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Inward or Outward Costophrenic Angles : A Simple Sign on Chest X-ray for the Screening of Metabolic Syndrome

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Abstract : Prevention of cardiovascular diseases is a top-priority issue in Japan. To this end, we have developed a new screening method for metabolic syndrome (MetS) using chest X-ray. We recruited 200 patients who visited our outpatient cardiology clinic from March 2014 to August 2014. Patients with severe lung disease, acute coronary syndrome, and end-stage renal failure were excluded. We collected data on each patient's medical history, laboratory results, waist circumference (WC), body weight, and height. Additionally, we measured two parameters from the chest X-ray: (A) width at the level of right dome of diaphragm and (B) width between the costophrenic (CP) angles. We classified the CP angles as either inward ($A \geq B$) or outward ($A < B$). Increased WC was defined as ≥ 85 cm in males and ≥ 90 cm in females. Patients with outward CP angles had a significantly larger WC compared to those with inward CP angles (92.3 ± 8.9 vs. 80.5 ± 7.8 cm, $P < 0.001$). In particular, the percentage of male patients with increased WC (≥ 85 cm) was significantly higher in patients with outward CP angles than in those with inward CP angles (89.2% vs. 41.3%, $P < 0.001$). Body weight and BMI were both significantly higher in patients with outward CP angles than in those with inward CP angles in both gender groups. When laboratory data and risk factors were compared, patients with outward CP angles and those with positive WC criteria consistently tended toward high morbidity from hypertension, dyslipidemia, and diabetes. The inward/outward CP identified candidates for MetS, especially in the male subjects. Chest X-ray could become a useful screening tool for the detection of increased WC and coronary risk factors.

Key words : metabolic syndrome, cardiovascular diseases, preventive medicine, obesity, visceral fat

Introduction

Metabolic syndrome (MetS) is a constellation of atherosclerotic risk factors, including obesity,

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hypertension, insulin resistance, and dyslipidemia¹⁾. The incidence of cardiovascular disease (CVD) and all-cause mortality is increased in patients with MetS, even in the absence of baseline CVD or diabetes²⁻⁵⁾. Due to the increasing trends towards a Westernized diet, Japanese people have gained visceral fat, which is associated with atherosclerotic diseases and cardiovascular events^{6,7)}. Thus, prevention of atherosclerosis in high-risk middle-aged adults is now a top priority issue for healthcare in Japan, a country of aging population.

The Japanese version of diagnostic criteria for MetS was established in 2005 by the Japanese Committee of the Criteria for Metabolic Syndrome⁸⁾ and is now widely used in routine health checkups; however, the required measurement of waist circumference (WC) can be time-consuming and inaccurate in busy daily practice⁹⁻¹¹⁾. On the other hand, chest X-ray is one of the most common imaging modalities used for diagnosis and the chronological evaluation of diseases, and such imaging often reveals a dilated lower thorax in obese patients, possibly due to the accumulation of visceral fat. We therefore hypothesized that WC could be routinely assessed by frontal chest X-ray.

Methods

Study population

A total of 200 patients who visited our outpatient cardiology clinic from March to August 2014 were recruited to the study. Exclusion criteria were emergency presentations such as acute coronary syndrome, severe lung disease, disabilities, and end-stage renal failure. Informed consent was obtained from all patients regarding the use of clinical data.

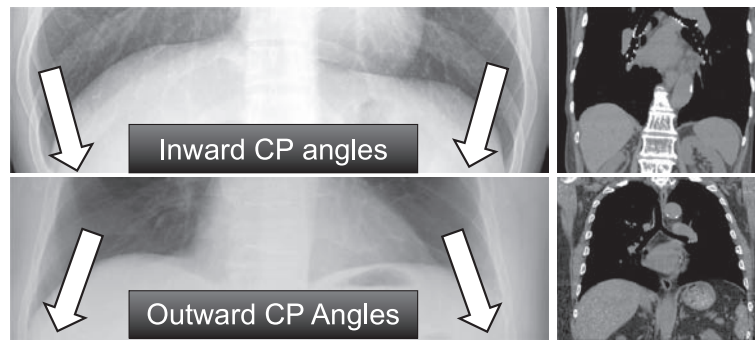
Data collection

Risk factors were collected by interview and from the medical records. WC was measured to the nearest 0.5 cm at the umbilical level with the patient in a standing position. Body mass index (BMI) was calculated as the patient's body weight (in kilograms) divided by body height squared (in meters). Blood pressure measurements were taken twice in a sitting position using a stethoscope and a standard sphygmomanometer. Various biochemical parameters were evaluated; however, plasma glucose was not measured if a fasting state was not possible.

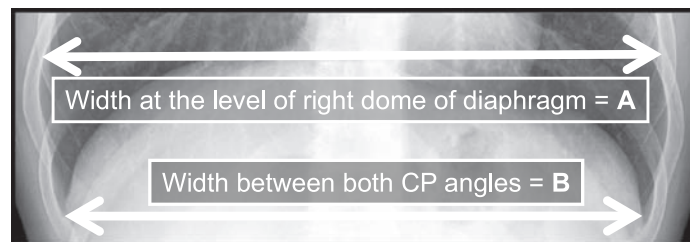
MetS was diagnosed according to the guidelines of the Japanese Committee of the Criteria for Metabolic Syndrome. WC criteria were judged as positive when the measurement was 85 cm or more in men and 90 cm or more in women. Patients with positive WC criteria were diagnosed as having MetS in the presence of two or more of the following risk factors of metabolic disorders: dyslipidemia (triglycerides ≥ 150 mg/dl, HDL-cholesterol < 40 mg/dl, or receiving lipid-lowering medication), hypertension (systolic blood pressure ≥ 130 mmHg, diastolic blood pressure ≥ 85 mmHg, or receiving anti-hypertensive medication), and hyperglycemia (fasting plasma glucose ≥ 110 mg/dl or receiving hypoglycemic medication).

Measurement of chest X-ray

A frontal chest X-ray taken during the initial hospital visit was assessed visually and quanti-



Visual assessment : upper X-ray image shows inward costophrenic (CP) angles and lower shows outward CP angles with corresponding coronal computed tomography image on the right, respectively.



Quantitative assessment : patient's CP angles were classified as inward ($A \geq B$) or as outward ($A < B$).

Fig. 1. Concept of inward /outward costophrenic (CP) angles

tatively (Fig. 1). For the study purpose, we performed quantitative measurements using an electronic medical record system HOPE / EGMAIN (Fujitsu Inc., Tokyo, Japan) for the following parameters : (A) width at the level of right dome of diaphragm ; and (B) width between the costophrenic (CP) angles. We classified each patient's CP angles as either inward ($A \geq B$) or outward ($A < B$).

Statistical analysis

Statistical analysis was performed with JMP software, version 11 (SAS Institute Inc., Cary, NC). Categorical variables were presented as frequencies and compared with chi-square statistics or the Fisher exact test. Continuous variables were expressed as mean \pm SD and assessed by Student's t-test. A P value < 0.05 was considered to indicate statistical significance.

Results

Baseline patient characteristics

Gender, age, risk factors, medication, blood pressure, and reason for hospital visit are listed in Table 1. Male patients were significantly younger (61.8 ± 12.5 vs. 65.4 ± 13.4) and had higher rates of hypertension (58% vs. 43%) and smoking history (68% vs. 18%) than female patients. Diastolic blood pressure was also significantly higher in males compared to females (79 ± 10 vs. 75 ± 12). Chest discomfort was the most common reason of hospital visit (43.5%).

Table 1. Patient characteristics and reason for hospital visit

Patient characteristics	All (n = 200)	Males (n = 111)	Females (n = 89)	P-value
Age, years \pm SD	63.4 \pm 13.0	61.8 \pm 12.5	65.4 \pm 13.4	< 0.05
Hypertension, n (%)	102 (51)	64 (58)	38 (43)	0.04
Anti-hypertensive drug usage, n (%)	94 (47)	52 (47)	42 (47)	0.96
Dyslipidemia, n (%)	94 (47)	56 (52)	38 (43)	0.27
Lipid-lowering drug usage, n (%)	79 (40)	43 (39)	36 (40)	0.81
Family history, n (%)	8 (4)	6 (5)	2 (2)	0.30
Smoking, n (%)	91 (46)	75 (68)	16 (18)	< 0.0001
Current smoking, n (%)	32 (16)	27 (24)	5 (6)	< 0.0001
Diabetes, n (%)	38 (19)	22 (20)	16 (18)	0.74
Oral diabetic agent usage, n (%)	24 (12)	16 (14)	8 (9)	0.24
Insulin usage, n (%)	2 (1)	1 (1)	1 (1)	1.0
Systolic blood pressure, mmHg	132 \pm 18	131 \pm 15	133 \pm 20	0.35
Diastolic blood pressure, mmHg	77 \pm 11	79 \pm 10	75 \pm 12	0.03
Pulse rate, beats / min	67 \pm 13	66 \pm 14	69 \pm 13	0.07
Reason for hospital visit	All (n = 200)	Males (n = 111)	Females (n = 89)	P-value
Chest discomfort, n (%)	87 (43.5)	42	45	
ECG abnormalities, n (%)	25 (12.5)	12	13	
Follow-up visit after PCI, n (%)	21 (10.5)	15	6	
Arrhythmia-related symptoms, n (%)	17 (8.5)	11	6	0.14
Dyspnea, n (%)	16 (8)	7	9	
Abnormal carotid echo findings, n (%)	13 (6.5)	9	4	
Edema, n (%)	4 (2)	4	0	
Others, n (%)	17 (8.5)	11	6	

Body measurements by type of CP angles

As shown in Fig. 2, WC was significantly larger in patients with outward CP angles than in patients with inward CP angles (92.3 ± 8.9 cm vs. 80.5 ± 7.8 cm). In particular, the percentage of male patients with WC ≥ 85 cm was significantly higher in patients with outward CP angles compared to those with inward CP angles (89.2% vs. 41.3%). Table 2 lists the results of body measurements. Body weight and BMI were significantly higher in patients with outward CP angles compared to those with inward CP angles, while WC, height, and body weight values were significantly more in male patients than in female patients. Table 3 shows the numbers of patients who meet the WC criteria for MetS (only in patients with fasting glucose measurement) according to inward or outward CP angles. Patients with outward CP angles had higher percentages of positive WC criteria (74%) and MetS (67%). When divided by gender, positive predictive values (PPV) of outward CP angles for positive WC criteria and MetS were 80% and 88%, respectively. On the other hand, negative predictive values (NPV) of inward CP angles

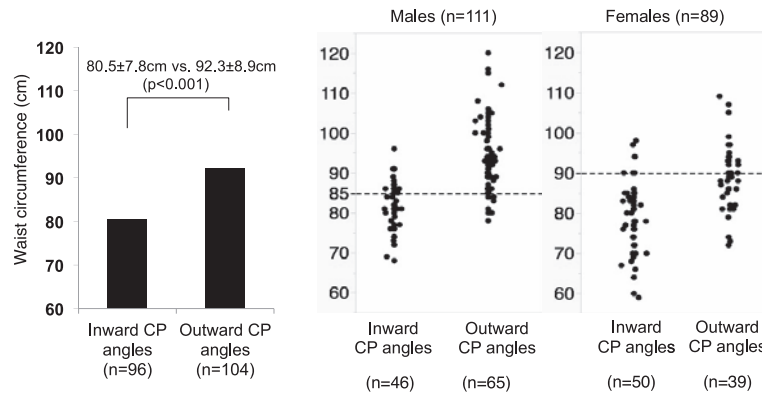


Fig. 2. Waist circumferences in patients with inward vs. outward costophrenic (CP) angles

Table 2. Comparison of body measurements between groups

Variable		Inward CP angles (M = 46, F = 50)	Outward CP angles (M = 65, F = 39)	P-value
Waist Circumference (cm)	Male (n = 111)	82.0 ± 6.5	94.4 ± 8.7	< 0.0001
	Female (n = 89)	79.0 ± 8.8	89.1 ± 8.3	< 0.0001
Body weight (kg)	Male (n = 111)	60.5 ± 8.8	73.2 ± 14.7	< 0.0001
	Female (n = 89)	51.8 ± 9.4	58.3 ± 8.5	0.0010
Height (cm)	Male (n = 111)	166.9 ± 6.7	168.0 ± 7.0	0.42
	Female (n = 89)	154.9 ± 6.3	152.3 ± 7.2	0.08
BMI (kg / m ²)	Male (n = 111)	21.8 ± 3.6	25.8 ± 4.0	< 0.0001
	Female (n = 89)	21.6 ± 3.6	25.2 ± 3.4	< 0.0001
Variable		WC criteria (-) (M = 34, F = 63)	WC criteria (+) (M = 77, F = 26)	P-value
Waist Circumference (cm)	Male (n = 111)	78.5 ± 4.4	94 ± 7.8	< 0.0001
	Female (n = 89)	78.7 ± 7.1	94.9 ± 5.2	< 0.0001
Body weight (kg)	Male (n = 111)	58.4 ± 7.2	72.2 ± 14.3	< 0.0001
	Female (n = 89)	52.1 ± 8.4	61 ± 9.1	< 0.0001
Height (cm)	Male (n = 111)	165.8 ± 6.8	168.3 ± 6.7	0.08
	Female (n = 89)	153.9 ± 6.5	153.5 ± 7.5	0.80
BMI (kg / m ²)	Male (n = 111)	21.3 ± 3	25.4 ± 4.2	< 0.0001
	Female (n = 89)	22 ± 3.5	25.9 ± 3.6	< 0.0001
Variable	Overall (n = 200)	Males (n = 111)	Females (n = 89)	P-value
Waist Circumference (cm)	86.7 ± 10.3	89.3 ± 10.0	83.5 ± 9.9	< 0.0001
Body weight (kg)	62.1 ± 13.9	67.9 ± 14.0	54.7 ± 9.5	< 0.0001
Height (cm)	161.4 ± 9.7	167.5 ± 6.8	153.8 ± 6.8	< 0.0001
BMI (kg / m ²)	23.7 ± 4.1	24.2 ± 4.3	23.1 ± 3.9	0.09

Values are mean ± SD. WC criteria, waist circumference criteria; CP angle, costophrenic angle; BMI, body mass index. WC criteria was judged positive when WC was 85 cm or more in men or 90 cm or more in women.

Table 3. Numbers of patients with inward / outward CP angles

	Overall (n = 200)		Males (n = 111)		Females (n = 89)	
	Outward CP angles	Inward CP angles	Outward CP angles	Inward CP angles	Outward CP angles	Inward CP angles
WC criteria (+)	77	26	58	19	19	7
WC criteria (-)	27	60	7	27	20	43
	Overall (n = 134)		Male (n = 78)		Female (n = 56)	
	Outward CP angles	Inward CP angles	Outward CP angles	Inward CP angles	Outward CP angles	Inward CP angles
MetS (+)	50	12	39	9	11	3
MetS (-)	25	47	10	20	15	27

CP angles, costophrenic angles ; WC, waist circumference ; MetS, metabolic syndrome. WC criteria was judged positive when WC was 85 cm or more in men or 90 cm or more in women.

MetS was assessed only in patients with fasting plasma glucose measurement according to the definition by Japanese Committee of the Criteria for Metabolic Syndrome.

for negative WC criteria and MetS were 86% and 90%, respectively.

Comparison of laboratory data between groups

As shown in Table 4, patients with outward CP angles had significantly higher values of all parameters except for LDL-C compared to those with inward CP angles. Similarly, patients meeting positive WC criteria had significantly higher values of parameters except for LDL-C and HbA1c compared to those who were WC negative.

Prevalence of coronary risk factors

Fig. 3 demonstrates that hypertension, dyslipidemia, and current smoking were more common in patients with positive than negative WC criteria. Likewise, hypertension, dyslipidemia, and diabetes were more common in patients with outward CP angles compared to those with inward CP angles. Thus, both positive WC criteria and outward CP angles well reflected the metabolic tendency of the patients.

Discussion

The main findings of this study are as follows: 1) In patients with outward CP angles, we observed larger WC, heavier body weight, and higher BMI; 2) Outward CP angles identified most patients with positive WC criteria, especially in males; 3) Both laboratory data and risk factors showed similar results when patients with / without WC criteria and those with inward / outward CP angles were compared.

Table 4. Comparison of laboratory data between groups

Variable	Inward CP angle	Outward CP angle	P-value
PG, mg / dl	105.4 ± 35.2 (n = 59)	127.2 ± 40 (n = 75)	0.001
HbA1 c, %	5.9 ± 0.6 (n = 90)	6.2 ± 0.8 (n = 98)	0.0031
IRI, μU / ml	10.9 ± 9.9 (n = 24)	25.6 ± 27.4 (n = 31)	0.0085
LDL-C, mg / dl	119.6 ± 28.6 (n = 93)	113.4 ± 31.4 (n = 100)	0.16
HDL-C, mg / dl	62.1 ± 16.6 (n = 95)	51.3 ± 13.3 (n = 102)	< 0.0001
TG, mg / dl	115.6 ± 62.6 (n = 95)	193.9 ± 280.7 (n = 102)	0.0071
UA, mg / dl	5 ± 1.2 (n = 95)	5.9 ± 1.5 (n = 102)	< 0.0001
Cr, mg / dl	0.7 ± 0.2 (n = 96)	0.8 ± 0.2 (n = 103)	0.0418
hs-CRP, mg / dl	0.06 ± 0.07 (n = 24)	0.16 ± 0.2 (n = 36)	0.012

Variable	WC criteria (-)	WC criteria (+)	P-value
PG, mg / dl	108.4 ± 38.7 (n = 58)	124.4 ± 38.6 (n = 77)	0.018
HbA1 c, %	5.9 ± 0.6 (n = 89)	6.1 ± 0.8 (n = 99)	0.10
IRI, μU / ml	11.7 ± 10.3 (n = 19)	23.2 ± 26.2 (n = 36)	0.025
LDL-C, mg / dl	119.1 ± 31.6 (n = 94)	113.8 ± 28.7 (n = 99)	0.23
HDL-C, mg / dl	62.4 ± 16.6 (n = 95)	51.1 ± 13 (n = 102)	< 0.0001
TG, mg / dl	111.1 ± 49 (n = 95)	198 ± 282 (n = 102)	0.0028
UA, mg / dl	4.9 ± 1 (n = 95)	6.1 ± 1.5 (n = 102)	< 0.0001
Cr, mg / dl	0.7 ± 0.2 (n = 96)	0.8 ± 0.2 (n = 103)	< 0.0001
hs-CRP, mg / dl	0.06 ± 0.07 (n = 19)	0.15 ± 0.18 (n = 41)	0.0063

Values are mean ± SD. WC criteria, waist circumference criteria; CP angle, costophrenic angle; PG, plasma glucose; IRI, immunoreactive serum insulin; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; TG, triglyceride; UA, uric acid; Cr, creatinine; hs-CRP, high sensitive c-reactive protein. WC criteria was judged positive when WC was 85 cm or more in men or 90 cm or more in women.

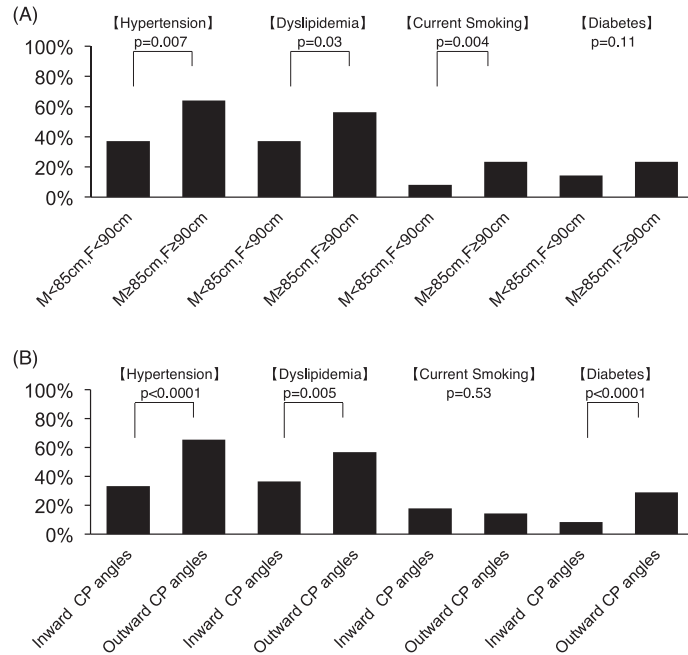


Fig. 3. Prevalence of risk factors between groups

Patients were divided into two groups by (A) waist circumference and (B) inward /outward costophrenic angles.

Body measurements in patients with inward/outward CP angles

Our study clearly showed differences in WC, body weight, and BMI in patients with inward versus outward CP angles (Table 2). We also observed the same results in patients with negative versus positive WC criteria. Compared with WC criteria, CP angles have similar meaning to WC because the measured areas of CP angles and WC are anatomically close (Fig. 1).

Usefulness of CP angles to predict larger WC and MetS

As shown in Table 3, PPV of outward CP angles for positive WC criteria and MetS were higher in male than in female patients, whereas NPV of inward CP angles for negative WC criteria and MetS were higher in females. The different results between males and females might reflect the different visceral/subcutaneous fat distribution between males and females^{12,13}, particularly since the CP angles are located inside the chest wall region connected to the abdominal wall, and thus the inward/outward CP angles might be influenced by the amount of visceral rather than subcutaneous fat. In contrast, WC measurement (a required component of MetS) includes both visceral and subcutaneous fat^{14,15}.

Laboratory data and risk factors analyzed by two different classifications

We observed similar trends in laboratory data and risk factors for both the CP angles and WC criteria analyses. In addition, it seemed that CP angles discriminated diabetes numerically better than WC criteria (Table 3 and Fig. 2). Visceral fat accumulation has a strong correlation with abnormal glucose metabolism¹⁶, and it is plausible that outward CP angles could reflect visceral fat, and therefore abnormal glucose metabolism, better than positive WC criteria.

Uncertainty about the current cut-offs of WC criteria

Although we started this study to reproduce the result of WC measurement with the parameters obtained from chest X-ray, it also raised some discussion points regarding the Japanese MetS criteria. The original WC criteria (≥ 85 cm in males and ≥ 90 cm in females) were derived from the cut-off value for visceral fat area of 100 cm^2 at which the average number of component risk factors goes beyond 1.0¹⁷). However, some studies have proposed gender-specific cut-off values instead of the original threshold of 100 cm^2 ^{18,19}). In addition, a number of studies reported different cut-offs of WC to predict the clustering of metabolic risk factors²⁰⁻²⁵). All of these analyses were performed to yield maximal sensitivity plus specificity for predicting the presence of one or more risks. In our study, we introduced a new simple screening method for identifying patients with visceral fat accumulation. Since inward/outward CP angles is a dichotomous criterion, we cannot set a cut-off point, but outward CP angles in an undiagnosed male patient could be an alarming sign and an early diagnostic clue.

Clinical implications of the study

This study highlights that chest X-rays obtained during routine practice could be used to identify a possible MetS patient, based on the CP angles, regardless of the reason for his/her

hospital visit. Further evaluation of the patient's metabolic status is recommended.

Limitations

Several limitations of the present study should be noted. This is a single-center observational study with a small number of patients. Accurate evaluation of blood pressure and laboratory data was difficult due to the significant number of patients receiving medication to control risk factors. Although we excluded patients with severe lung disease, there were a significant number of patients with a smoking history, which could also have affected the measurements on chest X-ray. The findings obtained from the patient population of our study are therefore not necessarily applicable to other patient populations or healthy individuals.

In addition, chronological changes in CP angles and long-term clinical outcomes of the patients were not included in the study. Therefore, further large-scale, long-term clinical studies are warranted to determine the clinical importance of inward/outward CP angles for MetS diagnosis and prevention.

In conclusions, chest X-ray is a useful and readily available screening tool for the detection of increased WC. In particular, the inward/outward CP angles by chest X-ray is a simple sign that could help identify the candidates of MetS, especially among the male population.

Conflict of interest disclosure

The authors have no conflict of interest to declare.

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