.010)	< 0.001
≥ 4	0.160 (0.015)	< 0.001	0.072 (0.015)	< 0.001	0.065 (0.015)	< 0.001	0.055 (0.015)	< 0.001
Per birth	0.061 (0.003)	< 0.001	0.024 (0.004)	< 0.001	0.020 (0.004)	< 0.001	0.016 (0.004)	< 0.001
Internal carotid IMT								
1	0		0		0		0	
2	0.037 (0.004)	< 0.001	0.019 (0.005)	< 0.001	0.016 (0.005)	< 0.001	0.010 (0.005)	0.043
3	0.059 (0.008)	< 0.001	0.028 (0.009)	0.002	0.024 (0.009)	0.006	0.018 (0.009)	0.041
≥ 4	0.092 (0.014)	< 0.001	0.057 (0.015)	< 0.001	0.053 (0.015)	< 0.001	0.044 (0.015)	0.003
Per birth	0.032 (0.003)	< 0.001	0.017 (0.003)	< 0.001	0.015 (0.003)	< 0.001	0.011 (0.003)	< 0.001

Note. Model 1: unadjusted; Model 2: adjusted for age; Model 3: adjusted for age, hypertension, diabetes mellitus and dyslipidemia; Model 4: adjusted for age, hypertension, diabetes mellitus, dyslipidemia, education level, income, current smoking, alcohol use, BMI, physical activity, antihypertensive medication, insulin or oral hypoglycemic drug, antilipemic agent, and oral contraceptives. IMT, intima-media thickness.

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REFERENCES

1. Fraser A, Nelson SM, Macdonald-Wallis C, et al. Associations of pregnancy complications with calculated cardiovascular disease risk and cardiovascular risk factors in middle age: The Avon Longitudinal Study of Parents and Children. Circulation, 2012; 125, 1367−80.
2. Humphries KH, Westendorp IC, Bots ML, et al. Parity and carotid artery atherosclerosis in elderly women: the Rotterdam Study. Stroke, 2001; 32, 2259−64.
3. Wolff B, Volzke H, Robinson D, et al. Relation of parity with common carotid intima-media thickness among women of the Study of Health in Pomerania. Stroke, 2005; 36, 938−43.
4. Lawlor DA, Emberson JR, Ebrahim S, et al. Is the association between parity and coronary heart disease due to biological effects of pregnancy or adverse lifestyle risk factors associated with child-rearing? Circulation, 2003; 107, 1260−4.
5. Kharazmi E, Moilanen L, Fallah M, et al. Reproductive history and carotid intima-media thickness. Acta Obstet Gynecol Scand, 2007; 86, 995−1002.
6. Stöckl D, Peters A, Thorand B, et al. Reproductive factors, intima media thickness and carotid plaques in a cross-sectional study of postmenopausal women enrolled in the population-based KORA F4 study. BMC Womens Health, 2014; 14, 17.
7. Skilton MR, Serusclat A, Begg LM, et al. Parity and carotid atherosclerosis in men and women: insights into the roles of childbearing and child-rearing. Stroke, 2009; 40, 1152−7.
8. Sanghavi M, Kulinski J, Ayers CR, et al. Association between number of live births and markers of subclinical atherosclerosis: The Dallas Heart Study. Eur J Prev Cardiol, 2016; 23, 391−9.
9. Mathieu RAt, Powell-Wiley TM, Ayers CR, et al. Physical activity participation, health perceptions, and cardiovascular disease mortality in a multiethnic population: The Dallas Heart Study. Am Heart J, 2012; 163, 1037−40.

Supplementary Table S1. Parity distribution in this study

Parity	Frequency	Percentage	Cumulative frequency	Cumulative percentage
0	23	0.67	23	0.67
1	2,498	73.28	2,521	73.95
2	633	18.57	3,154	92.52
3	186	5.46	3,340	97.98
4	53	1.55	3,393	99.53
5	13	0.38	3,406	99.91
6	2	0.06	3,408	99.97
7	1	0.03	3,409	100.00

Supplementary Table S2. Baseline characteristics of participants stratified by parity

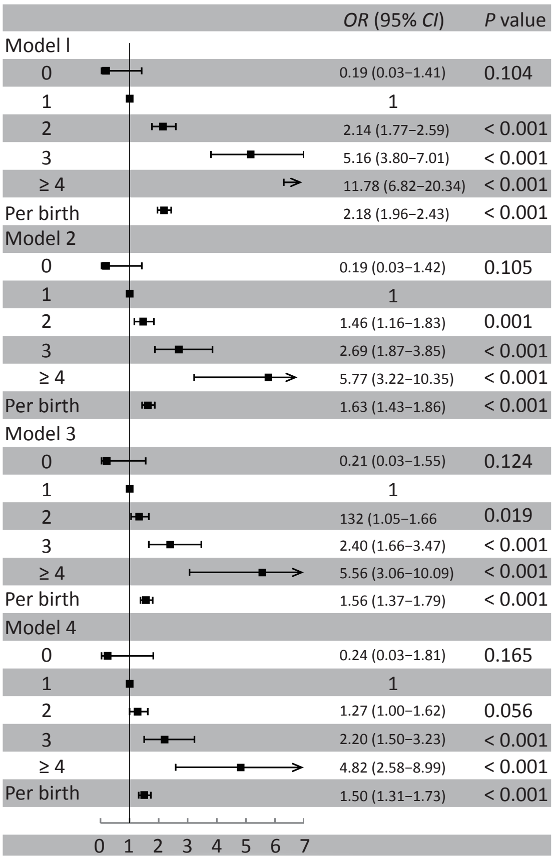
Characteristics	Overall	Parity groups					*P* value
		0	1	2	3	≥ 4	
Number, *n* (%)	3,409	23	2,498	633	186	69	
Age, year	52.5 ± 8.9	46.4 ± 5.1	49.2 ± 6.34	59.4 ± 7.3	66.5 ± 6.9	71.9 ± 6.9	< 0.001
Age at menopause, year	58.4 ± 7.4	52.9 ± 5.3	54.5 ± 5.4	61.4 ± 5.6	66.3 ± 5.7	72.3 ± 6.2	< 0.001
BMI, kg/m^2	24.5 ± 3.4	22.7 ± 2.2	24.2 ± 3.3	25.2 ± 3.5	25.3 ± 3.7	25.2 ± 3.4	< 0.001
Current smoking, *n* (%)	93 (2.7)	1 (4.4)	57 (2.3)	20 (3.2)	10 (5.4)	5 (7.2)	0.013
Alcohol use, *n* (%)*	86 (2.5)	2 (8.7)	71 (2.8)	13 (2.1)	0	0	0.011
Physical activity, *n* (%)							< 0.001
Inactive	1,115 (32.7)	9 (39.1)	831 (33.3)	196 (31.0)	62 (33.3)	17 (24.6)	
Moderate active	652 (19.1)	2 (8.7)	535 (21.4)	74 (11.7)	29 (15.6)	12 (17.4)	
Active	1,642 (48.2)	12 (52.2)	1,132 (45.3)	363 (57.4)	95 (51.1)	40 (58.0)	
Hypertension, *n* (%)	1,216 (35.7)	6 (26.1)	720 (28.8)	331 (52.3)	115 (61.8)	44 (63.8)	< 0.001
Diabetes mellitus, *n* (%)	304 (8.9)	0	168 (6.7)	92 (14.5)	32 (17.2)	12 (17.4)	< 0.001
Dyslipidemia, *n* (%)	1,440 (42.2)	6 (26.1)	960 (38.4)	320 (50.6)	115 (61.8)	39 (56.5)	< 0.001
Antihypertensive medication, *n* (%)	592 (17.42)	2 (8.7)	301 (12.1)	189 (29.9)	69 (37.1)	33 (47.8)	< 0.001
Insulin or oral hypoglycemic drug, *n* (%)	178 (5.22)	0	91 (3.6)	61 (9.6)	17 (9.1)	9 (13.0)	< 0.001
Antilipemic agent, *n* (%)*	72 (2.11)	0	41 (1.6)	17 (2.7)	12 (6.5)	2 (2.9)	0.002
Oral contraceptives, *n* (%)	119 (3.5)	0	67 (2.7)	32 (5.1)	11 (5.9)	9 (13.0)	< 0.001
Estrogen replacement therapy, *n* (%)*	33 (1.7)	0	26 (2.2)	5 (1.0)	2 (1.2)	0	0.415
Education level, *n* (%)							< 0.001
Illiteracy/primary school	281 (8.2)	1 (4.4)	76 (3.0)	129 (20.4)	46 (24.7)	29 (42.0)	
Middle/high school	2,195 (64.4)	8 (34.8)	1,588 (63.6)	444 (70.1)	121 (65.1)	34 (49.3)	
College or above	933 (27.4)	14 (60.9)	834 (33.4)	60 (9.5)	19 (10.2)	6 (8.7)	
Income, ¥/month, *n* (%)							< 0.001
≤ ¥3,000	2,454 (72.0)	10 (43.5)	1,721 (68.9)	511 (80.7)	155 (83.3)	57 (82.6)	
¥3,001–5,000	824 (24.2)	11 (47.8)	670 (26.8)	105 (16.6)	27 (14.5)	11 (15.9)	
> ¥5,000	131 (3.8)	2 (8.7)	107 (4.3)	17 (2.7)	4 (2.2)	1 (1.5)	
Plaques, *n* (%)	854 (25.1)	1 (4.4)	484 (19.4)	215 (34.0)	103 (55.4)	51 (73.9)	< 0.001
Mean common carotid IMT, mm	0.72 ± 0.13	0.66 ± 0.07	0.70 ± 0.11	0.76 ± 0.13	0.84 ± 0.14	0.86 ± 0.13	< 0.001
Mean internal carotid IMT, mm	0.65 ± 0.09	0.62 ± 0.08	0.63 ± 0.08	0.67 ± 0.10	0.69 ± 0.10	0.73 ± 0.10	< 0.001

Note. *Use Fisher's exact test.

Supplementary Table S3. Association between parity and carotid artery IMT

Parity	Model 1		Model 2		Model 3		Model 4	
	β (SE)	*P value*	*β* (SE)	*P value*	*β* (SE)	*P value*	*β* (SE)	*P value*
common carotid IMT								
0	−0.043 (0.025)	0.084	−0.042 (0.024)	0.083	−0.035 (0.023)	0.136	−0.026 (0.023)	0.272
1	0		0		0		0	
2	0.062 (0.005)	< 0.001	0.017 (0.006)	0.003	0.010 (0.006)	0.077	0.005 (0.006)	0.373
3	0.136 (0.009)	< 0.001	0.056 (0.010)	< 0.001	0.046 (0.010)	< 0.001	0.040 (0.010)	< 0.001
≥ 4	0.160 (0.015)	< 0.001	0.072 (0.015)	< 0.001	0.065 (0.015)	< 0.001	0.055 (0.015)	< 0.001
Per birth	0.058 (0.003)	< 0.001	0.023 (0.004)	< 0.001	0.019 (0.003)	< 0.001	0.016 (0.003)	< 0.001
internal carotid IMT								
0	−0.013 (0.019)	0.489	−0.013 (0.019)	0.503	−0.010 (0.019)	0.588	−0.002 (0.019)	0.924
1	0		0		0		0	
2	0.037 (0.004)	< 0.001	0.019 (0.005)	< 0.001	0.016 (0.005)	< 0.001	0.010 (0.005)	0.046
3	0.059 (0.008)	< 0.001	0.028 (0.009)	0.002	0.024 (0.009)	0.006	0.018 (0.009)	0.043
≥ 4	0.092 (0.014)	< 0.001	0.056 (0.015)	< 0.001	0.053 (0.015)	< 0.001	0.044 (0.015)	0.003
Per birth	0.030 (0.003)	< 0.001	0.016 (0.003)	< 0.001	0.014 (0.003)	< 0.001	0.010 (0.003)	0.001

Note. Model 1: unadjusted; Model 2: adjusted for age; Model 3: adjusted for age, hypertension, diabetes mellitus and dyslipidemia; Model 4: adjusted for age, hypertension, diabetes mellitus, dyslipidemia, education level, income, current smoking, alcohol use, BMI, physical activity, antihypertensive medication, insulin or oral hypoglycemic drug, antilipemic agent, and oral contraceptives.



Supplementary Figure S1. Association between parity and carotid artery plaques. Model 1: unadjusted; Model 2: adjusted for age; Model 3: adjusted for age, hypertension, diabetes mellitus and dyslipidemia; Model 4: adjusted for age, hypertension, diabetes mellitus, dyslipidemia, education level, income, current smoking, alcohol use, BMI, physical activity, antihypertensive medication, insulin or oral hypoglycemic drug, antilipemic agent, and oral contraceptives.