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Original Article

Evaluating additive relationship between metabolic syndrome and anthropometrics indices with carotid intima media thickness in diabetic , metabolic syndrome and control groups: a Bayesian nonparametric functional latent variable model

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Summary. *Background:* Cardiovascular disease represents a major cause of morbidity and mortality in patients with psoriatic diseases**.** Carotid intima-media thickness is an index of atherosclerosis in the vascular bed and is highly predictive of the development of atherosclerosis; therefore investigating the effective factors in carotid intima-media thickness seems an essential issue. *Objectives:* The relationship between Metabolic Syndrome and Anthropometric indices and carotid intima-media thickness has been studied separately in the literature. However such associations may be much more complex than a simply supposed linear relationship. The aim of this study is to evaluate the functional relationship of both Metabolic Syndrome and Anthropometric indices on carotid intima-media thickness. *Patients and Methods:* The total sample of study included 632 participants. Three groups have been compared with regard to their measures of carotid intima-media thickness: patients suffering from Diabetic disease, patients with high risk in Metabolic Syndrome, and healthy people. The present study used a latent variable model to evaluate the relationship between carotid intima-media thickness as an outcome variable and two cause factors of Metabolic Syndrome and Anthropometric indices as the explanatory variables. All of three variables were treated as latent. Using Bayesian Nonparametric functional latent variable model, the study is free from condition and fits a nonlinear functional relationship. *Results:* The obtained results showed the most standard deviations Varity of carotid intima-media thickness in diabetic group. Accordingly, in Diabetic and Metabolic Syndrome groups all of the items are important in the structure of their factors. Based on the findings 'Waist' plays the most important role in Metabolic Syndrome and Anthropometric indices variations (p-value<0.0001). Measures indicated that there is significant relationship between two independent latent variables. *Conclusions:* The findings are consistent with other studies showing the effect of Metabolic Syndrome and Anthropometric indices on displaying greater carotid intima-media thickness than those without them. These latent variables and their items had significant effect on carotid intima-media thickness in this study, and the relationship is showed in functions and graphs. These functions disclosed all details of the relationship between variables.

Key words: Metabolic syndrome, anthropometrics indices, carotid intima media thickness, nonparametric functional model, Bayesian P-spline

Background

Cardiovascular disease (CVD) represents a major cause of morbidity and mortality in patients with psoriatic diseases (1, 2). Extracranial carotid atherosclerosis is the most common cause of stroke in western part of the world. Several studies have identified carotid intima-media thickness (CIMT) to be independently associated with cerebrovascular and CVD (3). There are some papers which review CIMT as a risk factor for coronary artery disease, stroke, death from myocardial infarction, or a combination of these events (4, 6). CIMT has also been consistently linked to CVD. As one of the better CVD and stroke markers, (7, 8) CIMT can be measured noninvasively throughout life, yielding a risk assessment for future events (7, 12). CIMT is an index of atherosclerosis in the vascular bed and is highly predictive of the development of atherosclerosis (9, 13,17). Therefore studying the effective factors on CIMT is considered to be an essential subject.

In order to investigate atherosclerosis, B-mode ultrasounography enables non-invasive, direct vitalization of the arterial wall. The CIMT quantified using this technique is a reliable marker of atherosclerosis burden. Furthermore, it demonstrates greater sensitivity in detection of early atherosclerosis compared with angiography (18).

The relationship between Metabolic Syndrome (MetSyn) and Anthropometric indices (AI) and CIMT has been studied distinctly in the literature, including (19), (20), (21) and (22). The aim of this study is to evaluate the relationship between MetSyn and AI and CIMT. One important aspect of the MetSyn regardless of definition, lies in the 1.5- to 2.0- fold increased risk of CVD and stroke mortality in patients with the MetSyn relative to those without the syndrome (23, 24).

MetSyn is a cluster of cardiometabolic abnormalities that increases the risk of CVD (23). MetSyn affects approximately 15% to 25% of the general population (25, 26) and is considered a strong predictor of CVD, diabetes, and stroke (27, 28). The combination of all its components confers a significant greater risk of development of CVD than the attributable risk of each individual component risk factor (29).

Adiposity is becoming an increasingly prevalent problem in the Western society. The most recent estimates from the National Health and Nutrition Examination Survey (NHANES 2007-2008) indicated that approximately one-third of the American adult population is obese (30). Numerous epidemiological studies link obesity to increased rates of cardiovascular and all-cause mortality (31, 32). Furthermore, the link of obesity to metabolic risk and diabetes has been well documented (33, 34). Associations between adiposity and vascular function have been variably demonstrated in the literature. One of the earliest studies in this area is a small-scale study by Brook et al., in which a correlation between abdominal adiposity and vascular endothelial function was found (35). A recent study conducted by the Framingham group included over 3,000 patients who had visceral adiposity assessed using both computed tomography scans and waist circumference and endothelial function assessed using both macro and microvascular methods (36) . Both BMI and visceral adiposity were found to be significantly correlated with macrovascular function in multivariable adjusted models.

Most of above-mentioned papers studied the impact of MetSyn or AI on CIMT separately. In addition, they test significance of individual variables about MetSyn and AI on CIMT without details of trend and assumed linear relationship between them. This paper plans a nonlinear function to evaluate relationship between the mentioned variables. These functions may show the value of CIMT by any change on MetSyn or AI. On the other hand CIMT, MetSyn and AI are multi-dimensional variables and computing from several items; therefore in this paper they are treated as latent variable and are modeling with additive association model of MetSyn and AI on CIMT.

A common choice of modeling the current relationship is applying common regression model. There are two important problems in using this models, first is the non-normality of some variables, and second one is that there are nonlinear relationships between latent variables. We can solve both of them by using Bayesian Nonparametric functional latent variable model. The aim of this study is evaluating the additive relationship of MetSyn and AI with CIMT by appling Bayesian Nonparametric functional latent variable model.

Method

Study design

The current study uses a latent variable model (LVM) in evaluating the relationship between CIMT as an outcome variable and two important cause factors MetSyn and AI as explanatory variables. All of three variables are treated as latent. The role of CIMT is endogenous and MetSyn and AI are exogenous variables in the model.

Two items which are used to measure CIMT include Right CIMT (IMTR) and Left CIMT (IMTL). For all people, Ultrasound B-mode with high separation power and 7.5mh transducer have been used to measure CIMT in both sides. In addition, MetSyn has measured with 5 criteria Fast Blood Sugar (FBS), Systolic Blood Pressures (SBP), High-density lipoproteins (HDL), Waist and Triglycerides (TG). Finally, AI measured two items Waist and Body Mass Indexes (BMI). With this explanation, the full model of relationship is presented as follow (Fig. 1).

Figure1 shows the design of standard structural equation model (SEM). Common SEMs use linear relationship between items and factors and also assumed variables following multivariate normal distribution. There are two important problems in using this model, first refers to non-normality of variables, some variables due to their scales may not have normal distribution. Second one is that there were nonlinear relationships between latent variables. Considering the relationship as linear is inefficient however, we are interested in clarifying all scenario of the relationship.

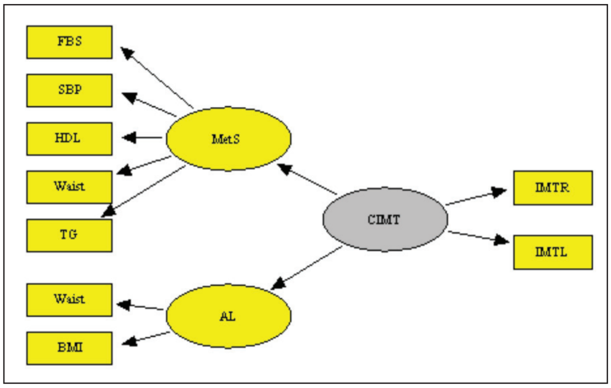

Figure 1. Diagram of Structural Equation Model of Relationship between MetSyn and AI with CIMT

Both problems can be solved by using Bayesian Nonparametric functional latent variable model.

Data Sources and participants:

This study uses the data, which belongs to a cross-sectional design and collected during 2009. The number of cases in the range during the study period determined the sample size. Sampling framework is the list of Outpatients. Non-probabilistic convenience sampling method with sectional census has been used for sample choosing. Target population includes persons who attended to check periodical TG, FBS and BP at biochemical laboratory and medical clinic of Emam Reza hospital. Sampling continued until collection of the intended sample size (37).

The study collected measures of CIMT participants in Emam Reza hospital of Tabriz. Data collection took place during 12 month. Measure of CIMT have compared three groups, persons suffering from Diabetic disease, patients with high risk in MetSyn, and healthy people.

Variables and Measurements:

MetSyn Diagnosis uses the NCEP ATP III criteria, as affirmed and slightly modified by the American Heart Association and the National Heart, Lung, and Blood Institute (38). Persons classified as MetSyn group should have any 3 of the following 5 criteria:

Increased waist circumference (90 cm in Asian men, and 80 cm in Asian women); Elevated triglycerides (150 mg/dl or treatment with fibrates or nicotinic acid); Reduced high-density lipoprotein (HDL) Cholesterol (40 mg/dl in men and 50 mg/dl in women or treatment with fibrates or nicotinic acid); elevated blood pressure (130 mm Hg systolic and 85 mm Hg diastolic or treatment for hypertension); or elevated fasting glucose (100 mg/dl or treatment for elevated glucose). All of diabetic persons lack high risk MetSyn, so there was not common case between two groups.

Statistical methods:

This study applied another kind of SEM model in which a nonparametric structural equation is used to model the functional relationships among latent variables and covariates. The Bayesian approach, together with a Bayesian analogue of P-splines, is used to estimate the nonparametric functions and unknown parameters in the model.

The nonparametric structural equation in the model can be regarded as a generalization of the ordinary nonparametric regression model with the new inclusion of unknown smooth functions of latent variables. The Bayesian P-splines approach, together with a Markov Chain Mount Carlo (MCMC) algorithm will be introduced to estimate smooth functions, unknown parameters, and latent variables in the model. Details of the model can be found at (39).

Based on the model proposed by Xin-Yuan Song and Sik-Yum Lee (39) the functional effects of age as a covariate and MetSyn and AI as explanatory latent variables on the outcome latent variable CIMT which shows by η_i are characterized by the nonparametric structural equation: $\eta_i=g(x_i)+f_1(\xi_{i1})+f_2(\xi_2)+\delta_i$

Where x is observed covariate, g, f_1 *and* f_2 are the unspecified univariate smooth functions, ξs are explanatory latent variables and δ_i is the residual error independent of ξ_i and distributed as normal.

This study uses the modified R code of Song and Lee (40) for fitting and evaluating the proposed model. Also, there were some missing data in diabetic group which have been omitted from the study. The effects of confounding variables, groups matching for smoking, nonalcoholic fatty liver, traditional cardiovascular risk factors of diabetes and other effective features are eliminated.

Results

Total samples of study included 632 participants and sample size of per group was 212, but because of losing 4 persons in diabetic group, this group conducted with 208 participants (37). The main objective of this analysis is to investigate the functional influences of MetSyn and AL on CIMT. The following observed variables were selected in establishing a model to achieve the objective: Fast Blood Sugar (FBS), Systolic Blood Pressure (SBP), High-density lipoprotein (HDL), Waist, and Triglyceride (TG), Body Mass Indexes (BMI). Moreover, age was also included as covariates. All of the above-mentioned continuous measurements were standardized.

Based on the medical meaning of the observed variables, we identified three latent variables through the measurement equation. More specifically, IMTR and IMTL were grouped into a latent variable 'CIMT'; similarly, {FBS, SBP, HDL, Waist, TG}, {Waist, BMI}

Table 1. Characteristics of the Study Base at Enrollment

		Total	Diabetic +	MetSyn +	healthy
Gender (%)	male	354(56)	103(49)	119(56)	132(62)
	female	278(44)	105(50)	93(44)	80(38)
Age (%)	Range				
	16-25	75(12)	5(2.4)	2(1)	68(32)
	26-35	157(25)	38(18)	40(19)	79(37)
	36-45	203(32)	73(35)	81(38)	49(23)
	46-55	197(31)	92(44)	89(42)	16(7)

Table 2. Mean(standard deviation) of variables in study groups

Index	Total	Diabetic+	MetSyn+	Healthy
Age	39.0 (10.0)	43.0 (8.5)	43.0 (8.0)	31.0 (10.0)
Weight kg	76.0 (14.0)	81.0 (13.5)	82.0 (11.0)	64.0 (9.0)
Height cm	166.0 (9.0)	165.0 (10.0)	166.0 (9.0)	167.0 (8.0)
BMI	27.5 (4.7)	29.5 (3.4)	29.7 (2.9)	23.4 (4.5)
SBP mmHg	12.5 (1.3)	12.9 (1.3)	12.9 (1.3)	11.5 (0.8)
DBP mmHg	8.1 (0.9)	8.4 (0.9)	8.5 (0.9)	7.5 (0.6)
TG mg/dl	188.0 (117.0)	232.0 (135.0)	231.0 (106.0)	102.0 (32.0)
LDL mg/dl	120.0 (36.0)	129.0 (37.0)	130.0 (39.0)	101.0 (20.0)
HDL mg/dl	46.0 (9.5)	42.0 (8.6)	44.0 (10.0)	51.5 (7.0)
FBS mg/dl	110.0 (34.5)	144.0 (40.0)	101.5 (11.0)	86.0 (10.0)
Waist cm	96.0 (11.5)	102.0 (9.0)	102.0 (8.0)	83.5 (5.0)
IMTR mm	0.7 (0.9)	0.8 (0.2)	0.75 (0.1)	0.5 (0.1)
IMTL mm	0.7 (0.2)	0.8 (0.2)	0.75 (0.1)	0.5 (0.1)

were grouped into two latent variables which could be interpreted as 'MetSyn', and 'AI', respectively.

Table 1 Shows distribution of participants' gender and age classifications in separated groups. Results show that participants of healthy group are younger than the other group. Mean of age in this group is 31 years old.

Shown in Table2 all indices of the healthy group are conditions in better than the two other groups. As it is seen, measures of CIMT, both in right and left sides are high in Diabetic and MetSyn but it is low in Healthy group. In addition, most standard deviations Varity of CIMT happen in diabetic group but it is more stable in Healthy group.

Table 3 shows the results of standardized factor loading with tems significance. To solve identification problems in every measurement model one item is treated as referent and fixed to 1. As the result shows in Diabetic and MetSyn groups all of items are important to structure of their factors. Measures revealed that 'Waist' plays the most important role in MetSyn and AI variations (p-value<0.0001). All of factors loading in modeling groups Diabetic and MetSyn are significant. However, as we see in Healthy group, effects of TG in MetSyn modeling and BMI in AI modeling are not significant. Also other factor loadings signs are Reversing. Results showed that in Healthy group being higher of SBP and Waist or lower of HDL not only are not threatening, but also are beneficial. In other words, high risk of metabolic syndrome in low muscles people is more than well-formed people.

Comparing two Diabetic and MetSyn groups displays that impact of items in MetSyn group is higher than Diabetic. This result is normal because persons who classified into MetSyn group have high risk of metabolic syndrome. In addition, analysis of all participants without classification shows that all of items in measurement models are significant.

Table 4 represents Bayesian estimation of items standardized mean (standard error mean) in measurement models. According to standardized translation, these values should be evaluated considering normal distribution with mean 0 and standard deviation equals to1. Results show that values of IMTR are higher than IMTL. Comparing groups with each other shows Diabetic group have higher values than others, except HDL. Healthy group has high HDL and low amount

Table 3. Parameter Estimates under Four Models

Intimae- Media Thickness (Outcome)

	IMT			MetS									AL		
GROUP	IMTR	IMTL	P	FBS	SBP	P	HDL	P	WAIST	P	TG	P	WAIST	BMI	P
Total	Referent	0.99 (0.14)	<0.001	Referent	0.98 (0.07)	<0.001	-0.87 (0.07)	<0.001	1.48 (0.07)	<0.001	1.00 (0.07)	<0.001	Referent	0.54 (0.04)	<0.001
Diabetic+	Referent	0.96 (0.04)	<0.001	Referent	0.37 (0.12)	0.002	-0.32 (0.10)	0.003	1.10 (0.09)	<0.001	0.36 (0.13)	0.008	Referent	0.85 (0.05)	<0.001
MetSyn+	Referent	0.96 (0.37)	0.013	Referent	1.44 (0.33)	<0.001	-1.01 (0.30)	0.001	1.80 (0.21)	<0.001	1.63 (0.27)	<0.001	Referent	0.80 (0.07)	<0.001
Healthy	Referent	0.83 (0.07)	<0.001	Referent	-0.77 (0.21)	<0.001	1.17 (0.28)	<0.001	-0.92 (0.16)	<0.001	-0.15 (0.11)	0.157	Referent	0.38 (0.25)	0.125

Values are factor loading of each item in measurement model with p-value. Wald test has been used for significance of Statistics.

Table 4. Bayesian Estimations of Standardized Mean (standard error mean) of Items in Measurement Models Separated with Different Groups

Index	Total	Diabetic+	MetSyn+	Healthy
IMTR mm	0.34 (0.02)	1.00 (0.04)	0.60 (0.04)	-0.60(0.03)
IMTL mm	0.00 (0.02)	0.70 (0.04)	0.30 (0.04)	-0.90(0.03)
FBS mg/dl	0.00 (0.05)	1.00 (0.09)	-0.30 (0.04)	-0.70(0.03)
SBP mmHg	0.00 (0.04)	0.30 (0.07)	0.30 (0.07)	-0.70(0.04)
HDL mg/dl	-0.00 (0.04)	-0.40 (0.06)	-0.20 (0.07)	0.60(0.05)
TG mg/dl	0.00 (0.04)	0.40 (0.08)	0.40 (0.07)	-0.70(0.02)
Waist cm	0.00 (0.05)	0.60 (0.05)	0.50 (0.05)	-1.10(0.04)
BMI	0.00 (0.04)	0.40 (0.05)	0.50 (0.05)	-0.90(0.06)

of other indices. Values of all items in Diabetic+ and MetSyn+ groups are right skewed except HDL but in Healthy group they are left skewed. This means except HDL, measures in Diabetic+ and MetSyn+ are high and in healthy group is low.

Bayesian standard error mean of indices indicated high precisions of estimation method. All of them are lower than 0.1 and result in short confidence interval.

Bayesian estimations of standardized error variance (Standard Error of Error Variance) in measurement and standardized disturbance (Standard Error of Disturbance) of latent response variable in structural model are low and show high accuracy of estimation methods. Correlation coefficients between MetSyn and AI in Diabetic+, MetSyn+ and Healthy groups are 0.90, 0.69 and -0.52, respectively. Measures indicate that there is firmly relationship between two independent latent variables. In Healthy group, the relationship is inversely.

The point wise posterior means of unknown smooth functions, together with the 10% and 90% point wise quantiles, are depicted in Figure 2. It is observed that some of the fitted curves are neither linear nor quadratic. This fact provides verification that traditional parametric SEMs with linear and/or quadratic terms of latent variables may not correctly reflect the true functional relationships between latent and observed variables, and would give misleading conclusions if the data were analyzed via a parametric approach.

As it has seen relationship between MetSyn and CIMT in total participant and Diabetic group are cubic form and similar to logistic function. Intensity of relationship in middle values is strong, but it is lightly in tails. It seems relationship in MetSyn+ and Healthy groups are linear. In Healthy group, line is near to flat and show weakly relationship and it changed direction from positive to negative, indicating a negative effect for subjects with low MetSyn and a positive effect for those with moderate or high MetSyn. Also notice the range of values in these groups, both MetSyn and CIMT are narrower than (-0.5 , 0.5). This result means that, in Healthy people Varity of metabolic syndrome

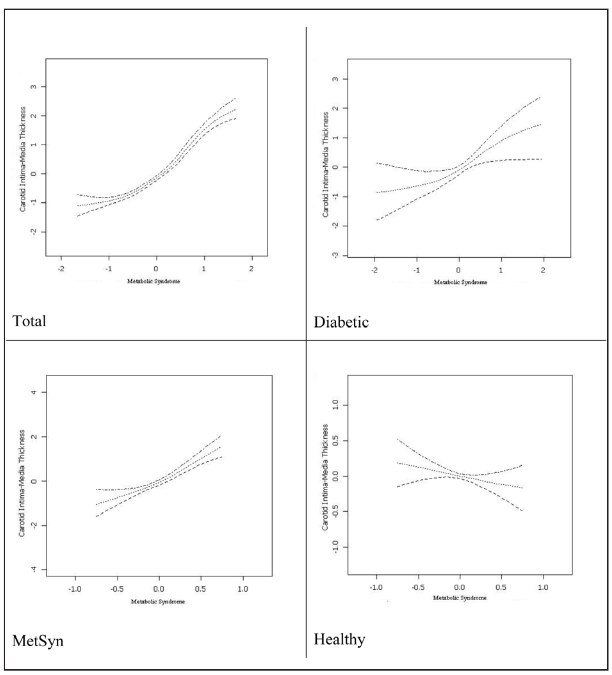

Figure 2. From left to right, top to bottom Estimates of the unknown smooth functions relationship between MetSyn and IMT separated with groups. The solid curves show the point wise posterior mean curves, while the dashed curves represent the 2.5% and 97.5% point wise quantiles.

indices and carotid intima-media thickness are very little.

The point wise posterior means of unknown smooth functions, together with the 10% and 90% point wise quantiles in Figure 3 indicate the relationship between AI and CIMT. Relationship between two factors in all cases at low values is almost flat but for high values of AI it drops down gradually. The relationship curves shows the necessity of using Bayesian nonparametric latent variable model. As it has seen the relationship between AI and CIMT in total participant and MetSyn group are similar to each other. It seems that the relationship in both Diabetic and Healthy groups are linear, but in opposite sign of slop. In Diabetic group, line is descending but in Healthy group ascending one. It seems that Varity of CIMT is more stable by changing AI. Comparing these functions with above it becomes clear that CIMT is most affected from MetSyn than AI.

The effect of age on CIMT is basically positive. This positive effect is more significant for old people.

Discussion and Conclusion

In this paper, a nonparametric LVM with unknown marginal effects of explanatory latent variables is applied to assess the functional relationships between latent and observed variables. We applied the proposed methodology to model the additive effects of MetSyn and AI on CIMT outcome. Model is applied in tree deferent groups and results compared with each other.

The study evaluated the functional effects of MetSyn and AI on CIMT. Results show that both of intended factors have significant effects. In addition, age is included as covariate and its functional relationship showed increasing trend in CIMT by aging. Measures of CIMT, both in right and left sides were high in Diabetic and MetSyn but it is low in Healthy group. Also most standard deviations Varity of CIMT happened in diabetic group but it was more stable than two others in Healthy group.

Result in Diabetic and MetSyn groups show that all of items including FBS, SBP, HDL, Waist, TG,

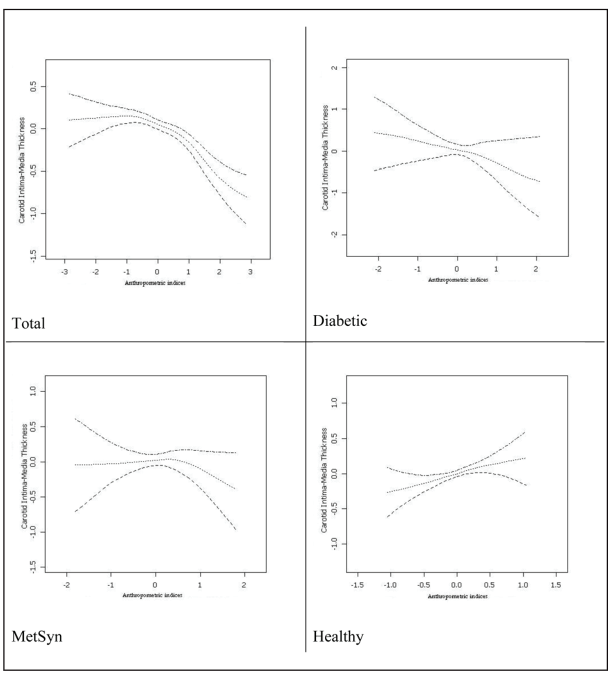

Figure 3. From left to right, top to bottom Estimates of the unknown smooth functions relationship between AL and IMT separated with groups. The solid curves show the point wise posterior mean curves, while the dashed curves represent the 2.5% and 97.5% point wise quantiles.

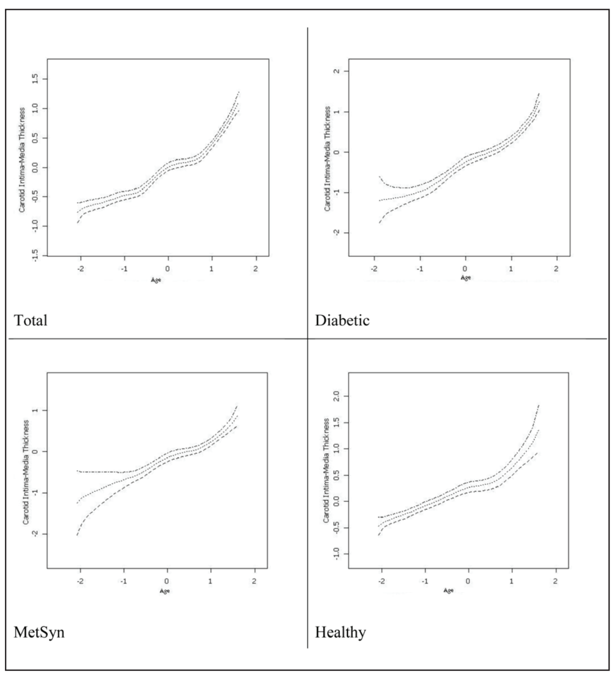

Figure 4. Estimates of the unknown smooth functions relationship between Age and IMT separated with groups. The solid curves show the point wise posterior mean curves, while the dashed curves represent the 2.5% and 97.5% point wise quantiles.

and BMI are important to structure of their factors. Measurement illustrated that Waist plays the most important role in MetSyn and AI variations. All of factor loading in modeling groups Diabetic and MetSyn are significant. The study of Karin Wallenfeldt, et. al showed CIMT change was associated with total cholesterol, LDL cholesterol, Triglycerides, and inversely with HDL cholesterol and LDL particle size at entry (41). However, in Healthy group effects of TG in MetSyn modeling and BMI in AI modeling were not significant and other factor loadings signs were reversing.

Results show that in Healthy persons have higher amount of SBP and Waist or lower amount of HDL that is not only threatening, but also beneficial. In other words, high risk of metabolic syndrome in low muscle people is more than well-formed people. Ji Hyun Moon, et. al show that, low muscle mass and metabolic syndrome was associated with each other -after adjusting for age- and the risk of metabolic syndrome was increased according to the grade increase in low muscle mass class. They find that for old people with normal BMI, low muscle mass is a risky factor of metabolic syndrome. Furthermore, in normal BMI men, when the degree of low muscle mass was enhanced, the risk of metabolic syndrome was increased (42).

Comparing groups with each other show Diabetic+ group have higher values than others, except HDL. Healthy groups had high HDL and low in others indices. Bayesian standard error mean of indices indicated high precisions of estimation method. All of them were lower than 0.1 and result in short confidence interval. Results indicated that there is firmly relationship between two independent latent variables MetSyn and AI, so evaluation of interaction effects has suggested in other studies.

The important part of results declared some of the fitted curves are neither linear nor quadratic. This fact provided verification that traditional parametric SEMs with linear and/or quadratic terms of latent variables may not correctly reflect the true functional relationships between latent and observed variables, and would give misleading conclusions if the data were analyzed via a parametric approach. Different shape of curves showed the necessity of new methods. Functional curves between latent factors stated all scenarios of relationships.

In addition, area of curve in both axes showed Varity of latent variable and this were deferent in groups, and it means that Varity of variables in some group were little than others. Relationship between MetSyn and CIMT in total participant and Diabetic group are cubic form and similar to logistic function. Intensity of relationship in middle values is strong, but it is lightly in tails. It seemed that the relationship in MetSyn and Healthy groups are linear. Line in Healthy group is near to flat and shows weakly relationship and changed direction from positive to negative, indicating a negative effect for subjects with low MetSyn and a positive effect for those with moderate or high MetSyn. Also range of both MetSyn and CIMT in these groups was narrow and means Varity of MetSyn in healthy people and CIMT was very little.

Deferent types of functional forms cleared detail of relationships between latent variables. These functions are nonlinear, but have different form in three groups and pointed the usefulness of Bayesian nonparametric latent model. The results obtained from the present study are consistent with those of other studies showing that participants with MetSyn exhibit greater carotid CIMT than those without MetSyn (14, 43, 45) and some papers that discussed the effects of AI and its components on CIMT (46, 48).

Kolluru, et al. examined the relationship of CIMT and anthropometric measures, BMI, and percentage body fat after controlling for CVD risk factors. They found that among risk factors, only age and hypertension were associated with increased CIMT and among anthropometric measures, BMI, waist circumference and waist to height ratio were significantly associated with increased CIMT. As we saw, not only these items had significant effects on CIMT in our study, but also the relationship is shown in functions and perspicuous graphs. These functions disclose all details of relationships between variables. Therefore, we concluded that the increasing CIMT with aging is more intensity for elderly.

A potential limitation of the study is that, some important items are not included in measurement model, because study used provided data which didn't used this items, especially AI factor can be measured with more items. The presented method can be applicable in most clinical, social, psychological and other sciences where variables which are treated as latent don't follow normal distribution and also the relationship between variables is complex and cannot be explained as linear. In addition, we need more details of relationship scenario.

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