Sex modifies the association between body mass index and carotid artery intima media thickness in the multi-ethnic Singapore population

R. Dalan[1], T. Mina[2], N.A. Nur Azizah[2], T. Tong[2], M. Loh[2], G. Wansaicheong[3], J. Chambers[2]

[1]Tan Tock Seng Hospital, Endocrinology, Singapore, Singapore; [2]Lee Kong Chian School of Medicine, Cardiovascular Epidemiology, Singapore, Singapore; [3]Tan Tock Seng Hospital, Singapore, Singapore

Funding Acknowledgement: Type of funding sources: None.

Background and aims: Globally cardiovascular disease (CVD) risk is higher in men than in women in the younger age group but the risk is attenuated in later life with an unexpected higher risk in women in some populations. A better understanding of sex differences in CVD is needed. Carotid artery intima-media thickness (CIMT) has been proposed for CVD risk assessment in individuals at intermediate risk. We study the gender interactions in the associations of the traditional cardiovascular risk factors with CIMT.

Methods: We performed carotid ultrasonography in the large population health study-HELIOS conducted in Singapore. Measurements were performed as per Mannheim consensus, at the far wall of bilateral common carotid artery at 8 sites in each participant. We report the average of all measurements (avgCIMT) and maximum value (maxCIMT). We analysed 2061 healthy participants recruited between 2018–2020. Inclusion criteria for this analysis: non-smokers, not known to have diabetes, hypertension, hyperlipidemia or ischemic heart disease. Individuals with systolic blood pressure >160 mm Hg or fasting glucose >7.0 mmol/L on recruitment were excluded. Multivariable linear regression analysis was performed to examine the association between CIMT and cardiovascular risk factors in the healthy population adjusting for age, sex and ethnicity. All analysis was performed using Stata version 16.0.

Results: After exclusion, 1407 healthy participants were included in the analysis. Median (IQR) avgCIMT: 0.56 (0.50, 0.65) in men; 0.54 (0.50, 0.58) in women. Median (IQR) maxCIMT: 0.64 (0.57, 0.76) in men; 0.61 (0.54, 0.70) in women. The avgCIMT and the maxCIMT were higher in males when compared to women and all traditional cardiovascular risk factors associated with CIMT after adjustment for age, sex and ethnicity (P<0.05) (Table 1). Interaction tests in multivariable model adjusted for age, ethnicity, pulse pressure, non HDL-C and HbA1c showed a significant interaction between sex and body mass index (BMI) with predicted effects on avgCIMT and maxCIMT being relatively higher in males at the same BMI when compared to females (P-interaction <0.01) (Figure 1).

Conclusion: Sex modifies the relationship between BMI and CIMT in Singapore's multi-ethnic population. Understanding the intermediary mechanisms involved will help in developing personalized preventive strategies.

Table 1: Linear regression analysis in this cohort of selected **normal** individuals, with lnavgCIMT/lnMaxCIMT as dependent variable and the stated variable as independent variable adjusted for age, sex and race. Exponentiated coefficients are presented

Variable	Mean (SD)	Average CIMT (ln)			Maximum CIMT(ln)		
		Coeff#	95% CI #	P value#	Coeff#	95% CI #	P value#
Age, years	47.1(10.5)	1.011	1.010,1.011	<0.0001*	1.0118	1.011,1.013	<0.0001*
Gender							
Male	506(36.0)	Ref	Ref	Ref	Ref	Ref	Ref
Female	901(64.0)	0.947	0.934,0.961	<0.0001*	0.925	0.909,0.942	<0.0001*
Race							
Chinese	1118 (80%)	Ref	Ref	Ref	Ref	Ref	Ref
Malays	107 (8%)	1.010	0.984,1.037	0.4484	1.010	0.977,1.044	0.5639
Indians	182 (12%)	1.007	0.987,1.028	0.4961	1.007	0.980,1.032	0.6467
BMI, kg/m2	24(4.1)	1.009	1.007,1.010	<0.0001*	1.010	1.008,1.012	<0.0001*
Systolic Blood pressure, mm Hg	115.8(15.6)	1.002	1.002,1.003	<0.0001*	1.003	1.002,1.003	<0.0001*
Diastolic Blood Pressure, mm Hg	68.2(10.8)	1.002	1.002,1.003	<0.0001*	1.003	1.002,1.003	<0.0001*
Pulse Pressure, mm Hg	47.54(9.80)	1.003	1.002,1.004	<0.0001*	1.003	1.002,1.004	<0.0001*
Total Cholesterol, mmol/L	5.27(0.89)	1.012	1.005,1.021	0.0021*	1.020	1.009,1.030	0.0001*
HDL-C, mmol/L	1.57(0.42)	0.959	0.942,0.977	<0.0001*	0.949	0.928,0.970	<0.0001*
LDL-C, mmol/L	3.18(0.79)	1.021	1.012,1.030	<0.0001*	1.032	1.020,1.043	<0.0001*
Triglycerides, mmol/L	1.16(0.78)	1.022	1.013,1.031	<0.0001*	1.027	1.015,1.038	<0.0001*
Non HDL-C, mmol/L	3.70(0.89)	1.021	1.013,1.029	<0.0001*	1.031	1.021,1.042	<0.0001*
Fasting glucose, mmol/L	4.80(0.50)	1.030	1.015,1.044	<0.0001*	1.044	1.025,1.062	<0.0001*
HbA1c, %	5.39(0.39)	1.028	1.010,1.047	0.0030*	1.044	1.020,1.068	0.0003*

#Adjusted for age, race and gender; exponentiated coefficients, *p<0.05

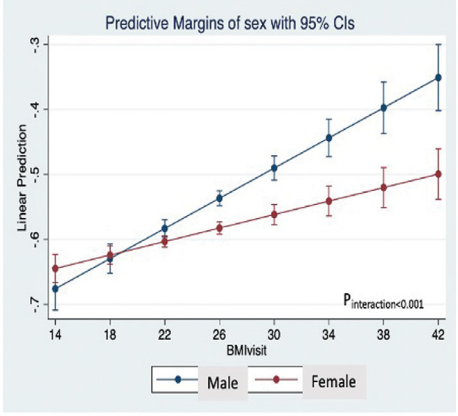

Figure 1A: Predictive margins of AvgCIMT(ln) for males and females

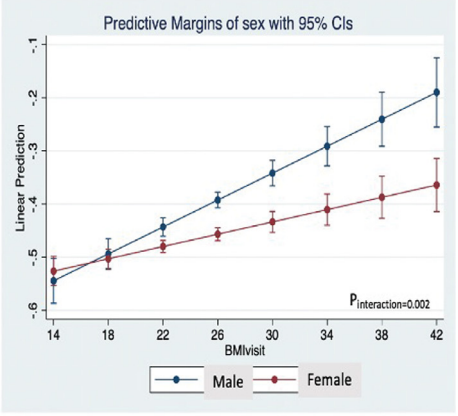

Figure 1B: Predictive margins of MaxCIMT(ln) for males and females

Figure 1