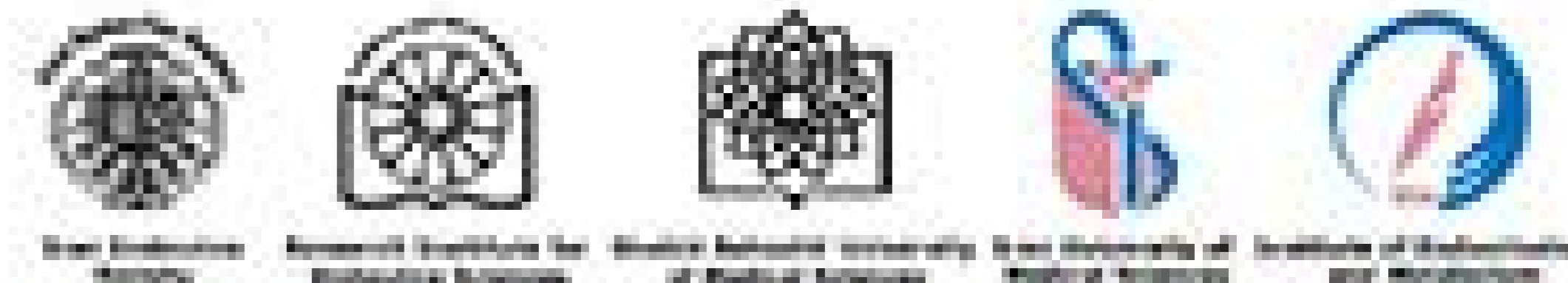


In The Name of GOD





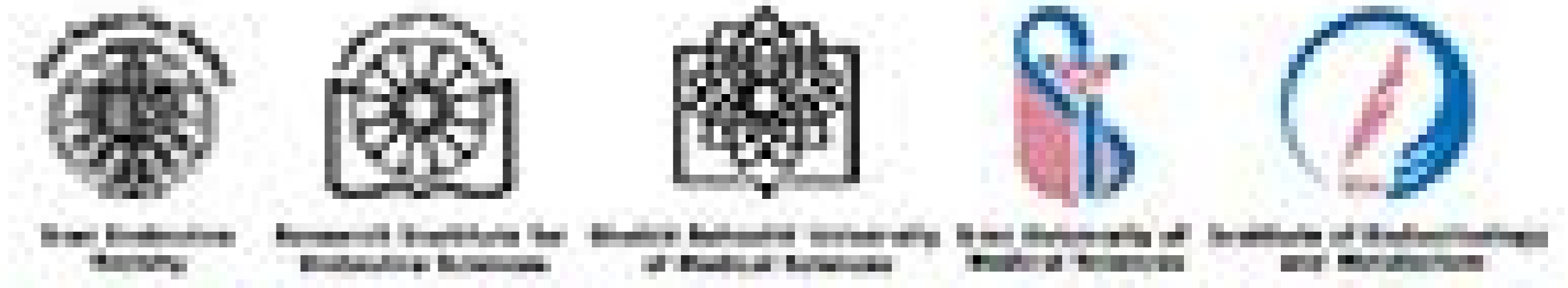
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## **Association between new indices and the carotid intima-media thickness in type 2 diabetes mellitus**

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Shahmiri, MD, PhD<sup>1\*</sup>

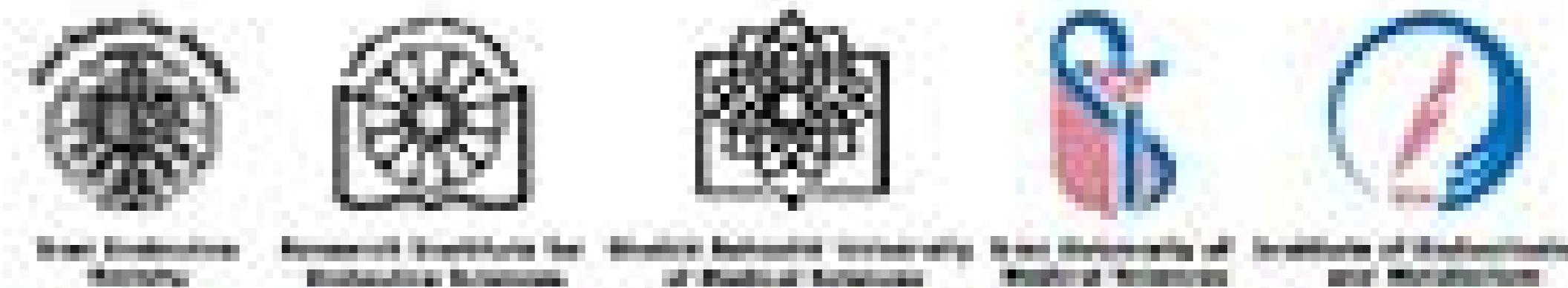


# AIM



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- This study aimed to investigate the relationship between triglyceride glucose (TyG) index and monocyte/high-density lipoprotein cholesterol ratio (MHR) and carotid intima-media thickness (CIMT) in type 2 diabetes mellitus (T2DM).



# INTRODUCTION

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- Atherosclerosis is a picture of CVD
- Characterized by the accumulation of fatty streaks in arterial walls and as well as a chronic inflammatory state
- Progression into plaque formation (atheroma)
- Plaque rupture
- Eventually thrombotic occlusion of the vessels



# CONT...

- This process may cause mortality and morbidity, such as IHD, stroke, and PAD.
- It is crucial for the early identification of high-risk people and the timely control of AS progression.
- Risk factors: HTN and DM, can accelerate the progression of AS at different levels.



# CONT...



- During systemic inflammation and atherogenesis, macrophages and monocytes are the most prominent sources of proinflammatory and pro-oxidant cytokines. In AS, macrophages and monocytes remove modified and oxidized LDLs, which are then attracted into the artery wall, causing the release of inflammatory cytokines in inflamed tissue.



# CONT...

- As a result, monocyte accumulation and HDL-C decrease may play a role in AS and CVD.
- Monocyte/HDL-C ratio (MHR) could be a useful marker for predicting the development and progression of inflammatory processes such as AS.



# CONT...



- In this context, it was also demonstrated that insulin resistance (IR) plays an essential role in the development of DM, HTN, and AS and it is a well-known predictor of a wide range of CVDs.





# CONT...

- The triglyceride glucose (TyG) index, has been introduced as a reliable and affordable marker for IR prediction, more accurately than HOMA-IR.
- Given that both hypertriglyceridemia and impaired glucose metabolism are commonly related to IR and AS.



# CONT...



- Growing attention is now attracted to assessing the association of the TyG index and MHR with AS .



# CONT...

- Carotid intima-media thickness (CIMT) is a widely used imaging marker for the diagnosis of preclinical carotid AS, which was shown to have predictive value for future cardio/cerebrovascular events.



# METHODS

- Cross-sectional study
- Between 2019 to 2021
- A total of 244 participants.
- Endocrine Research Center and Firoozgar teaching tertiary hospital in Tehran, Iran
- T2DM, age range of 30-60Y/O, DM duration > 5 Yrs.



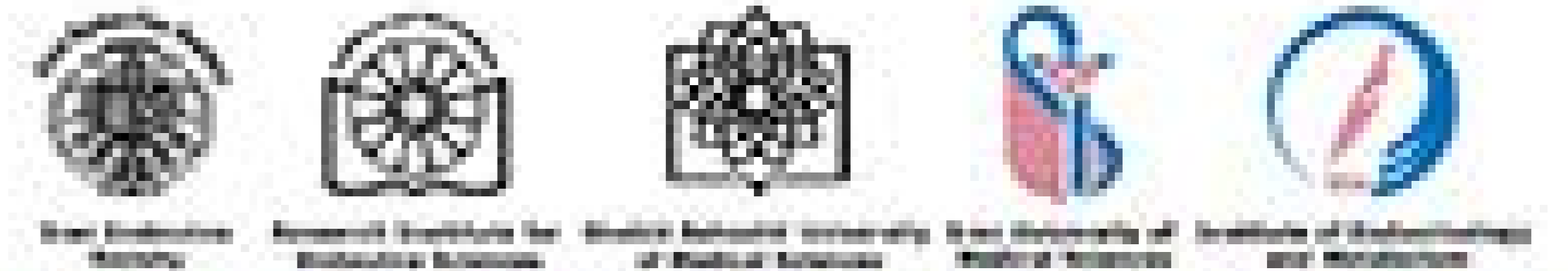
## EXCLUSION CRITERIA



- Smoking and drug abuse
- Pregnancy
- Using medications (the corticosteroid, immunosuppressants, ...)
- Renal transplantation
- Systemic diseases (CVD, autoimmune disease, Cushing, adrenal hyperplasia, chronic lung or renal disease, chronic or acute infection, malignancy, thrombocytopenia)
- Albuminuria, HbA1C  $\geq 9$ , LDL-C  $\geq 100$ , TG  $\geq 250$ , BP  $\geq 160/100$ , e-GFR  $< 30$  and BMI  $\geq 35$ .



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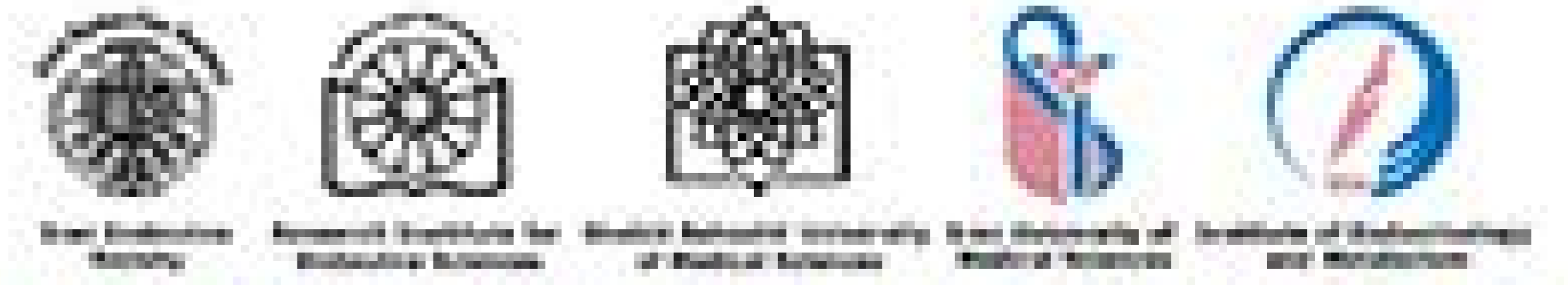


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- The research protocol (IR.IUMS.REC.1397.1118) was approved by the ethics committee of the Iran University of Medical Sciences, and all participants signed and gave written informed permission.



# CONT...

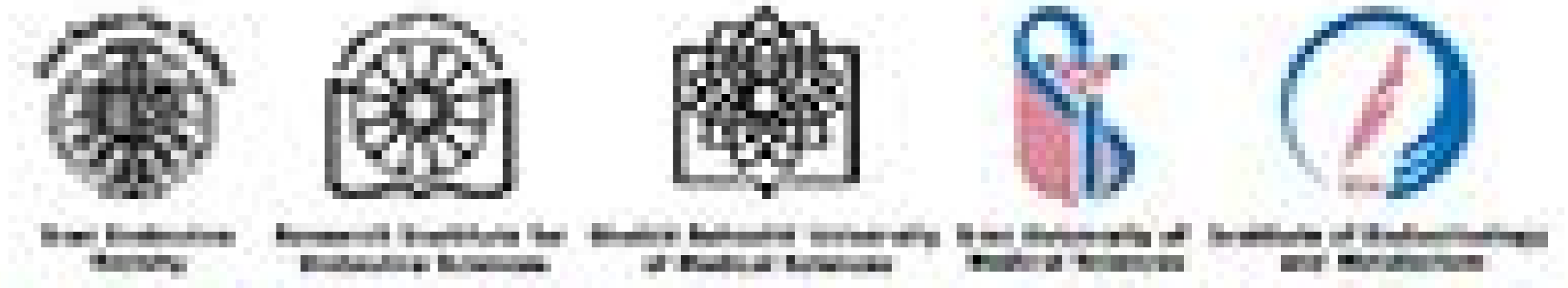


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- Duplex ultrasonography parameters and demographic, physical, and paraclinical assessments were recorded.



# MHR



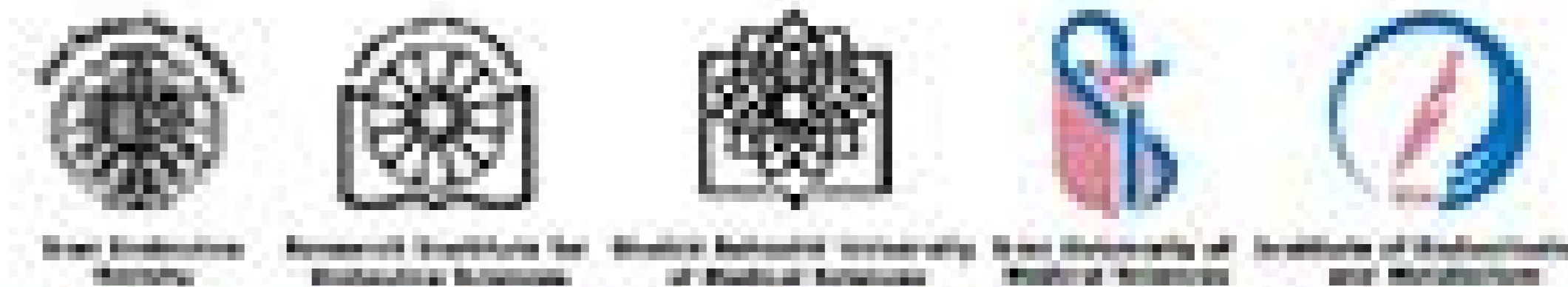
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- The monocyte count was evaluated by applying data provided by the CBC differential analysis.
- The MHR was computed for both groups by monocyte counts ( $\times 10^6/L$ )/HDL-C (mg/dL)<sup>®</sup>.





# TYG

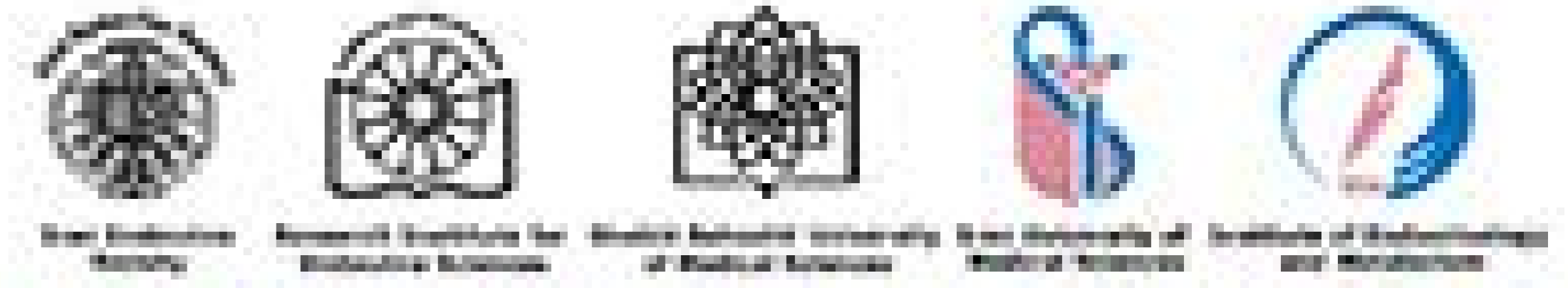


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- The TyG index was calculated as  $\text{Ln} [\text{TG (mg/dl)} \times \text{fasting glucose (mg/dl)} / 2] ^{\text{®}}$ .



# CIMT



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- The CIMT was evaluated by a single professional and experienced neurologist (neurosonologist and blinded).
- A duplex ultrasound system (B-Mode) with an 8-Hz linear probe (Sonosite M Turbo, Fuji Film, Japan).

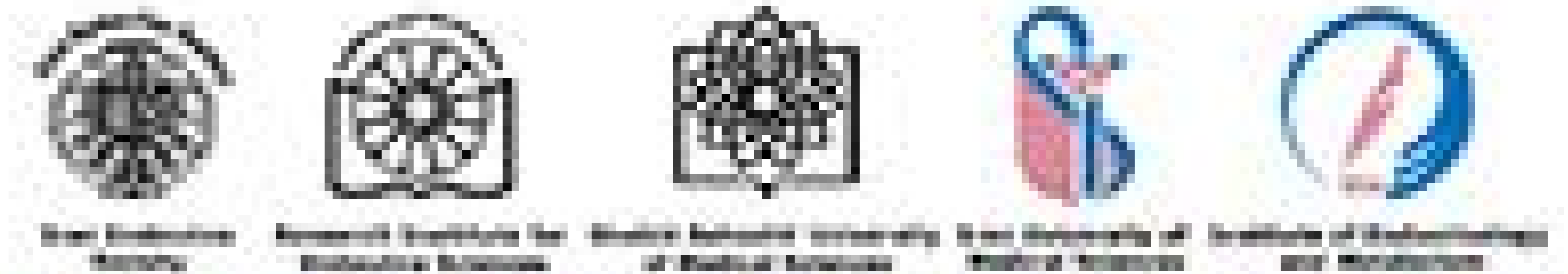


# CONT...

- The mean CIMT was calculated by estimating the thickness of the innermost two layers of intima-media in 10 mm before the bifurcation of CCA.
- No atherosclerotic plaques were present.
- The average of the RT and LT CIMT was employed.
- Mean CIMT > 75th percentile for age, race, and gender was recognized as a risk factor for CV events by the American Echocardiographic Association<sup>®</sup>.



# RESULTS

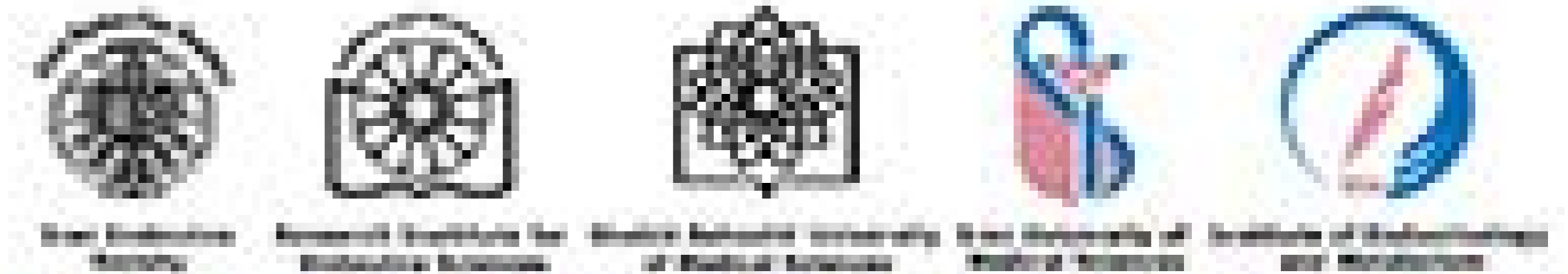


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- 118 DM and 126 non-DM
- Sex ratio F/M= 1.16
- Median age of 47 Yrs.
- Diabetes duration is 7 (5-10) yrs.



# CONT...



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- Individuals with T2DM were older and had significantly higher BP, and FBG, and lower e-GFR, total cholesterol, and LDL-C than non-DM (P values <0.05).

# Characteristics of the study participants by diabetes status.

	Non-diabetic group (n= 126)	Diabetic group (n=118)	P- value
Age (year)	42.71±9.82	50.31±9.59	<0.001
Gender (Female, n (%))	69 (54.8%)	62 (52.5%)	0.73
BMI (kg/m <sup>2</sup> )	26.32 (23.39-28.48)	26.12 (24.22-28.89)	0.68
SBP (mmHg)	120.0 (110.0-120.0)	120.0 (120.0-130.0)	<0.001
DBP (mmHg)	76.86±7.69	80.08±9.22	0.003
FBG (mmol/l)	5.33 (5.11-5.72)	6.39 (5.72-7.67)	<0.001
TG (mmol/l)	1.07 (0.85-1.67)	1.17 (0.95-1.39)	0.40
Total cholesterol (mmol/l)	3.85 (3.18-4.70)	3.41 (3.15-3.77)	0.001
LDL-C (mmol/l)	2.46 (2.07-3.05)	1.81 (1.50-2.15)	<0.001
HDL-C (mmol/l)	1.11 (1.06-1.24)	1.14 (1.06-1.24)	0.57
e-GFR (mL/min/1.73m <sup>2</sup> )	84.3 (69.0-98.4)	73.3 (64.8-87.6)	0.006
Diabetes duration (year)	-	7.0 (5.0-10.0)	-
<b>Medical history</b>			
Hypertension	28 (22.2%)	33 (28.0%)	0.30
Dyslipidemia	18 (14.3%)	26 (22.0%)	0.51
TyG	8.44 (8.21-8.93)	8.76 (8.48-8.96)	<0.001
CIMT (mm)	0.42±0.10	0.40±0.13	0.29
MHR	2.65(1.87-4.37)	3.14(2.18-4.93)	0.13



# CONT...

- There was no significant difference between CIMT and MHR evaluated in the two groups.
- However, individuals with T2DM had significantly higher TyG index.

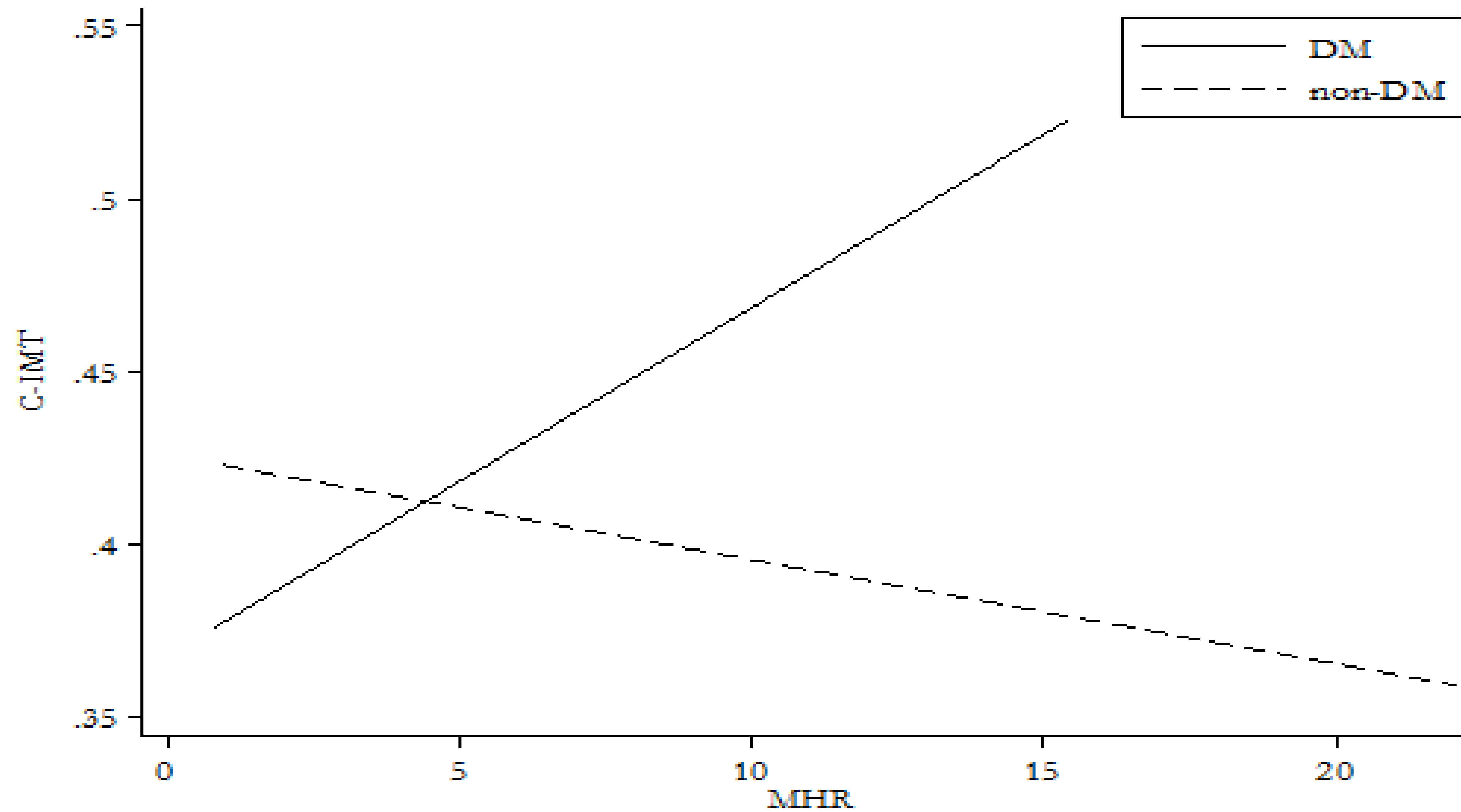


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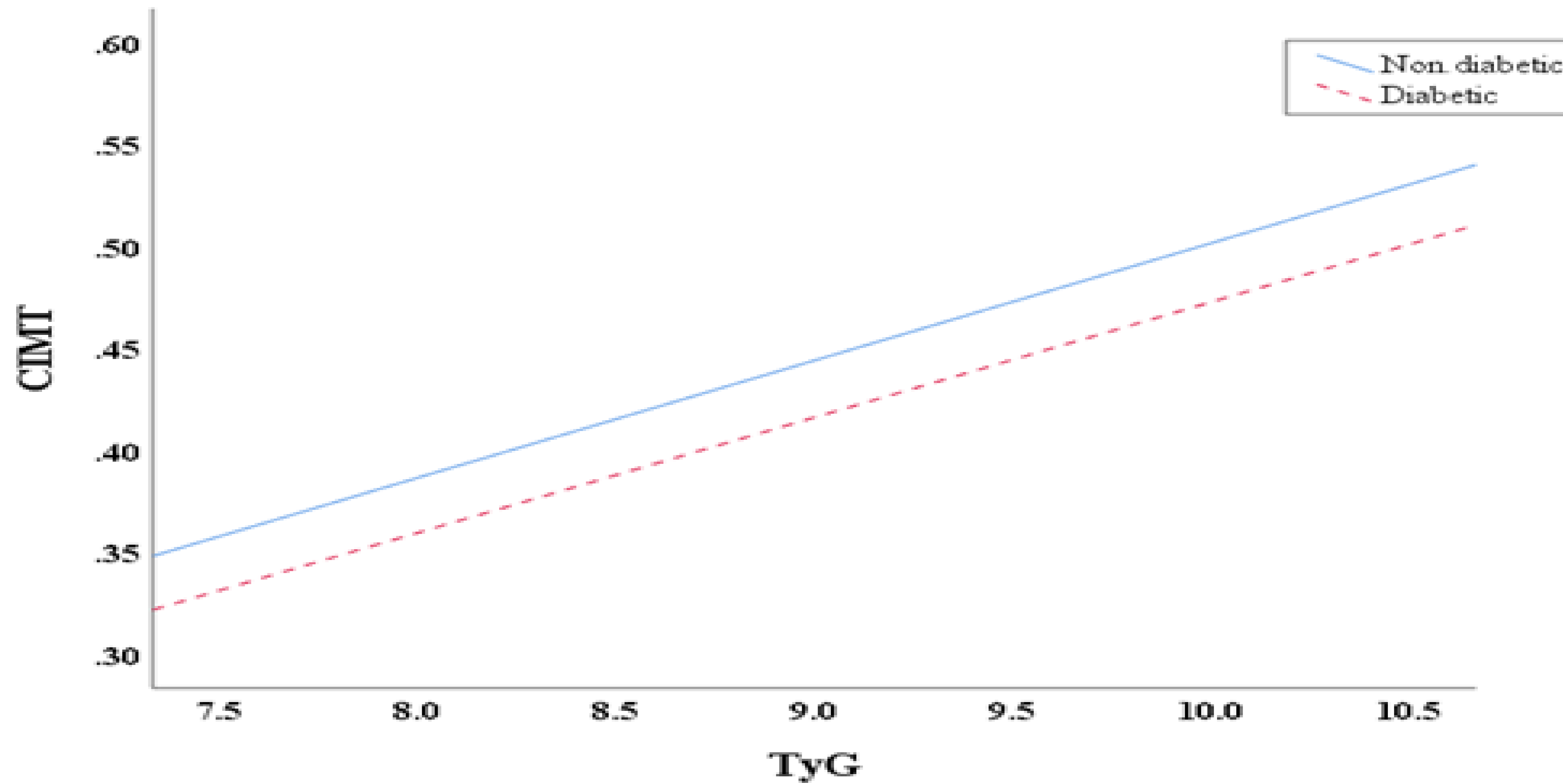
- In correlation analyses, CIMT was directly related to age ( $r_s=0.288$ ,  $P<0.001$ ), BMI ( $r_s=0.203$ ,  $P=0.001$ ), TG ( $r_s=0.153$ ,  $P=0.016$ ), cholesterol ( $r_s=0.174$ ,  $P=0.007$ ), LDL-C ( $r_s=0.313$ ,  $P<0.001$ ), TyG index ( $r_s=0.190$ ,  $P=0.003$ ), and MHR ( $r_s=0.32$ ,  $P=0.001$ ).



# Association of the CIMT and the MHR.



# Association of the CIMT and the TyG index



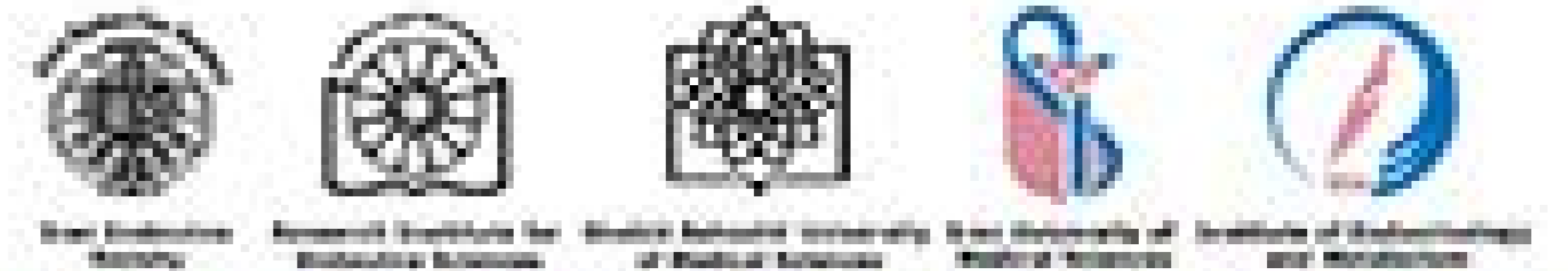


# CONT...

- Stratified by sex, the median (IQR) of MHR values in DM and non-DM male groups were 2.42 (1.75-4.11) and 3.39 (2.36-5.09), respectively (P=0.035).
- However, there was no difference between the DM and non-DM female groups, with (P=0.962).



# CONT...



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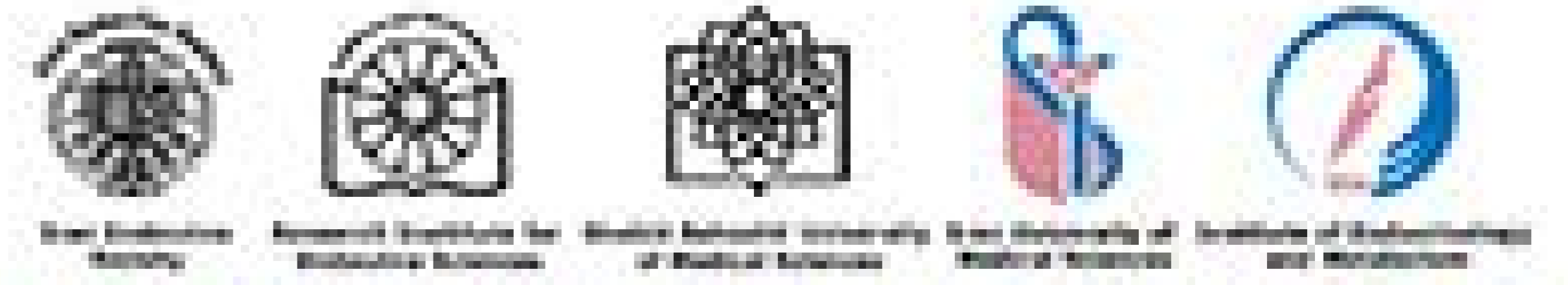
- Finally, the regression models were built to quantify the influence of MHR on CIMT (corrected for any of the covariates' BMI as a clinical factor<sup>®</sup>, age, LDL, and e-GFR, and completely adjusted, stratified by diabetes and sex status).

Univariate and multivariate regression analysis were performed on CIMT.

Variable	DM <sup>†</sup> -Female		Non-DM-Female		DM-Male		Non-DM-Male	
	Beta	P-value	Beta	P-value	Beta	P-value	Beta	P-value
<b>Crude</b>	0.127	0.32	-0.065	0.59	0.294	0.02*	-0.097	0.47
<b>Age-adjusted</b>	0.128	0.32	-0.032	0.76	0.248	0.04*	-0.093	0.46
<b>BMI<sup>α</sup> -adjusted</b>	0.097	0.44	-0.046	0.70	0.290	0.03*	-0.082	0.54
<b>LDL- C<sup>β</sup> -adjusted</b>	0.033	0.76	-0.081	0.49	0.282	0.03*	-0.060	0.65
<b>e-GFR<sup>γ</sup>-adjusted</b>	0.106	0.40	-0.061	0.61	0.248	0.05*	-0.081	0.54
<b>Fully-adjusted**</b>	0.028	0.80	-0.024	0.80	0.220	0.07	-0.042	0.74



# CONT...



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- MHR was shown to be a significant predictor of CIMT in only male DM participants when crudely and adjusted for confounders.



# CONT...

- Additionally, the univariate linear regression analyses performed on the whole data and two study groups separately.
- A significant association was revealed between CIMT and TyG index (on the whole data ( $\beta = 0.197$ ,  $P=0.002$ ) and two study groups (DM:  $\beta = 0.192$ ,  $P=0.037$  & non-DM:  $\beta = 0.256$ ,  $P=0.004$ ) respectively).

# Univariate and multivariate regression analyses of CIMT by diabetes status



Groups	Model	Variable	Unstandardized	Standardized	P-value	95.0% Confidence Interval for B	
			Coefficients B	Coefficients Beta		Lower Bound	Upper Bound
Entire Data	Model 1	TyG	0.050	0.197	0.002	0.019	0.082
		Age	0.003	0.264	0.000	0.002	0.004
	Model 2	Gender	0.036	0.154	0.010	0.008	0.063
		BMI	0.003	0.118	0.041	0.000	0.007
		LDL-C	0.054	0.362	<0.001	0.037	0.072
		e-GFR	-0.001	-0.134	0.039	-0.001	0.000
DM Group	Model 1	TyG	0.057	0.192	0.037	0.003	0.110
	Model 2	Age	0.003	0.224	0.008	0.001	0.005
		LDL-C	0.080	0.395	<0.001	0.047	0.114
Non-DM Group	Model 1	TyG	0.058	0.256	0.004	0.019	0.096
		Age	0.003	0.322	<0.001	0.002	0.005
	Model 2	Gender	0.040	0.199	0.010	0.010	0.071
		BMI	0.003	0.128	0.081	0.000	0.006
		SBP	0.002	0.188	0.015	0.000	0.003
		Chol	0.030	0.301	<0.001	0.016	0.045
		e-GFR	-0.001	-0.210	0.010	-0.002	0.000







# CONT...

- Multivariate linear regression analyses performed; (age, gender, BMI, LDL-C, and e-GFR were the main determinants of CIMT in the best-fit model ( $R^2: 0.242$ )).
- Accordingly; LDL-C and age having the most influence in whole data (LDL-C;  $\beta = 0.362$ ,  $P < 0.001$  and age;  $\beta = 0.26$ ,  $P = 0.000$ ).

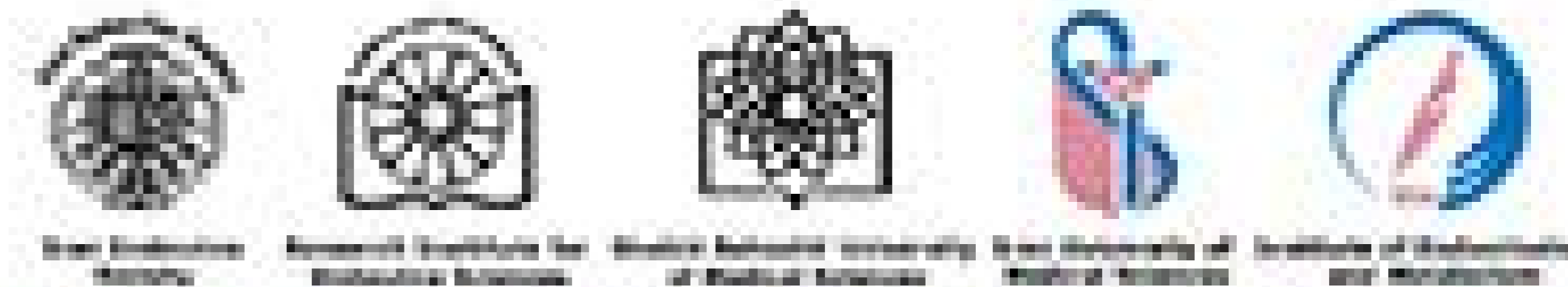


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- A subsequent separate analysis for both groups revealed that age and LDL-C were significant predictors of CIMT in individuals with DM ( $R^2$ : 0.192).
- Age, gender, SBP, total cholesterol, and e-GFR levels in non-DM ( $R^2$ : 0.400).



# LIMITATIONS



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# CONCLUSIONS

- Using the MHR and TyG index may improve the prediction of subclinical carotid atherosclerosis of DM II patients in clinical settings.
- More comprehensive research with a larger sample size is required to confirm these results.

Thanks for Your Attention

