TYPES OF LESIONS AND THE INCIDENCE OF TOTAL OCCLUSION OF CORONARY ARTERY IN METABOLIC SYNDROME

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Abstrak: Sindroma metabolik merupakan gabungan kelainan-kelainan metabolik, termasuk obesitas sentral, penurunan *high density lipoprotein*, peningkatan trigliserida, peningkatan tekanan darah, dan hiperglikemia, yang berpotensi meningkatkan risiko aterosklerosis. ACC/AHA membuat klasifikasi lesi koroner (tipe A, B, dan C) untuk memrediksi tingkat keberhasilan dan risiko tindakan intervensi. Beberapa studi lain menunjukkan derajat keparahan dari jenis lesi koroner terkait dengan *outcome* jangka panjang. Penelitian ini bertujuan untuk mengetahui perbedaan jenis lesi dan insidensi dari lesi oklusi total pada pasien dengan sindrom metabolik. Sejumlah 43 pasien berturut-turut dengan atau tanpa sindrom metabolik yang menjalani angiografi koroner di Rumah Sakit Awal Bros sejak tanggal 1 Jan sampai 15 Februari 2013 dimasukkan sebagai sampel penelitian. Pasien dikategorikan sebagai penyandang sindrom metabolik bila memenuhi definisi NCEP ATP III untuk populasi Asia. Hasil penelitian memperlihatkan bahwa dari 43 pasien, 25 (58%) didiagnosis sebagai sindrom metabolik. Pada kelompok sindrom metabolik ditemukan jenis lesi koroner tipe A 0%, tipe B 40%, dan tipe C 60%, dengan insidensi oklusi total 48%. Pada kelompok bukan sindrom metabolik ditemukan bahwa lesi koroner yang tidak bermakna 16,5%, tipe A 22,5%, tipe B 55,5%, dan tipe C 5,5%, dengan insidensi oklusi total 0%. Terdapat perbedaan bermakna dalam tingkat keparahan lesi koroner dan insidensi oklusi total arteri koroner di antara kedua kelompok (P < 0,001). **Simpulan:** Sindrom metabolik berhubungan dengan tingkat keparahan jenis lesi koroner dan peningkatan insidensi oklusi total pada arteri koroner.
Kata kunci: sindroma metabolik, tipe lesi, penyakit arteri koroner.

Abstract: The constellation of metabolic abnormalities including centrally distributed obesity, decreased high-density lipoprotein, elevated triglycerides, elevated blood pressure, and hyperglycaemia are known as the metabolic syndrome. Metabolic syndrome amplifies and accelerates the risk of atherosclerosis. ACC/AHA classified coronary lesions into type A, B, and C to predict successful intervention rates and risks. Other studies show the severity of coronary type lesions associated with long-term outcomes. This study aimed to find out the difference in types of lesions and incidence of total occlusion lesions in patients with metabolic syndrome. A total 43 consecutive patients with or without metabolic syndrome who underwent coronary angiography in Awal Bros Hospital were enrolled from 1st January until 15th February 2013. Patients were categorized as having metabolic syndrome when they met the NCEP ATP III definition for Asian Population. The results showed that from 43 patients, 25 (58%) considered as having metabolic syndrome. In the metabolic syndrome group, it was

found that the coronary type lesion A was 0%, B was 40%, and C was 60%, with the incidence of total occlusion being 48%. In non-metabolic syndrome, it was found that non-significant coronary lession was 16.5%, type A was 22.5%, B was 55.5%, and C was 5.5%, with the incidence of total occlusions being 0%. There was a significant difference in the severity of coronary lesions and the incidences of total occlusion in the coronary artery between the two groups ($P < 0.001$). **Conclusion:** Metabolic syndrome was associated with changes in severity of types of coronary lesions and an increased incidence of total occlusions in the coronary artery.

Keywords: metabolic syndrome, type of lesion, coronary artery disease.

The constellation of metabolic abnormalities including centrally distributed obesity, decreased high-density lipoprotein cholesterol (HDL-C), elevated triglyceride, elevated blood pressure, and hyperglycaemia is known as the metabolic syndrome.[1] The National Cholesterol Education Program's Adult Treatment Panel III report (NCEP-ATP III) identified the metabolic syndrome as a multiplex risk factor for cardiovascular diseases (CVD) that is deserving of more clinical attention (Table I).[2] Two definitions of metabolic syndrome predominate in the literature: the National Cholesterol Education Program (NCEP) and the WHO (Table I).[3] For the Asian population, the ATP III modified Asian criteria requires the presence of 3 or more of the following: 1) Abdominal obesity (waist circumference >90 cm in males and >80 cm in females; 2) A high triglyceride level (>150 mg/dL); 3. A low HDL-cholesterol level <40 mg/dL for males and <50 mg/dL for females); 4) A high blood pressure (systolic >130 mmHg or diastolic >80 mmHg); and 5) A high fasting plasma glucose concentration (>110 mg/dL).[4]

The prevalence of metabolic syndrome in the adult population in developing countries is 22-39%. A study from the University of Indonesia in 2006 showed that the prevalence of metabolic syndrome using ATP III modified Asian criteria was 28.4%. The most prevalent found in males was hypertension while in females it was central obesity.[3,4]

The ACC and AHA derived a lesion classification published in 1988 and has just been renewed unchanged. This system

Table 1. Definitions of metabolic syndrome[4]

Variable	NCEP ATP III	WHO
Absolutely required	None	Insulin resistance (IGT, IFG, T2D, or other evidence of IR)
Criteria	Any of the 5 criteria below	IR or diabetes, plus 2 of the 5 criteria below:
Obesity	Waist circumstance >40 in (M), >35 in (F)	Waist/hip ratio: >90 (M), >0.85 (F); or BMI >30 kg/m^2
Hyperglycemia	Fasting glucose 100 mg/dL, *or* on therapy	IR already required
Dyslipidemia	Triglyserides ≥150 mg/dL, *or* on therapy	Triglyserides ≥150 mg/dL, *or* HDL-C <35 mg/dL (M), <39mg/dL (F)
Dyslipidemia (second, separate criteria)	HDL-C <40 (M), <50 mg/dL (F); *or* on therapy	
Hypertension	>130 mmHg systolic, *or* >85 mm Hg diastolic; *or* on therapy	≥140/90 mmHg

ATP=Adult Treatment Panel III; BMI=body mass index; F=Female; HDL-C=high density lipoprotein cholesterol; IGT=impaired glucose tolerance; IFG=impaired fasting glucose; IR=insulin resistance; M=male; NCEP=National Cholesterol Education Program; T2D=type 2 diabetes; WHO=world Health Organization.

grouped the individual criteria into three large categories (Table 2). Initially, it was expected that type A lesions (low-risk) would have a success rate of 80%, type B lesions 60-85%, and type C lesions <60%. The characteristics of the lesion classification differed by greater amounts of tortuosity, angulation of the segment, length of the vessel, presence of occlusions, issues with side branches, and potential for protection.[5]

Coronary chronic total occlusion (CTO) is characterized by heavy atherosclerotic plaque burdens within the artery, resulting in complete (or nearly complete) occlusions of the vessel. Although the duration of the occlusion is difficult to determine on clinical grounds, a total occlusion must be present for at least 3 months to be considered a true CTO.[5,6] Patients with CTO typically have collateralization of the distal vessel in their coronary angiography, but these collaterals may not provide sufficient blood flow to the myocardial beds, resulting in ischemia and anginal symptoms. CTO is clinically distinct from the acute coronary occlusions, which occur in the setting of ST-segment-elevation myocardial infarction, or sub-acute coronary occlusion discovered with delayed presentation after ST-segment elevation myocardial infarction. Clinical features and treatment considerations of these entities differ considerably from CTO.[5,7,8]

Among patients who have a clinical indication for coronary angiography, the incidence of CTO has been reported to be as high as 15-30%.[11,12] Patients with CTO are referred for angiography because of anginal symptoms or significant ischemia in non-invasive ischemia testing. Patients who are symptomatic will have stable exertional angina resulting from a limitation of collateral vessel flow to meet myocardial oxygen demands with stress. Of patients referred for PCI in clinical trials of CTO PCI, only 10-15% of the patients were asymptomatic. It is likewise uncommon for patients with CTO to have an acute coronary syndrome caused by the CTO itself.[5,9-11]

This study was aimed to find out the differences in types of lesions and the incidence of total occlusion lesions in patients with metabolic syndrome.

METHODS

A total 43 consecutive patients with or without metabolic syndrome who underwent coronary angiography in Awal Bros Hospital Makassar were enrolled from 1st Jan until 15th Feb 2013. The patients were categorized as having metabolic

Table 2. Characteristics of type A, B, and C coronary lesions[5]

Type A lesions (high success, >85%; low risk	
Discrete (<10mm)	Little or no calcium
Concentric	less than totally occlusive
Readily accesible	Not ostial in location
Nonangulated segment, <45 degress	No major side branch involvement
Smooth Countour	Absence of thrombus
Type B lesions (moderate success, 60-85%; moderate risk	
Tubular (10 to 20 mm in length)	Moderate to heavy calcification
Eccentric	Total occlusion <3 month old
Moderate turtuosity of proximal segment	Ostial in location
Moderately angulated segment	Bifurcation lesion requiring double guidewire
Irregular contour	Some thrombus present
Type C lesions (low Success, <60%; high risk)	
Diffuse (>2 cm in length)	Total occlusion >3 month old
Excessive turtuosity of proximal segment	Inability to protect major side branches
Extremely angulated segment, >90 degrees	Degenarated vein grafts with friable lessions

syndrome when they met the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) definition for Asian Population. Data was statistically analyzed by using the chi-square test.

The chi-square test was used to analyze the correlation between the differences in types of lesions and the incidences of total occlusion lesions in metabolic syndrome and non-metabolic syndrome groups. A *P*-value < 0.001 was considered as statistically significant. The statistical analysis was carried out with SPSS software.

RESULTS

From 43 patients, 34 (79.9%) were male. Twenty-five patients (58%) were considered as having metabolic syndrome and 18 (42%) as having non-metabolic syndrome (Table 3).

In the metabolic syndrome group, it was found that coronary type lesion A was 0%, type B was 40%, and type C was 60%, with the incidence of total occlusion being 48%. In non-metabolic syndromes, it was found that non-significant coronary lessions were 16.5%, type A was 22.5%, type B was 55.5%, type C was 5.5%, with the incidence of total oclussions being 0% (Table 4,5).

After statistically being compared with chi-square, there was a significant difference in the severity of coronary lesions ($P < 0.001$) and incidences of total occlusions in coronary arteries ($P < 0.001$) between the two groups (Table 6,7).

Table 3. Characteristics of samples

	Metabolic Syndrome (n=25)	**Non-metabolic Syndrome (n=18)**
Age	60.8 ± 9.5	56.22 ± 9.74
Male	22(88%)	12 (66%)
Weight	77.68 ± 14.62	68.27 ± 11.10
Height	164.6 ± 6.05	162.72 ± 7.06
Waist Circumference	101.98 ± 10.48	89.11 ± 9.53
Blood Pressure	144.4/81.80 ± 18.94/8.27	135.83/78.88 ± 24.68/8.14
Fasting Glucose	140.64 ± 59.45	108.5 ± 45.80
HDL - C	40.36 ± 11.18	49.88 ± 11.37
Triglycerida	164.52 ± 51.56	128.94 ± 38.10

Table 4. Distribution of type of lession

Type of lesion		**Group**		**Total**
		metabolic syndrome	**Non-metabolic syndrome**	
A	Count	0	4	4
	Expected Count	2.3	1.7	4.0
B	Count	10	10	20
	Expected Count	11.6	8.4	20.0
C	Count	15	1	16
	Expected Count	9.3	6.7	16.0
N	Count	0	3	3
	Expected Count	1.7	1.3	3.0
Total	Count	25	18	43
	Expected Count	25.0	18.0	43.0

Table 5. Distribution of total occlusion coronary artery

Total occlusion		Group		Total
		Metabolic syndrome	Non Metabolic syndrome	
No	Count	13	18	31
	Expected Count	18.0	13.0	31.0
Yes	Count	12	0	12
	Expected Count	7.0	5.0	12.0
Total	Count	25	18	43
	Expected Count	25.0	18.0	43.0

Table 6. Chi-square analysis for comparation type lesion in metabolic syndrome vs non-metabolic syndrome

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	18.603[a]	3	.000
Likelihood Ratio	23.259	3	.000
N of Valid Cases	43		

a. 4 cells (50.0%) have expected count less than 5. The minimum expected count is 1.26.

Table 7. Chi-square analysis for coronary total occluded in metabolic syndrome vs non-metabolic syndrome.

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	11.985[a]	1	.001		
Continuity Correction[b]	9.717	1	.002		
Likelihood Ratio	16.301	1	.000		
Fisher's Exact Test				.000	.000
N of Valid Cases	43				

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 5.02.
b. Computed only for a 2x2 table.

DISCUSSION

We found that metabolic syndrome was associated with more severe coronary artery lesions. Type C lesion considered as the worst type appeared in 15 from 25 patients (60%) compared with the non-metabolic syndromes in which it appeared in only 1 of 18 patients. However, if we judge from the type B lesions, the result can be said to be almost the same in both groups: 10 of 25 (40%) in the metabolic syndrome group versus 10 of 19 (55.5%) in the non-metabolic group. From the above result, it can be concluded that the probability of occurence of type C lesions was higher in the metabolic syndrome group.

Why was metabolic syndrome associated with more severe lesions compared to non-metabolic syndrome? First, the metabolic syndrome consisted of metabolic abnormalities including centrally distributed obesity, decreased high-density lipoprotein, elevated triglyceride, elevated blood pressure, and hyperglycaemia.[1-3] It means that in metabolic syndrome, individual patient will have equal to or more than a 3-risk factor compared to non-metabolic syndrome, which means that the more the risk factors the worse the lesion. Second, metabolic syndrome itself amplifies and accelerates the risk of atherosclerosis with its associated effect on morbidity and mortality. Redox homeo-

stasis describes the normal physiologic process of reduction and oxidation in order to repair unstable, damaged, reduced reactive oxygen species (ROS) which will include the following oxygen free radicals (superoxide, hydrogen peroxide, hydroxil radical, singlet oxygen) and organic analogues which include reactive nitrogen species (RNS) primarily peroxynitrite. In metabolic syndrome, this homeostatic balance between ROS and antioxydant capacity is in contrast to redox stress which implies a loss of this unique homeostatis resulting in an excess production of ROS either trhough the process of reduction or oxidation. Oxidative stress implies a loss of redox homeostasis (imbalance) with an excess of ROS by the singular process of oxidation. Both redox and oxidative stress may be associated with an impairment of antioxidant defensive capacity as well as an overproduction of ROS.[12]

It has been known for some time that ROS are detrimental and toxic to cells and tissues as a result of injury to lipids, nucleic acids, and proteins, such as: 1) Lipid peroxidation of membranes (loss of membrane function and increased permeability) and generation of lipid autoperoxidation reaction, 2) DNA damage leading to mutation and death, and (3) Cross linking or vulcanization of sulfhydryl rich proteins (leading to stiff aged proteins specifically collagen of the extracellular matrix). The evolutionary process of redox homeostasis allows humans to survive in an atmosphere of high oxygen content. In addition, our bodies have become "hard wired" to utilize the mechanism of redox stress injury to fend off invading infectious organisms and survive our environment. Paradoxically, (when there is a loss of homeostasis resulting in redox or oxidative stress) this protective mechanism turns on our own cells and tissues, and causes damages, especially the intima. Metabolic syndrome is associated with an elevated tension of redox stress within the intima due to multiple toxicities. Each of these toxicities results in the formation of damaging ROS. The redox stress associated with these reactive oxygen species contributes to the development, progression, and the final fate of the arterial vessel wall in atherosclerosis.[13-16.]

We also found that the incidence of coronary total occlusion was higher in the metabolic syndrome group. From 25 patients, we found 12 patients with coronary total occlusions (48%) compared to 0 from 18 patients (0%), in non-metabolic syndrome. From the data above we can conclude that metabolic syndrome was associated with a higher incidence of coronary total occlusion.

CONCLUSION

As compared to non-metabolic syndrome, metabolic syndrome was associated with changes in the severity of types of coronary lesions and increased incidences of total occlusions in coronary arteries. Furthermore, both patients and health care providers should pay more attention when faced with metabolic syndrome because of all the consequences that can result. Future research with larger populations and samples will be necessary to confirm our findings.

ACKNOWLEDGEMENTS

We would like to thank the director of Awal Bros Hospital Makassar who permitted us to carry out our study in this hospital.

Presented as a Free Paper - Oral Presentation at the 22nd Annual Scientific Meeting of Indonesian Heart Association (Asmiha), Jakarta, Indonesia, April 5-7, 2013.

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