THE OPTIMAL CUT-OFF POINTS OF WAIST CIRCUMFERENCE AND BODY MASS INDEX FOR IDENTIFICATION OF METABOLIC SYNDROME IN ROYAL THAI ARMY PERSONNEL IN BANGKOK AND SUBURBAN

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ABSTRACT

The aim of the study was to determine the optimal cut-off points of waist circumference (WC) and body mass index (BMI) for identification of metabolic syndrome in Royal Thai Army (RTA) personnel aged 35-60 years in Bangkok and suburbs. The design of this study was a cross sectional research conducted with 2,809 samples (1,549 males and 1,260 females). The metabolic syndrome is defined according to Joint Interim Statement (JIS) criteria. WC was measured horizontally at the umbilicus level. Data collection was by using existing annual health checkup data in the fiscal year 2014 from Armed Forces Research Institute of Medical Sciences. Receiver operating characteristic (ROC) curve analysis was used for identifying the cut-off points of WC and BMI with sensitivity and specificity for metabolic syndrome. The sensitivity of at least 80 percent was used for determining the appropriate WC and BMI cut-off points. The area under the curve (AUC) with 95% confidence interval (CI) was used as an indicator of the diagnostic performance of WC and BMI for identifying metabolic syndrome.

The ROC analysis showed that the WC optimal cut-off points for detection of the metabolic syndrome in male were 82.5 cm (sensitivity 81.9%, specificity 43.2%, AUC=0.686, 95% CI=0.659-0.712) and in female were 77.5 cm (sensitivity 81.3%, specificity 53.1%, AUC=0.755, 95% CI=0.727-0.783). Furthermore, BMI optimal cut-off points for detection of the metabolic syndrome was 23.14 kg/m^2 (sensitivity 80.0%, specificity 47.1%, AUC=0.690, 95% CI=0.671-0.710). The parallel combined test we proposed will be a powerful and cost-effective tool for initial screening for the detection of metabolic syndrome. It may also increase the sensitivity of metabolic syndrome diagnosis.

These finding suggest that WC and BMI are potential as screening tools for classifying metabolic syndrome. Especially in a field setting, screening by using WC and BMI would be more convenient than a laboratory test in order to prevent and carry out surveillance of the occurrence of metabolic syndrome.

KEY WORDS: METABOLIC SYNDROME / WAIST CIRCUMFERENCE AND BODY MASS INDEX / CUT-OFF POINTS / RECEIVE OPERATING CHARACTERISTIC CURVE / ROYAL THAI ARMY

116 pages

การหาค่าจุดตัดที่เหมาะสมของเส้นรอบวงเอวและดัชนีมวลกายเพื่อบ่งชี้ถึงภาวะเมตาบอลิคซินโดรมในกำลังพลกองทัพบกสังกัดกรุงเทพมหานครและปริมณฑล

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บทคัดย่อ

การศึกษาในครั้งนี้เป็นการศึกษาแบบภาคตัดขวาง มีวัตถุประสงค์เพื่อหาจุดตัดที่เหมาะสมของเส้นรอบวงเอวและดัชนีมวลกายเพื่อใช้ในการบ่งชี้ถึงภาวะเมตาบอลิคซินโดรมในกำลังพลกองทัพบกสังกัดกรุงเทพมหานครและปริมณฑล โดยใช้ข้อมูลผลการตรวจสุขภาพประจำปีของกำลังพลกองทัพบกจากสถาบันวิจัยวิทยาศาสตร์การแพทย์ทหาร ในช่วงวันที่ 1 ตุลาคม 2556 ถึง 30 กันยายน 2557 อายุตั้งแต่ 35-60 ปี โดยมีจำนวนกำลังพลที่ใช้ในการศึกษาทั้งหมด 2,809 คน ประกอบด้วย กำลังพลชายจำนวน 1,549 คน และกำลังพลหญิงจำนวน 1,260 คน สำหรับการวินิจฉัยภาวะเมตาบอลิคซินโดรมใช้เกณฑ์ของ Joint Interim Statement (JIS) และใช้วิธีการวิเคราะห์ Receiver operating characteristic (ROC) curve ในการหาจุดตัดของเส้นรอบวงเอวและดัชนีมวลกาย โดยการเลือกจุดตัดที่เหมาะสมจะใช้จุดตัดที่ให้ค่าความไวตั้งแต่ร้อยละ 80 ขึ้นไป และใช้พื้นที่ใต้กราฟในการประเมินประสิทธิภาพของจุดตัดเส้นรอบวงเอวและดัชนีมวลกายที่จะนำมาใช้เป็นเครื่องมือคัดกรองภาวะเมตาบอลิคซินโดรม

จากผลการวิเคราะห์ ROC พบว่าจุดตัดของเส้นรอบวงเอวที่เหมาะสมในการบ่งชี้ภาวะเมตาบอลิคซินโดรมในกำลังพลชายอยู่ที่ 82.5 ซม. (Sensitivity 81.9%, specificity 43.2%, AUC=0.686, 95% CI=0.659-0.712) และกำลังพลหญิงที่ 77.5 ซม. (Sensitivity 81.3%, specificity 53.1%, AUC=0.755, 95% CI=0.727-0.783) ส่วนจุดตัดของดัชนีมวลกายที่เหมาะสมในการบ่งชี้ภาวะเมตาบอลิคซินโดรมอยู่ที่ 23.14 กก/ม^2 (Sensitivity 80.0%, specificity 47.1%, AUC=0.690, 95% CI=0.671-0.710) และเมื่อนำทั้งสองเครื่องมือมาใช้ร่วมกันโดยวิธีแบบขนานจะช่วยเพิ่มประสิทธิภาพในการคัดกรองภาวะเมตาบอลิคซินโดรมได้ดียิ่งขึ้น โดยผลการศึกษานี้มีข้อเสนอแนะว่าเส้นรอบวงเอวและดัชนีมวลกายเหมาะสมนำมาใช้เป็นเครื่องมือคัดกรองภาวะเมตาบอลิคซินโดรมอีกทั้งยังสะดวกที่จะนำไปใช้ในภาคสนามเพื่อเป็นการป้องกันและเฝ้าระวังการเกิดภาวะเมตาบอลิคซินโดรมในกำลังพลกองทัพบก

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ABBREVIATIONS

AACE	American Association of Clinical Endocrinologists
AFRIMS	Armed Forces Research Institute of Medical Sciences
ATP III	Adult Treatment Program III
AUC	Area under the curve
BMI	Body mass index
CHD	Coronary heart disease
CVD	Cardiovascular disease
DBP	Diastolic blood pressure
DALYs	Disability Adjusted Life Years
ECS	European Cardiovascular Societies
FFA	Free fatty acid
FPG	Fasting plasma glucose
HDL-C	High density lipoprotein cholesterol
IDF	International Diabetes Federation
JIS	Joint Interim Statement
LDL-C	Low density lipoprotein cholesterol
MetS	Metabolic syndrome
NCDs	Noncommunicable diseases
NCEP	National Cholesterol Education Program
NHANES	National Health and Nutrition Examination Survey
OR	Odds ratio
ROC	Receiver operating characteristic
RR	Relative risk
RTA	Royal Thai Army
SBP	Systolic blood pressure
TC	Total cholesterol
TG	Triglyceride
VLDL	Very low density lipoprotein cholesterol

ABBREVIATIONS (cont.)

WC	Waist circumference
WC-U	Waist circumference measurement at the site of the umbilicus level
WHO	World Health Organization
WHR	Waist-to-hip ratio

CHAPTER I
INTRODUCTION

Background and Rationale

Worldwide, noncommunicable diseases (NCDs), mainly cardiovascular disease (CVD), diabetes mellitus, hypertension and cancer, are majors cause of illness and death in both developed and developing countries (1-3). NCDs are related to the interaction of various genetic, environmental and especially lifestyle risk factors, including smoking, alcohol consumption, unhealthy diet (high total energy, fat, salt, and sugar, low in fruit and vegetables), physical inactivity and chronic stress (4). According to the World Health Organization (WHO) report in 2012, over 36 million people or 63% around the globe had died of NCDs. The leading causes of NCDs deaths were CVD, which contributes to 17.5 million deaths or 45% of all NCDs death. Of these, 7.4 million people (13.2 %) died of ischaemic heart disease and 6.7 million (11.9%) from stroke (5, 6). WHO estimates that total deaths from NCDs will increase by a further 17% or 41 million people and predicts the greatest increase in incidence of NCDs in the African region with a 27% rise and in the Eastern Mediterranean region with 25% rise in 2015. The highest absolute number of deaths will occur in the Western Pacific and South-East Asia region (7).

In Thailand, NCDs are one of top five leading causes of illness and death among the Thai population. WHO-NCDs Country Profiles, 2014 reported total Thai deaths 501,000; NCDs are estimated to account for 71% of total deaths (8). National health statistics show that the leading burden of disease in the Thai population has been shifting to NCDs. The Bureau of Health Policy and Strategy (BHPS), Ministry of Public Health and the International Health Policy Program (IHPP) reported the Disability Adjusted Life Years (DALYs) lost from NCDs increased from 5.6 to 6.5 and 10.2 million in 1999, 2004, and 2009, respectively (9). In 2009, the DALYs in Thai population are 4.4 million and 5.8 million for female and male, respectively; with CVD, cancer, and diabetes are among the top five leading causes. (10). Thus, from the data and statistics, it is clearly shown that CVD is one of Thailand's largest health problems.

The major risk factors of CVD is metabolic syndrome (MetS), a cluster of risk factors including abdominal obesity, atherogenic dyslipidemia, elevated blood pressure, insulin resistance, and proinflammatory and prothrombotic states (11) . The importance of MetS is its association with subsequent development of type 2 diabetes mellitus and cardiovascular events, patients with MetS have a 2-fold increase risk of mortality from coronary heart disease and an increased risk of developing type 2 diabetes mellitus (12). A recent meta-analysis including 43 cohorts (172,573 individuals) reported that MetS conveyed a relative risk (RR) for CVD events and death of 1.78, with higher risk in women (RR 2.63). In addition, risk was still associated with the syndrome after adjusting for traditional CVD risk factors (RR=1.54) (13). At present, it is generally accepted that MetS is a major contributor for the development of CVD, type 2 diabetes mellitus and many NCDs. Thus, early MetS detection, prevention and management offer the best solution for reduction of risk for CVD and other NCDs.

Metabolic syndrome detection criteria have evolved over the past decade. The recommended measurements for detection have been conditioned in part by views of the pathogenesis of the syndrome. For example, in 1998, WHO task force on diabetes indicated that insulin resistance is the dominant cause of the MetS. By these criteria, clinical indicators of insulin resistance were required for the diagnosis (14). Thereafter, several organizations such as the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III), the American Heart Association (AHA)/ National Heart, Lung, and Blood Institute (NHLBI) and the International Diabetes Federation (IDF) have published diagnostic criteria, differing with respect to glucose and/or waist circumference (WC) cut-off levels (11, 15). The two major sets of criteria that have been used are those of ATPIII and IDF. The main difference between the two criteria is that central obesity, as measured by WC, is a prerequisite in the IDF definition, with cut-off points of WC being ethnic specific and lower than in the ATPIII definition. Recently, an additional definition of MetS was proposed as a joint interim statement (JIS) by several organizations in an attempt to harmonize the definition of MetS. The available information based on ATPIII and IDF criteria suggests that MetS is pandemic but that prevalence varies widely depending on the ethnic groups studied and criteria applied. Thus, the definition proposed is appropriate to use in epidemiologic studies, it does not built in any preconceived notion of the underlying cause of metabolic syndrome, whether it is insulin resistance or obesity. The proposed criteria does not require any specific criterion, only at least any three of five criteria as following are met; elevated waist circumference (population and country specific definitions) , elevated triglycerides (≥150 mg/dL) , reduced HDL-C (<40 mg/dL in males and <50 mg/dL in females), elevated blood pressure (SBP ≥130 and/or DBP ≥85 mm Hg), and elevated fasting glucose (≥100 mg/dL) (16).

Abdominal obesity is the major disorder constituting the basic for the development of MetS. It is categorized as abdominal obesity due to fat accumulation in visceral abdomen. Theoretically, abdominal obesity should be determined by visceral adipose tissue (VAT) precisely measured by magnetic resonance imaging (MRI) or computerized tomography (CT) scanning. In practice WC is widely used clinically to estimate the abdominal fat for its convenience and strong correlation with VAT (17). Furthermore, BMI is presently the most often used and widely satisfactory methods of distribution of body weight and classification of obesity. It is a useful determinant of adiposity in early and middle-aged adults (18). However, an important restriction of BMI is its inability to recognize between fat mass and fat free mass, which is a good indicator of health status. In addition to BMI in clinical practice and suggesting that a combination of BMI and WC may be preferable to BMI alone for obesity risk assessment. Such a combination measure would require little extra cost or equipment and could increase the clinician's ability to identify individuals at high risk for diseases that correlate with excess adiposity (19). Therefore, WC and BMI are recommended anthropometric indicators assessment of abdominal obesity and suitable screening tools for early MetS detection, they have been widely used in epidemiologic studies because of their ease in field work. They are simple, most practical and expedient (20). It was found that WC and BMI measurements have strong positive correlations to the biochemical markers such as blood glucose and lipid profile (21-24). WHO suggests using cut-off points for WC and BMI concurrently but declares that the use of WC to assess health risk would need to be population specific and depends on the presence or absence of other risk factors, i.e. CVD, type 2 diabetes, hypertension. The Asia-Pacific recommendations of WC cut-off points for Asia population is <90 cm in male and <80 cm in female (25). However, these cut-off points were discussed by several Asia researchers such as Japan, China and India (26-28), lower WC cut-off points were suggested for diagnosis of abdominal obesity for these populations. The WC cut-off points proposed by the Asia-Pacific may not be appropriate for Thai population. In Thailand, studies found that WC cut-off points were 82-88 cm in male and 80-85 cm in female with the BMI cut-off points were 23-25 kg/m^2 in both sexes, a few studies indicated that WC and BMI cut-off points seemed to be increasing in general population (29-31). However, there was no study in Royal Thai Army (RTA) personnel.

It is interested to study these issues in RTA personnel. The Royal Thai Army has 4 core missions which are defense external threat, upholding the public security, sustaining internal public order and developing country. Currently, the RTA has taken more responsibility in civic action, for example, humanitarian assistance during disaster and road construction in remote areas. From all the duties, the RTA personnel obviously have a significant role for the country. They all need to obtain special training and maintaining excellence in physical fitness to perform their duty all the time. Moreover, to efficiently complete the assignments, commander in chief of the RTA has assigned the policy with regulations and instructions to enhance health of the RTA personnel as follows; to enhance physical performance by introduce physical testing for their developing and renovating fitness stimulation, to create well-being in various aspects such as soul, mood, social life, and nutrition, to inspect physical condition through health risk assessment, weight control, annually health check-up, and take the result of checking plus the number of BMI to be a part of performance evaluation, information of developing management, and considering for yearly bonus (32-35).

A study of MetS in RTA personnel, 2011 found that 19.6% of RTA personnel had MetS (male 21.1% and female 13.8%) (36). From the importance of the problem as mentioned above, the researchers realize that MetS is a major health problem in the RTA personnel. Therefore, we are interested in the study of the optimal cut-off points of WC and BMI for identification of MetS in RTA personnel. Different behavior and lifestyles between RTA personnel and general population, for instance the majority of RTA personnel training is resistance exercise, might boost up BMI of RTA personnel due to increase in muscle mass but not fat. Furthermore, the researcher also studies the prevalence of high level of LDL-C because dyslipidemia is the major constituent of the MetS and related to the incidence of CVD, particularly high LDL-C. In clinical practice, LDL-C is the target to be reduced in order to effectively prevent CVD. Thus, we expected that the WC and BMI with appropriate cut-offs points in the RTA personnel can be used as the effective screening tools for early MetS detection and for planning of the preventive strategies for MetS in high-risk RTA populations and for planning of health promotion programs.

Research Question

What are the optimal cut-off points of WC and BMI in the selected Royal Thai Army personnel population in Bangkok and suburban for identification of metabolic syndrome?

Research Objectives

Primary Objective

1. To study the prevalence of metabolic syndrome using JIS criteria.
2. To identify the optimal cut-off points of WC in male and female for identification of metabolic syndrome compared to JIS criteria.
3. To identify the optimal cut-off points of BMI in male and female for identification of metabolic syndrome compared to JIS criteria.

Secondary Objectives

1. To study association between smoking, alcohol consumption, exercise and metabolic syndrome.
2. To study the prevalence of high LDL cholesterol.

Research Hypothesis

1. WC might be used as a predictor for metabolic syndrome.
2. BMI might be used as a predictor for metabolic syndrome.
3. Smoking, alcohol consumption and exercise associate with metabolic syndrome.

Scope of the study

The subjects of this study were Royal Thai Army personnel male and female aged 35-60 year old in Bangkok and suburban who received annual health checkup from Armed Forces Research Institute of Medical Sciences (AFRIMS) in fiscal year 2014.

Definition of Terms

1. Royal Thai Army personnel means commissioned officers, non-commissioned officers, recruits, civilian employees and other personnel in this Royal Thai Army.

2. Fiscal year 2014 means duration from 1^{st} of October, 2013 to 30^{th} September, 2014

3. Suburban is defined to Nonthaburi, Samutprakarn, Samutsakorn and Nakhon Pathom province.

4. Metabolic Syndrome is a cluster of risk factors for CVD and type 2 diabetes mellitus. The risk factors include raised blood pressure, dyslipidemia (raised triglycerides and lowered high-density lipoprotein cholesterol), raised fasting glucose, and central obesity. MetS is defined according to the JIS criteria except that central obesity requirement is omitted since it will be treated as an independent variable. Subjects with two or more of risk factors from the JIS criteria were identified as having MetS.

5. A Joint Interim Statement criteria (JIS) is definition of MetS was proposed by several organizations in an attempt to harmonize the definition of MetS.

The consensus criteria define MetS as the presence of three or more of the following metabolic risk factors: elevated WC (≥90 cm for males and ≥80 cm for females), elevated serum triglycerides (≥150 mg/dL or using drug treatment), reduced HDL-C (<40 mg/dL in males, <50 mg/dL in females or using drug treatment), elevated blood pressure (SBP ≥130 and/or DBP ≥85 mmHg or using antihypertensive drug), elevated fasting glucose (≥100 mg/dL or using drug treatment) (16).

6. Waist circumference (WC) is defined as the measurement indicating abdominal obesity level. WC is measured at the umbilicus level (WC-U), unit is centimeter (cm). The measuring tape is placed in a horizontal plane around the abdomen at the level of this marked point. The plane of the tape is parallel to the floor and the tape is snug, but does not compress the skin. The measurement is made at a normal minimal respiration.

7. Body Mass Index (BMI) is a simple index of weight-for-height that is commonly used to classify underweight, overweight and obesity in adults. It is defined as the weight in kilograms divided by the square of the height in meters (kg/m^2)

$$BMI = \text{Body weight (kg)} / \text{Body height squared (m)}^2$$

8. High blood pressure is one of criteria for identifying metabolic syndrome; consist of high systolic blood pressure (SBP ≥130 mmHg) and/or high diastolic blood pressure (DBP ≥85 mmHg) or use of antihypertensive drug treatment, based on JIS criteria (16).

9. Dyslipidemia means abnormal level of lipids in the blood; consist of triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) and total cholesterol (TC).

9.1 Triglyceride (TG), based on JIS criteria (16).

- Optimal level means TG < 150 mg/dL.
- High risk level means TG ≥ 150 mg/dL.

9.2 HDL-C, based on JIS criteria (16)

- Optimal level means HDL-C ≥ 40 mg/dL. (men), ≥ 50 mg/dL. (women)
- High risk level means HDL-C < 40 mg/dL. (men), < 50 mg/dL. (women)

9.3 LDL-C, based on AACE (37).

- Optimal level means LDL-C < 130 mg/dL.
- Borderline level means LDL-C 130-159 mg/dL.
- High risk level means LDL-C 160-189 mg/dL.
- Very high risk level means LDL-C ≥ 190 mg/dL.

9.4 Total Cholesterol (TC), based on AACE (37).

- Optimal level means TC < 200 mg/dL.
- Borderline level means TC 200-239 mg/dL.
- High risk level means TC ≥ 240 mg/dL.

10. Hyperglycemia means high level of fasting plasma glucose (FPG). It is the primary symptom of diabetes. FPG level were classified according to the JIS criteria (16).

- Normal level blood glucose means FPG < 100 mg/dL.
- High level blood glucose means FPG ≥ 100 mg/dL.

11. Smoking is recognized as one of risk factor. Smokers are the subjects who smoke cigarette, tobacco and cigars. Smoking was classified as

- Non-smoker means the subjects who never smoked.
- Ex-smoker means the subjects who smoked previously.
- Current smoker means the subjects who smoked regularly.

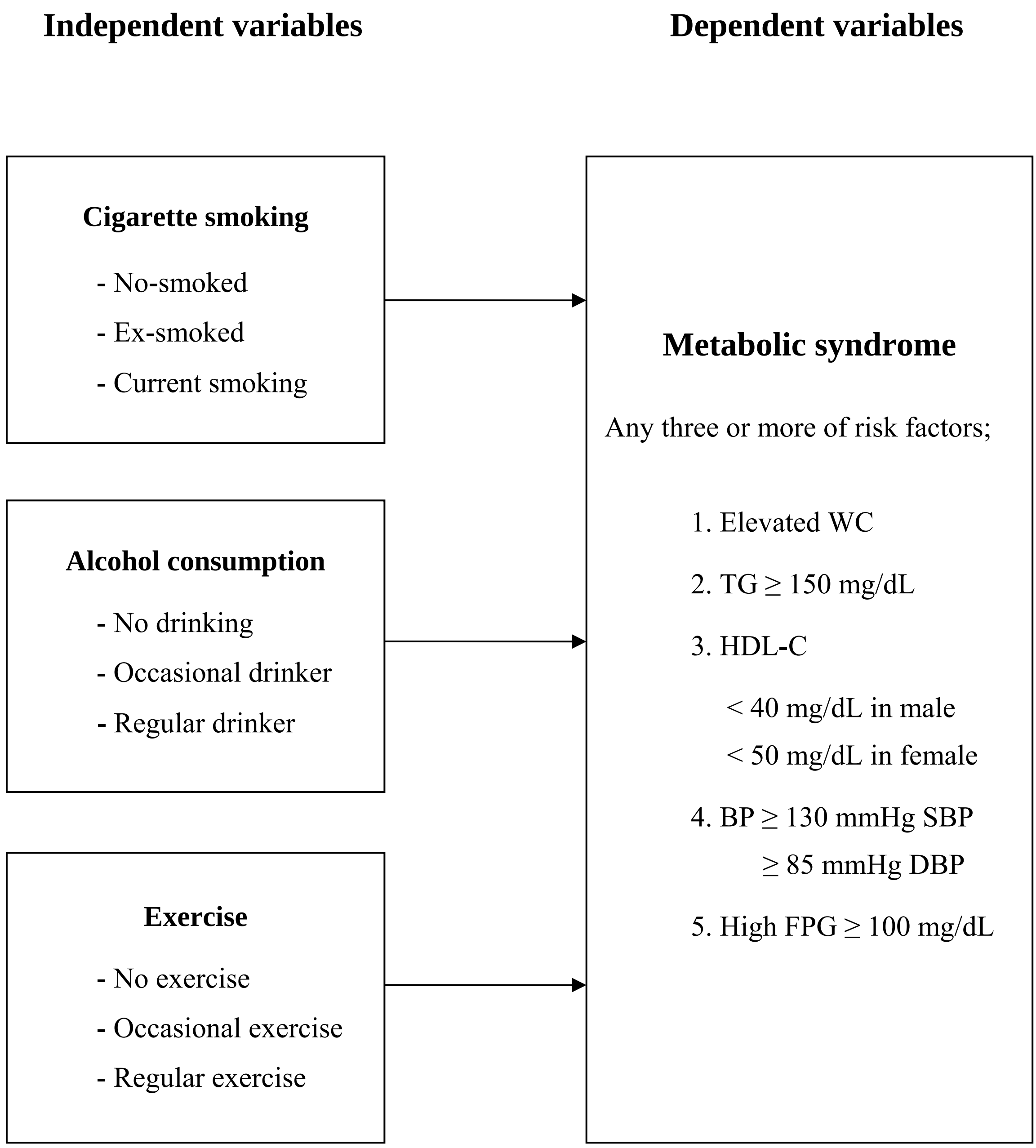
12. Alcohol consumption: Several health problems including hypertension and hyperglycemia are related to a high alcohol intake. Alcohol consumption was classified as

- Regular drinker means the subjects who drank alcohol beverage more than 2 times per week.
- Occasional drinker means the subjects who drank alcohol beverage no more than 2 times per week.
- Non-drinker means the subjects who never drank alcohol beverage.

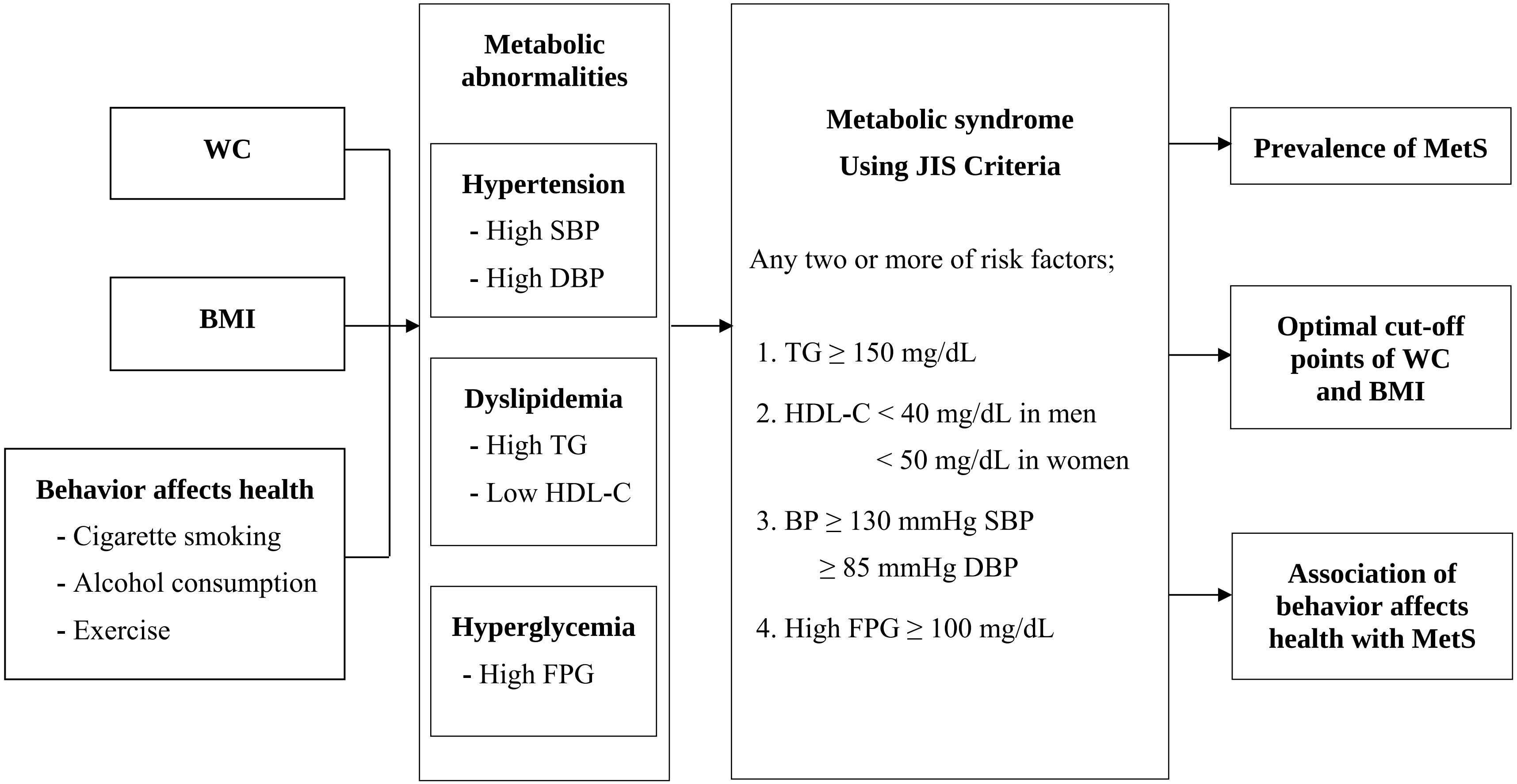
13. Exercise is a subcategory of physical activity that enhances or maintains physical fitness and overall health and wellness. It is performed for various reasons including strengthening muscles and the cardiovascular system, honing athletic skills, weight loss or maintenance, as well as for the purpose of enjoyment. This does not include the work force as usual. Exercise was classified as

- Regular exercise means the subjects who exercised at least 20 minutes at a time and 3 or more times per week.
- Occasional exercise means the subjects who exercised less than 3 times per week.
- No exercise means the subjects who hardly have any exercise activity or any movement at all.

Research conceptual framework



Research conceptual framework



CHAPTER II
LITERATURE REVIEW

Literature was reviewed as the following;

2.1 Scope of problem

2.2 Components of metabolic syndrome

2.3 Pathogenesis of metabolic syndrome

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The metabolic syndrome (MetS) can be considered as a clustering of several risk factors, including hypertension, dyslipidemia, impaired glucose tolerance, and central adiposity. The recognition of this clustering has evolved over almost 90 years. According to Panteleimon Sarafidis' and Peter Nilsson's historical account of the origins of the metabolic syndrome, during World War I, two Austrian physicians, Karl Hitzenberger and Martin Richter-Quittner, identified a link between hypertension and diabetes (38).

The metabolic syndrome is also referred to by various other names, such as the plurimetabolic syndrome (1988) (39), the deadly quartet (1989) (40), syndrome X plus (1991) (41), metabolic syndrome X (42), the metabolic syndrome (43), the insulin resistance syndrome (1991) (44), the cardiovascular disease risk factor cluster (1992) (45), and diabesity (1993) (46). However, from the mid-1990s onward, the term metabolic syndrome has been most used.

2.1 Scope of problem

The prevalence of metabolic syndrome (MetS) is increasing worldwide, which is one of the major public health problem, both in developing and developed countries. This prevalence appears to be increasing because of a parallel rise in the prevalence of obesity. The likelihood of a further increase in the MetS can be anticipated because of projections of a greater prevalence of obesity in the future (47). In the discussion to follow, the prevalence of obesity in various regions of the world will be reviewed. However, it must be noted that determining the prevalence of the MetS in different regions depends on defining criteria. Most reports have used the NCEP definitions of the MetS (48, 49). In some cases, the NCEP definition has been adjusted for WC differences in different population groups. One of the major unresolved issues for defining the syndrome is that of the appropriate WC. The primary difference between NCEP and IDF definitions is that WC cut points for Whites, Blacks, and Hispanics is higher in NCEP than in IDF. This could lead to a higher prevalence of the MetS with the IDF definition. In some reports, this is true, but in others, the differences are less than might be expected.

Numerous studies have examined the epidemiology of overweight and obesity worldwide. The current estimation reveals that about 20-30% worldwide people have some forms of this syndrome (50). Using data from NHANES III, Ford and colleagues calculated that 21.8% of US adults had MetS in the period between 1988 and 1994 (12). Between NHANES III (1988–1994) and the more recent NHANES 1999–2000, the age adjusted prevalence of MetS (using updated criteria) increased by 10.9% from 29.2% to 32.3% (51). In addition to an overall increased prevalence of MetS, several individual MetS components increased over this period: abdominal obesity (from 38.3% to 44.0% from 1988–1994 to 1999–2000), high serum TG (30.2% to 32.6%), and high BP (32.2% to 39.2%). In 2000, it was estimated that 50 million US adults had MetS. The high burden of MetS is not unique to the United States. In studies of European countries, the prevalence of MetS has ranged widely but has exceeded 50% in some studies and has routinely exceeded 20%. Similarly high rates have been noted in Asia countries. The prevalence of the MetS, as reported from several studies in European, Central Asia, Southeast Asia, China, and Japan are summarized in Table 2.1 and Table 2.2.

Table 2.1 Prevalence of Metabolic Syndrome in Europe

Country and Reference	Age Range (year)	No. of subjects	Criteria	Prevalence of MetS (%)		
				Male	Female	Total
France (52)	35–64	3359	NCEP	23.0	16.9	
France (53)	50–59	10,592	NCEP	29.7		
			IDF	38.9		
			WHO	35.5		
Germany (54)		M = 4,816	NCEP	23.5	17.6	
		F = 2,315	IDF	31.6	22.6	
Netherlands (55)	50–75	1,364	NCEP	19.0	32.0	
			WHO	26.0	26.0	
Italy (56)	45–64	1,877	NCEP	24.1	23.1	22.2
Italy (57)	40–79	888	NCEP WHO			17.8 34.1
Italy (58)	19+	2,100	NCEP	15.0	18.0	
Italy (59)	65–84	5,632	NCEP	29.9*	55.2*	
Spain (60)	35–64	2,540	NCEP	22.3	30.7	
			IDF	27.7	33.6	
Spain (61)	35-74	24,670	JIS	32.0	29.0	31.0
Portugal (62)	18–90	1,436	NCEP	19.1	27.0	23.9
Greece (63)	Adults	9,669	NCEP IDF			24.5 43.4
Greece†(64)		384	JIS	69.9	67.6	
Croatia (65)	18–88	996	NCEP			34.0
UK (66)	60–79	3,589	NCEP IDF		29.8 47.5	
			WHO		20.9	
Canada (67)	18+	1,800	NCEP	23.4	22.9	23.2
Canary Islands (68)	30+	1,193	NCEP	20.3	21.1	
			WHO	26.5	17.6	
Finland‡ (69)	Adults	5,698	NCEP	47.0	25.0	37.0
Luxembourg (70)	18-69	1,349	JIS	35.5	20.4	28.0

*In a subgroup with diabetes, 64.9% of male and 87.1% of female had NCEP MetS.

† In subgroup with hypertension ‡ In subgroup with depression and anxiety.

Table 2.2 Prevalence of Metabolic Syndrome in Asia

Country and Reference	Age Range (year)	No. of subjects	Criteria	Prevalence of MetS (%)		
				Male	Female	Total
Central Asia						
India (71)	20-70	26,001	IDF NCEP			25.8 18.3
			WHO			23.0
India (72)	20+	1,123	NCEP	22.9	39.9	31.6
India (73)	20–75	475	NCEP			41.1
Southeast Asia						
Thailand (74)	35+	404	NCEP			18.0
Thailand (75)	20–70	1,383	NCEP	15.7	11.7	12.8
Thailand (76)	Adult	3,209	JIS	26.5	13.7	16.1
Singapore(77)	Adult	3,954	NCEP	14.1	12.3	
Malaysia (78)	18+	4,341	WHO ATP III			32.1 34.3
			IDF JIS			37.1 42.5
China						
(79)	20–90	16,342	NCEP with BMI ≥25 kg/m^2	15.7	10.2	13.2
(80)	18–66	1,513	NCEP IDF WHO			9.6 7.4 13.4
(81)	25–64	18,630	NCEP (WC; M≥90 cm, F ≥80 cm)			9.5
			IDF			8.5
(82)	50–85	10,362	NCEP IDF			15.7 25.8
(83)*	30+	1,039	NCEP IDF			55.7 50.0
			WHO			70.0
(84)*	16–95	5,202	NCEP	23.9	12.8	16.8
Japan						
(85)	19–88	8,144	NCEP	19.0	7.0	
(86)	20–79	3,264	Japanese criteria	12.1	1.7	7.8
(87)	30–79	6,985	NCEP	30.2	10.3	
(88)	40+	11,941	3+ metabolic risk factors			14.9
Korea (89)	Adult	2,890	NCEP	29.0	32.9	31.3

*In subgroup with Type 2 Diabetes.

2.2 Components of metabolic syndrome

The National Cholesterol Education Program's (NCEP) Adult Treatment Panel (ATP III) reported six components of the metabolic syndrome that relate to CVD (11):

Abdominal obesity
Insulin resistance with or without glucose intolerance
Atherogenic dyslipidemia
Raised blood pressure
Proinflammatory state
Prothrombotic state

Abdominal obesity is the form of obesity most strongly associated with metabolic syndrome, such as dyslipidemia, hyperinsulinemia, insulin resistance, and glucose intolerance. It presents clinically as increased waist circumference (11).

Insulin resistance with or without glucose intolerance usually refers to the resistance to the metabolic effects of insulin, including the suppressive effect of insulin on endogenous glucose production, the stimulatory effects of insulin on peripheral (predominantly skeletal muscle) glucose uptake and glycogen synthesis, and the inhibitory effects of insulin on adipose tissue lipolysis. Insulin resistance is present in the majority of people with the metabolic syndrome. It strongly associates with other metabolic risk factor and correlates univariately with CVD risk. These associations, combined with belief in its priority, account for the term insulin resistance syndrome. Even so, mechanisms underlying the link to CVD risk factors are uncertain, hence the ATP III's classification of insulin resistance as an emerging risk factor. Patients with longstanding insulin resistance frequently manifest glucose intolerance, another emerging risk factor. When glucose intolerance evolves into diabetes-level hyperglycemia, elevated glucose constitutes a major, independent risk factor for CVD (90).

Atherogenic dyslipidemia manifests in routine lipoprotein analysis by raised triglycerides and low concentrations of HDL cholesterol. A more detailed analysis usually reveals other lipoprotein abnormalities, e.g., increased remnant lipoproteins, elevated apolipoprotein B, small LDL particles, and small HDL particles. All of these abnormalities have been implicated as being independently atherogenic (11).

Raised blood pressure is strongly associated with obesity and commonly occurs in insulin-resistant individuals. Some investigators believe that hypertension is less metabolic than other metabolic syndrome components. Certainly, hypertension is multifactorial in origin. For example, increasing arterial stiffness contributes significantly to systolic hypertension in the elderly. Even so, most conference participants favored inclusion of elevated blood pressure as one component of the metabolic syndrome (11).

Proinflammatory state, recognized clinically by elevations of C-reactive protein (CRP), is commonly present in persons with metabolic syndrome. Multiple mechanisms seemingly underlie elevations of CRP. One cause is obesity, because excess adipose tissue releases inflammatory cytokines that may elicit higher CRP levels (11).

Prothrombotic state, characterized by increased plasma plasminogen activator inhibitor (PAI)-1 and fibrinogen, also associates with the metabolic syndrome. Fibrinogen, an acute-phase reactant like CRP, rises in response to a high cytokine state. Thus, prothombotic and proinflammatory states may be metabolically interconnected (11).

2.3 Pathogenesis of metabolic syndrome

Obesity and Disorders of Adipose Tissue

Failure of weight regulation and the onset of obesity, particularly abdominal obesity, is central to the pathophysiology of the metabolic syndrome (91). The modern pandemic of obesity has been the driving force behind the increasing prevalence of the metabolic syndrome and its later progression to both type 2 diabetes and CVD (91-95). In the metabolic syndrome, visceral adipose tissue metabolism is altered, with decreased glucose uptake (due to insulin resistance), increased lipid uptake and increased storage of fat as well as increased lipolysis (also due to tissue insulin resistance), and crucially, increased release of non-esterified ("free") fatty acids (FFA) into the circulation. Hypertrophied intra-abdominal adipocytes are resistant to the antilipolytic effects of insulin (96). This leads to an increased flux of FFA from the visceral adipose tissue compartment to the liver, resulting in increased liver fat, increased hepatic glucose output and decreased overall liver function. Consistent with these abnormalities, the obesity pandemic has been associated with a dramatic and rapid increase in the prevalence of non-alcoholic hepatic steatosis, a serious chronic liver disease in its own right, with risk of progression to end stage liver disease and death (97). Insulin resistance in the liver is associated with decreased apolipoprotein B degradation and increased production of triglyceride-rich lipoproteins. In obesity, adipose tissue is infiltrated by macrophages, contributing to an increased state of chronic inflammation. Many of the cytokine products of adipose tissue are altered in character and concentration in viscerally obese subjects. Typically C-reactive protein (CRP), Interleukin (IL)-6 and tumour necrosis factor α (TNFα) are increased, while adiponectin is decreased. The overall effect of the increase in visceral adipose tissue is an alteration of FFA metabolism coupled with a proinflammatory profile, both of which are associated with insulin resistance and altered glucose homeostasis typical of pre-diabetes and progression to type 2 diabetes (98). Thus, the impact of changes in visceral adipose tissue can be described as a state of systemic lipotoxicity associated with low-grade systemic inflammation, mediated through changes in liver metabolism of both carbohydrate and fat (99).

Insulin Resistance

The metabolic syndrome since its first description has been intimately associated with insulin resistance. However, unlike previous definitions, the current definition of the syndrome does not include a specific reference to insulin resistance because difficult to measure in clinical practice and still remains a clinical research measurement. The gold standard measurement technique using the hyperinsulinaemic glucose clamp is time consuming (several hours minimum). The current definition of the metabolic syndrome comprises the most common clinical features of insulin resistance: central obesity, a characteristic classic dyslipidemia, hypertension and elevation in fasting glucose. The importance of insulin resistance as the underlying metabolic milieu is that insulin resistance is a major risk factor for the development of diabetes, and thus for the later complications of diabetes especially CVD, chronic kidney disease, retinopathy and neuropathy. As already described above, insulin resistance is the best unifying hypothesis for the pathophysiology of the metabolic syndrome. A major contributor to the development of insulin resistance is the alteration in fat metabolism, with an excess of circulating FFA originating either from adipose tissue triglyceride stores (released by hormone sensitive lipase) or from triglyceride-rich lipoproteins [by the action of lipoprotein lipase (LPL) (100, 101). Insulin plays a key role in the suppression of lipolysis by both these routes, and a very early sign of impaired insulin action is the failure of this mechanism. Increased circulating FFA further impairs the anti-lipolytic effect of insulin, exacerbating this effect. Excess FFA contributes to insulin resistance in insulin target tissues such as skeletal muscle and liver, through several cellular mechanisms (102). In addition to these effects, it has also been shown that insulin resistant subjects display abnormalities of mitochondrial oxidative phosphorylation that correlate with the accumulation of triglycerides and other related fat molecules in muscle tissue (103, 104). More recently, the field of metabolomics has begun to demonstrate a completely new profile of the metabolic “signature” of insulin resistance at a more fundamental level. Characteristic of this signature is a preponderance of branched chain amino acids (BCAA), along with the expected higher circulating concentrations of total and various species of FFA (105, 106). What is important about these new insights from metabolomics is that amino acid data have been shown to provide information on the future risk of diabetes beyond what could be known from standard risk factors (such as body mass index (BMI), diet pattern and fasting glucose). Thus, metabolomic patterns can be correlated with standard measures of insulin resistance and beta-cell function, but amino acid concentrations have been shown also to be accurately predictive of diabetes progression even among individuals with similar fasting insulin and glucose concentrations (99).

Independent Factors That Mediate Specific Components of the Metabolic Syndrome

Beyond obesity and insulin resistance, each risk factor of the metabolic syndrome is subject to its own regulation through both genetic and acquired factors. This leads to variability in expression of risk factors.

Blood Pressure

The relationship between elevated blood pressure and insulin resistance has been extensively studied. High blood pressure is a classical feature of the metabolic syndrome. It has been reported that up to one-third of hypertensive subjects have a clinical phenotype of the metabolic syndrome. A number of potential physiological mechanisms for this association have been documented (107). Insulin has vasodilatory effects in healthy subjects and also contributes to sodium retention in the kidney (108). There are important differences between white people, Africans and Asians in these mechanisms. In insulin-resistant subjects, the vasodilatory effect of insulin is lost (109), while the sodium retention is maintained, which may contribute to elevation of blood pressure. Another potential mechanism of blood pressure elevation is the effect of insulin to stimulate the sympathetic nervous system. Further possible mechanisms include oxidative stress, endothelial dysfunction and an activated renin–angiotensin system, all pro-hypertensive effects and all of which have been shown to be more common in subjects with the metabolic syndrome. However, large scale studies suggest that the overall contribution of insulin resistance per se to elevated blood pressure is modest (110). The mechanistic relationship between hypertension and the metabolic syndrome has been outlined in a recent review by Yanai and colleagues (99, 111).

Lipids

As already outlined, the metabolic syndrome is fundamentally a disorder of lipid metabolism. In clinical practice, the metabolic syndrome is associated with a “classic” dyslipidaemia phenotype of elevated triglycerides (and FFA), together with reduced high-density lipoprotein (HDL)-cholesterol and changes in the low-density lipoprotein (LDL) particle to a smaller, denser and more atherogenic variant. This classical plasma lipoprotein phenotype results from increased FFA flux to the liver, leading to increased production of apo B-containing triglyceride-rich very low-density lipoproteins (VLDL). Under conditions of normal physiology, insulin inhibits the secretion of VLDL into the circulation. In the setting of insulin resistance, this homeostasis is lost, and hypertriglyceridemia results, becoming a central component of the criteria for diagnosis of the metabolic syndrome. In the presence of hypertriglyceridemia, a decrease in the cholesterol content of HDL results from decreases in the cholesteryl ester content of the lipoprotein core, with variable increases in triglyceride making the particle small and dense (112). This alteration of the composition of the lipoprotein leads to increased clearance of HDL from the circulation. LDL is also changed in composition in the setting of insulin resistance and the metabolic syndrome. Subjects in whom triglycerides (in the fasting state) exceed 2.0 mmol/l usually have a predominance of small dense LDL circulating (113, 114). In this modified LDL particle, unesterified cholesterol, esterified cholesterol and phospholipid are depleted, while LDL triglyceride is either unchanged or increased. Small dense LDL is considered to be more atherogenic than buoyant LDL, for a number of possible reasons, including: it is more toxic to the endothelium, it has a greater ability to transit through the endothelial basement membrane, it adheres to glycosaminoglycans, it is more susceptible to oxidation, it is more selectively bound to scavenger receptors on monocyte-derived macrophages(115, 116). Taken together, the combined altered lipid phenotype, which is typical for the metabolic syndrome, constitutes an increased risk phenotype for CVD and is a key clinical characteristic of the syndrome (99).

Metabolic Flexibility

The concept of metabolic flexibility is the capacity of the organism to adapt fuel oxidation to fuel availability. For example, the inability to modify fuel oxidation in response to changes in nutrient availability has been implicated in the accumulation of intramyocellular lipid and insulin resistance in skeletal muscle (117). The epidemiology of the metabolic syndrome could be explained by the change in the dietary habits of modern populations to an energy-dense diet high in fats. Following on from these sustained (if even minor) changes in nutrient intake, an impaired capacity to up-regulate muscle lipid oxidation in the face of high lipid supply in some subjects may lead to increased muscle fat accumulation and insulin resistance. As outlined previously, the chronic accumulation of lipids as triglycerides and other molecular species including ceramides and diglycerides (lipotoxicity) can impair insulin action through a variety of mechanisms (102). Conversely, the ability to adjust and increase lipid oxidation in response to increased availability (or metabolic flexibility) reduces the formation of harmful lipid products such as ceramides and diglycerides, and thus protects against changes in insulin sensitivity. The term “metabolic flexibility” was first termed by Kelley and Mandarino as “the capacity to switch from predominantly lipid oxidation and high rates of fatty acid uptake during fasting conditions to the suppression of lipid oxidation and increased glucose uptake, oxidation, and storage under insulinstimulated conditions” (118). Consistent with this description, the switch from carbohydrate to lipid oxidation during an overnight fast or in response to high-fat diets [measurable by a reduction in respiratory quotient (RQ)] are examples of normal metabolic flexibility. An underlying component of the metabolic syndrome is the maladaptation of modern man to increased fat availability in typical western diets. Individuals who are metabolically inflexible are prone under these conditions to the accumulation of harmful lipid species in metabolically active tissues such as muscle, adipose tissue and liver, where these compounds may contribute to reduced insulin sensitivity. An important corollary to this is that lifestyle changes (reduction in dietary fat intake coupled with physical activity and weight loss) can restore or improve metabolic flexibility in skeletal muscle, thereby contributing to improved insulin action and prevention of diabetes (99).

2.4 Criteria for Clinical Diagnosis of metabolic syndrome

Several different sets of criteria have been proposed during the past decade for diagnosis of the metabolic syndrome. Their criteria are similar in many aspects, but they also reveal fundamental differences in positioning of the predominant causes of the syndrome. For example, the WHO proposed the diagnostic criteria required for the diagnosis of type 2 diabetes and the metabolic syndrome, it has given importance to insulin resistance and a prerequisite for the diagnosis (14). Organizations such as

NCEP ATP III, AHA-NHLBI and IDF have published diagnostic criteria, differing with respect to glucose and/or waist WC cutoff levels (11, 15). The IDF definition underlined the importance of central obesity considering elevated WC as a prerequisite for diagnosis. Recently, a unified definition was presented in a Joint Interim Statement (JIS) of several organizations. Central obesity was not considered essential for the diagnosis but different WC thresholds were proposed according to ethnicity (16).

World Health Organization (WHO) (14)

In 1999, the World Health Organization (WHO) criteria require presence of type 2 diabetes mellitus, insulin resistance, impaired fasting glucose (IFG) or impaired glucose tolerance (IGT), and plus any two additional risk factor of the following:

- Blood pressure: ≥140 mmHg systolic or ≥90 mmHg diastolic or on antihypertensive
- Plasma triglyceride: ≥150 mg/dL (≥1.7 mmol/L)
- Plasma HDL-C: <35 mg/dL (<0.9 mmol/L) in men or <39 mg/dL (1.0 mmol/L) in women
- Central obesity: BMI >30 and/or waist/hip ratio >0.9 in men, >0.85 in women
- Microalbuminuria: Urinary albumin excretion rate ≥20 μg/min or albumin/creatine ratio ≥30 mg/g

The National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) (11)

In 2001, the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) proposed a simple set of diagnostic criteria based on common clinical measures including waist circumference, triglycerides, HDL-C, blood pressure, and fasting glucose level. The presence of defined abnormalities in any 3 of these 5 measures constitutes a diagnosis of the metabolic syndrome.

- Waist circumference: >102 cm (>40 inches) in men, >88 cm (>35 inches) in women
- Triglycerides: ≥150 mg/dL (1.7 mmol/L)

- Low HDL cholesterol: Men <40 mg/dL (1.03 mmol/L) in men, women <50 mg/dL (1.3 mmol/L)
- Blood pressure: ≥130/85 mmHg or on antihypertensive drug
- Fasting glucose: ≥100 mg/dL (5.6 mmol/L), includes diabetes

The International Diabetes Federation (IDF) (15)

In 2005, the International Diabetes Federation (IDF) published their diagnostic version. The IDF agreed with the ATPIII that the ATPIII definition of the metabolic syndrome was simple and correctly considered that abdominal obesity was highly correlated with insulin resistance; so the laborious measurement of insulin was considered unnecessary. Consequently, the IDF considered obesity as a prerequisite and the presence of two other factors from the ATPIII criteria sufficient for the diagnosis. However, the IDF emphasized ethnic differences in the correlation between abdominal obesity and other metabolic risk factors. According to the IDF definition, for a person to be defined as having the metabolic syndrome they must have: Central obesity (defined as waist circumference* ethnicity-specific values: Europid men ≥ 94 cm and women ≥ 80 cm, South Asians men ≥90 cm and women ≥80 cm, Japanese men ≥85 cm and women ≥90 cm)

Plus any two of the following four factors:

- raised TG level: ≥ 150 mg/dL (1.7 mmol/L), or specific treatment for this lipid abnormality
- reduced HDL cholesterol: < 40 mg/dL (1.03 mmol/L*) in males and < 50 mg/dL (1.29 mmol/L*) in females, or specific treatment for this lipid abnormality
- raised blood pressure: systolic BP ≥ 130 or diastolic BP ≥ 85 mmHg, or treatment of previously diagnosed hypertension
- raised fasting plasma glucose (FPG) ≥ 100 mg/dL (5.6 mmol/L), or previously diagnosed type 2 diabetes If above 5.6 mmol/L or 100 mg/dL, OGTT is strongly recommended but is not necessary to define presence of the syndrome.

* If BMI is >30kg/m^2, central obesity can be assumed and waist circumference does not need to be measured.

A Joint Interim Statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity (16)

In 2009, an additional definition of metabolic syndrome was proposed as a joint interim statement (JIS) by several organizations in an attempt to harmonize the definition of metabolic syndrome. The available information based on ATPIII and IDF criteria suggest that metabolic syndrome is pandemic but that prevalence varies widely depending on the ethnic groups studied and criteria applied (119).

Any three of five risk factors constitutes a diagnosis of metabolic syndrome:

- Elevated waist circumference*: Population and country-specific definitions
- Elevated triglycerides: ≥150 mg/dL (1.7 mmol/L)

(drug treatment for elevated triglycerides is an alternate indicator**)

- Reduced HDL-C: <40 mg/dL (1.0 mmol/L) in males and <50 mg/dL (1.3 mmol/L) in females

(drug treatment for reduced HDL-C is an alternate indicator**)

- Elevated blood pressure: Systolic ≥130 and/or diastolic ≥85 mmHg

(antihypertensive drug treatment in a patient with a history of hypertension is an alternate indicator)

- Elevated fasting glucose***: ≥100 mg/dL

(drug treatment of elevated glucose is an alternate indicator)

* It is recommended that the IDF cut points be used for non-Europeans and either the IDF or AHA/NHLBI cut points used for people of European origin until more data are available.

** The most commonly used drugs for elevated triglycerides and reduced HDL-C are fibrates and nicotinic acid. A patient taking 1 of these drugs can be presumed to have high triglycerides and low HDL-C. High-dose ω-3 fatty acids presumes high triglycerides.

*** Most patients with type 2 diabetes mellitus will have the metabolic syndrome by the proposed criteria.

2.5 Risk factors of metabolic syndrome

The metabolic syndrome is a combination of interconnected risk factors for obesity, insulin resistance and glucose intolerance, dyslipidemia, and hypertension (120). It represents a complex disorder expressed by interrelated risk factors with unknown genetic and not well known environmental influences. Previous familial studies have shown that metabolic syndrome has an important heritable component (121-124). While the genetic aspects of metabolic syndrome are quite important, several studies have revealed that lifestyle modifications and/or medication use reduce the prevalence of metabolic syndrome (125, 126).

Risk factors most closely associated with metabolic syndrome include:

Age

The prevalence of metabolic syndrome increases with age, affecting less than 10 percent of people in their 20s and 40 percent of people in their 60s. However, prevalence declined in 80s of life. The large increase in the prevalence of the metabolic syndrome in adults older than 50 years of age can possibly be explained by a lifetime accumulation of risk factors. It has been postulated that accumulation of excess caloric intake, dyslipidemia, a sedentary lifestyle, hormonal changes in women, changes in the secretory functions of pancreatic β cells, and obesity can be environmental triggers for the genetic expression of the metabolic syndrome (11, 127).

Gender

The metabolic syndrome displays significant gender-associated differences in many parameters. These differences have been attributed to variations in fat distribution patterns and endocrine profiles, with the sex hormones being of major importance. Although metabolic syndrome generally has been more prevalent in men, there has been a steep increase in cases in women during the last decade due to a parallel increase in obesity among women (127).

Ethnicity

The prevalence of the metabolic syndrome varies between ethnic groups. African-Americans and Mexican Americans are more prone to metabolic syndrome. African-American women are about 60 percent more likely than African-American men to have the syndrome (127).

Obesity

Obesity is defined as a BMI of 25 or greater. Lowering BMI and losing just 5 percent to 7 percent of body weight can lower risk of developing type 2 diabetes significantly. Another measurement of obesity is the presence of abdominal fat. Generally a waist circumference of 90 cm. or greater for men and 80 cm. or greater for women is an indicator of risk for metabolic syndrome (11).

Family history of diabetes

Women who have experienced diabetes during pregnancy (gestational diabetes) or people who have a family member with type 2 diabetes are at greater risk for metabolic syndrome (11).

Other diseases

A diagnosis of high blood pressure, cardiovascular disease or polycystic ovary syndrome, a similar type of metabolic problem that affects a woman’s hormones and reproductive system. It also increases risk of metabolic syndrome (11).

Stress

An increased activity in this ‘stress system’ produces abnormal levels of mainly cortisol, norepinephrine and epinephrine, affect to insulin resistance and visceral obesity. A dose-response association exists between exposure to work stress and the metabolic syndrome. Employees with chronic work stress have more than double the odds of the syndrome than those without work stress (128).

Health behavior (Lifestyle)

Lifestyle means a pattern of individual practices and personal behavior choices that are related to elevated or reduced health risk, example alcohol coffee tea consumption, food intake, smoking, exercise, sleeping time (129).

2.6 Related studies in association of health behavior risk factors and metabolic syndrome

Smoking

Smoking use has been associated with an increased risk of developing metabolic syndrome. It acts at multiple levels in the etiopathogenesis of metabolic syndrome. The various pathways of etiopathogenesis of metabolic syndrome include increased adiposity, insulin resistance, leptin resistance, low-grade systemic inflammation, endothelial dysfunction, and autonomic dysfunction. Smoking has been associated with an increased waist circumference and increased waist–hip ratio (WHR), increased triglycerides, and reduced HDL cholesterol. WHR is positively associated with the number of pack-years of smoking, and there is a dose–response relation between WHR and the number of cigarettes smoked. The association among smoking amount and high triglyceride level and low HDL level has also been reported to be dose-dependent. It has been associated with endothelial dysfunction and a hypercoagulable state (130).

A national nutrition examination survey in USA reported an increase in risk of development of metabolic syndrome among women (OR, 1.8; 95% CI: 1.2–2.6) and men (OR, 1.5; 95% CI: 1.1–2.2) who were current smokers compared with those who never smoked (49). Exposure to tobacco smoke is associated with a 4-fold increased risk of development of metabolic syndrome among adolescents who are either overweight or at risk for overweight (131). Saarni et al. investigated the association between adolescent smoking and overweight or abdominal obesity in adulthood. They reported that smoking is a risk factor for abdominal obesity in both sexes and for overweight in women (132). Ching-Chu Chen et al. reported the adjusted odds ratios of current smoking amount showed a statistically significant dose-dependent association with metabolic syndrome, high triglyceride level, and low HDL-C level. Current smokers who smoke ≥20 pack-years have a significantly increased risk of developing metabolic syndrome (OR, 1.82; 95% CI: 1.26–2.65), high triglyceride level, and low HDL-C level. The higher risk of development of metabolic syndrome, high triglyceride level, and low HDL-C level was insignificant in former smokers (133). In Kawada's 1-year follow-up study, current smokers had a higher risk of metabolic syndrome than nonsmokers, independent of age, body mass index (BMI), insulin resistance, uric acid, and other lifestyle factors. In contrast, ex-smokers did not have a significantly greater risk of metabolic syndrome than nonsmokers. The most effective way for smokers to reduce their risk of metabolic syndrome and cardiovascular disease is to stop smoking (134). However, Nakanishi et al. highlighted that smoking cessation is also associated with a 1.3-fold risk of metabolic syndrome as a result of subsequent body weight gain (135). As for mechanism of weight gain after smoking cessation may include increased energy intake, decreased resting metabolic rate, decreased physical activity and increased lipoprotein lipase activity (136-138).

Alcohol Consumption

The association of alcohol consumption with the metabolic syndrome is complex and controversial, as both protective and detrimental effects have been reported. For example, the analysis of the data from the Third National Health and Nutrition Examination Survey, USA, found the prevalence of the metabolic syndrome to be higher in women (22.7%) compared to men (21.9%), as also that the current drinkers had a lower adjusted prevalence of metabolic syndrome than subjects not currently drinking [OR 0.57 (95% CI 0.45- 0.72)]. It reported that mild to moderate consumption of alcohol was associated with a lower prevalence of the metabolic syndrome, with a favorable influence on lipids, waist circumference, and fasting insulin in a comparison with current nondrinkers (139). From community-based study found the risk of developing metabolic syndrome is greater among current drinkers than among never drinkers. In addition, the increased risk of developing metabolic syndrome and many of its individual components, namely, high triglyceride and fasting glucose levels, was dose dependent. The type of alcoholic beverages consumed had different effects on the development of the individual components of metabolic syndrome; however, it was not related to the development of metabolic syndrome. And the consumption of a moderate amount of alcoholic beverages has been shown to have protective cardiovascular effects may outweigh the negative effects of consuming alcohol (140). Findings of a meta-analysis of prospective studies show an approximate J-shaped association between alcohol drinking and risk of metabolic syndrome. Heavy alcohol consumption was associated with an increased relative risk of metabolic syndrome while very light alcohol consumption seemed to be associated with a reduced relative risk of metabolic syndrome (141).

In contrast, the 1998 Korean National Health and Nutrition Examination Survey covering 7962 adults (3597 men, 4365 women), the prevalence of the metabolic syndrome has been reported as 20.8 percent in men and 26.9 percent in women. The adjusted odds ratio for the metabolic syndrome in the group with daily consumption of 1-14.9 g alcohol was 0.71 (95% CI: 0.53, 0.95) in men and 0.80 (95% CI: 0.65, 0.98) in women. Alcohol consumption had a significant inverse relation with the odds ratio for low HDL cholesterol in all alcohol subgroups. Heavy alcohol consumption (≥30 g/day) was associated with significantly higher odds ratios for high blood pressure and high TG in men and high FPG and high TG in women. It suggested that there were adverse effects of alcohol consumption on all components of the metabolic syndrome except low high-density lipoprotein cholesterol (HDL-C) (142). These discrepant results may be partly attributed to different consumption patterns in different study populations, even among those whose average daily alcohol consumption is similar (143).

Physical activity

Physical activity is defined as any bodily movement produced by skeletal muscles that result in energy expenditure. Total daily physical activity, which is the sum of all occupational, household, and leisure-time activities. Exercise is a subcategory of physical activity that is planned, structured, repetitive, and purposeful in the sense that the improvement or maintenance of one or more components of physical fitness is the objective (144). Forms of exercise include aerobic activity and resistance exercise, aerobic exercise consists of rhythmic, repeated, and continuous movements of the same large muscle for at least 10 minutes at a time and resistance exercise consists of activities that use muscular strength to move a weight or move against a resistive load. When performed regularly and at moderate to high intensity, resistance exercise increases muscular fitness and muscular endurance. By increasing muscle mass and endurance, resistance exercise training can produce more rapid changes in functional status and body composition than aerobic training. Resistance exercise also improves insulin sensitivity to a similar extent as aerobic exercise (145, 146).

Lack of physical exercise and excess caloric intake lead to the development of obesity and metabolic syndrome, which is associated with an increase in plasma free fatty acid (FFA) availability. The structural imbalance between FFA uptake, lipid storage, and fatty acid oxidation results in progressive intramuscular accumulation of both lipids and fatty acid metabolites, which could cause abnormal insulin signaling, leading to skeletal muscle insulin resistance. Furthermore, it has been suggested that excess lipid deposits are prone to enhanced lipid peroxidation, which could also lead to the development and/or progression of skeletal muscle insulin resistance by increasing tumor necrosis factor-α and/or by inducing mitochondrial damage. This results in an imbalance between plasma FFA uptake and fatty acid oxidation. In contrast, greater intramuscular lipid storage capacity in lean and physically active individuals could represent an adaptive response to physical training, allowing a greater contribution of the intramuscular lipid levels as a substrate source during exercise (146).

From Kerry J. Stewart et al. investigated the associations between older adults often have metabolic syndrome and exercise. They reported that 6 months of exercise training improved aerobic and strength fitness, reductions in general and abdominal fatness and increases in lean mass were more strongly related to improvements in risk factors associated with metabolic syndrome (147). Furthermore, the data from the Third National Health and Nutrition Examination Survey, USA found The OR was significantly increased for physical inactivity in men. Physical inactivity also imparts an increased risk for CHD and type 2 diabetes mellitus and exacerbates the severity of other risk factors. Increased physical activity promotes weight loss and maintenance in obese individuals and favorably modifies obesity-associated risk factors, including promoting visceral adipose tissue loss, improving insulin sensitivity, increasing HDL cholesterol levels, and lowering triglyceride levels (49).

2.7 The cut-off point and receiver operating characteristics analysis (148-150)

The cut-off point is the point (on a continuous scale) that the researcher decides is best in differentiating diseased and nondiseased persons in the population being screened. The cut-off point might be a standard, or an arbitrary one. For example, in the identification of hypertensive persons, it was arguable at what level of blood pressure a person could be called hypertensive and need treatment. And this could be different in different populations. Similarly, the cut-off point which should be applied to classifying other disease for further investigation and treatment. Consequently, the different levels of cut-off chosen would give different levels of sensitivity and specificity. If the cut-off point is too low, there would be a large number of normal or nondiseased persons who are incorrectly labeled as diseased. If the cut-off point is too high, there would be a large proportion of diseased persons who are mislabeled and then did not seek proper medical care.

Receiver Operating Characteristic (ROC) curves are a useful way to interpret sensitivity and specificity levels and to determine related cut-off points. ROC curves are a generalization of the set of potential combinations of sensitivity and specificity possible for predictors. ROC curve analyses not only provide information about cut-off points, but also provide a natural common scale for comparing different predictors that are measured in different units, whereas the odds ratio in logistic regression analysis must be interpreted according to a unit increase in the value of the predictor, which can make comparison between predictors difficult.

In a ROC curve the true positive rate (sensitivity) is plotted in function of the false positive rate (1-specificity) for different cut-off points. Each point on the ROC curve represents a sensitivity/specificity pair corresponding to a particular decision threshold. And this graph is best in displaying the optimal cut-off point for a particular screening test, as well as in comparing the efficiency of two screening tests. At a low cut-off point, sensitivity is high, with the expense of low specificity (as reflected in high (1-specificity)) . At a high cut-off point, sensitivity is low but the specificity becomes higher. The total area under ROC curve (AUC) is a measure of the performance of the screening test since it reflects the test performance at all possible cut-off levels. The area lies in the interval [0.5, 1] and the larger area, the better performance. Assume that a high value from the method indicates that diagnosis is positive and a low value indicates that diagnosis is negative. AUC values closer to 1 indicate the screening measure reliably distinguishes among the disease with non-disease subject.

Method to find the optimal threshold

Optimal threshold is the point that gives maximum correct classification. Three criteria are used to find optimal threshold point from ROC curve. First two methods give equal weight to sensitivity and specificity and impose no ethical, cost, and no prevalence constraints. The third criterion considers cost which mainly includes financial cost for correct and false diagnosis, cost of discomfort to person caused by treatment, and cost of further investigation when needed. This method is rarely used in medical literature because it is difficult to implement. These three criteria are known as points on curve closest to the (0, 1), Youden index, and minimize cost criterion, respectively.

Advantages of the ROC curve

ROC curve has following advantages compared with single value of sensitivity and specificity at a particular cut-off.

1. The ROC curve displays all possible cut-off points, and one can read the optimal cut-off for correctly identifying diseased or non-diseased subjects.

2. The ROC curve is independent of prevalence of disease since it is based on sensitivity and specificity which are known to be independent of prevalence of disease.

3. Two or more diagnostic tests can be visually compared simultaneously in one figure.

4. Sometimes sensitivity is more important than specificity or vice versa, ROC curve helps in finding the required value of sensitivity at fixed value of specificity.

5. Useful summary of measures can be obtained for determining the validity of diagnostic test such as AUC and partial area under the curve.

Assessment of a screening or diagnostic test

Sensitivity and Specificity

Two popular indicators of inherent statistical validity of a medical test are the probabilities of detecting correct diagnosis by test among the true diseased subjects and true non-diseased subjects.

Sensitivity is the probability of a positive test when the person is sick, or the proportion with a positive test among all people with the disease (people with the disease who have a positive test divided by all the people with the disease). Therefore, the sensitivity is calculated on the people who have the disease.

Specificity is the probability of a healthy individual testing negative, or the proportion of people with a negative test among the healthy persons. Therefore, the specificity is calculated in healthy people.

Predictive value

The whole purpose of a diagnostic test is to use its results to make a diagnosis, so we need to know the probability that the test result will give the correct diagnosis. The probability of having the disease, given the results of a test, is called the predictive value of the test.

Positive predictive value (PPV) is the probability that persons who are screened as positive would have the disease under investigation.

Negative predictive value (NPV) is the probability that persons who are screened as negative would not have the disease under investigation.

The predictive value of a test is determined by the test's sensitivity and specificity and by the prevalence of the condition for which the test is used. The more sensitive a test, the less likely an individual with a negative test will have the disease and thus the greater the negative predictive value. The more specific the test, the less likely an individual with a positive test will be free from disease and the greater the positive predictive value. Both PPV and NPV vary with changing prevalence of disease. It will therefore be wrong for clinicians to directly apply published predictive values of a test to their own populations, when the prevalence of disease in their population is different from the prevalence of disease in the population in which the published study was carried out.

Table 2.3 A 2 x 2 probability test

Screening test	**Disease**		**Total**
	Present	**Absent**	
Positive	a true positive	b false positive	a+b total test positive
Negative	c false negative	d true negative	c+d total test negative
Total	a+c total disease	b+d total non-disease	a+b+c+d grand total

Sensitivity (Se) = a/(a + c)

Specificity (Sp) = d/(b + d)

Accuracy = (a + d)/(a + b + c + d)

Pretest probability = prevalence of disease = (a + c)/(a + b + c + d)

Positive predictive value (PPV) = a/(a + b)

$$= \frac{\text{Se x Prevalence}}{\text{Se x Prevalence} + (1 - \text{Sp}) \text{ x } (1 - \text{Prevalence})}$$

Negative predictive value (NPV) = d/(c + d)

$$= \frac{\text{Sp x } (1 - \text{Prevalence})}{\text{Sp x } (1 - \text{Prevalence}) + (1 - \text{Se}) \text{ x } (\text{Prevalence})}$$

Youden's index

Youden's index is one of the oldest measures for diagnostic accuracy. It is also a global measure of a test performance, used for the evaluation of overall discriminative power of a diagnostic procedure and for comparison of this test with other tests. Youden's index is calculated by deducting 1 from the sum of test's sensitivity and specificity expressed not as percentage but as a part of a whole number: (sensitivity + specificity) – 1. For a test with poor diagnostic accuracy, Youden's index equals 0, and in a perfect test Youden's index equals 1. Youden's index is not sensitive for differences in the sensitivity and specificity of the test, which is its main disadvantage. Namely, a test with sensitivity 0,9 and specificity 0,4 has the same Youden's index (0,3) as a test with sensitivity 0,6 and specificity 0,7. It is absolutely clear that those tests are not of comparable diagnostic accuracy. If one is to assess the discriminative power of a test solely based on Youden's index it could be mistakenly concluded that these two tests are equally effective. Youden's index is not affected by the disease prevalence, but it is affected by the spectrum of the disease, as are also sensitivity and specificity.

Considerations for screening test with high sensitivity

We need the cut-off point which gives high sensitivity when:

1. The disease could be fatal or has bad prognosis if it is not identified in the early stage. The identification if the early stage of a disease would enable physicians to give effective treatment, with low cost and less complication. The examples are breast cancer and cervical cancer, in particular.

2. The disease could be easily transmitted to the population at large, if the diseased person is not correctly identified and treated as soon as possible. The examples are active tuberculosis and sexually transmitted diseases, etc.

3. The false positive has no strong physical and mental side effect.

4. The diagnosis and treatment facilities are readily available and accessible to those who are screened positive. The follow-up or confirmative process should also be cheap, easy to perform, acceptable, nontraumatic and not harmful to recipients.

5. The prevalence of disease is low and the health officer needs to identify all cases of the disease in the population.

Considerations for screening test with high specificity

We need the cut-off point which gives high specificity when:

1. The false positive would give strong unwanted effect for the screened population, either physically, emotionally or socially. In some circumstances, a false positive gives an unwanted effect on the family as well. A good example is HIV infection, which is wrongly associated as the drug users, homosexuals and prostitutes, and is correctly known as a life-long, incurable, fatal disease. If a person is screened positive, despite the fact that she/he is disease-free, that person and the family might be discriminated against, become unemployed, or even the children might receive discrimination by friends in school. The person and the family might lose all of their opportunity and some might commit suicide as the result of such social discrimination.

2. The disease is not easily transmitted to a population at large, even though there are some cases hidden. It has slow progress and might be able to be detected later without serious consequences.

3. The diagnosis and treatment is not readily available for all suspected cases. The diagnosis and treatment is expensive, traumatic, or even harmful to a person. The examples are cardiac catheterization in locating the blockage in the coronary artery, or using a microscopic examination of cells drawn from amniotic fluid in detecting chromosome abnormality in fetus. These processes are quite invasive and could have a bad side effect; therefore, the use is always limited to highly suspected diseases, not in ambiguous situations.

2.8 Cut-off points of WC and BMI in different ethnic groups

Waist circumference (WC)

Abdominal fat deposition is generally considered to be a key component of obesity. WC is a convenient way of measuring abdominal fat deposition; it is easy, cost effective, informative, and well suited for assessment in nearly all clinical settings. It is strongly correlated with, and used as a surrogate marker for, abdominal fat mass and has been associated with all-cause mortality. Increased WC is closely associated with alterations in carbohydrate and lipid metabolism as well as inflammation and atherosclerosis. WC has a stronger correlation with risk factors and intra-abdominal fat content than either BMI and is more reliable than WHR. In some populations, WC is a better indicator of relative disease risk than is BMI; examples include Asian-Americans or persons of Asian descent living elsewhere. WC also assumes greater value for estimating risk for obesity-related disease at older ages (20). For metabolic syndrome diagnosis, central obesity has been claimed to be the most important element, and is commonly assessed by gender and ethnicity-specific WC cut-off values. In 2005, IDF recommended using European cut-off values (94 cm for men and 80 cm for women) for Middle-Eastern populations and Asian population (90 cm for men and 80 cm for women) until more specific data is available (15). Table 2.4 showed current recommended WC thresholds for abdominal obesity by organization.

Table 2.4 Current recommended WC thresholds for abdominal obesity by organization

Population	Organization	Recommended WC threshold for Abdominal Obesity	
		Men	**Women**
Europid	IDF	≥94 cm	≥80 cm
Caucasian	WHO	>94 cm (increased risk) >102 cm (still higher risk)	>80 cm (increased risk) >88 cm (still higher risk)
United States	AHA/NHLBI (ATP III)	≥102 cm	≥88 cm
Canada	Health Canada	≥102 cm	≥88 cm
European	ESC	≥102 cm	≥88 cm
Asian (including Japanese)	IDF	≥90 cm	≥80 cm
Asian	WHO	≥90 cm	≥80 cm
Japanese	Japanese Obesity Society	≥85 cm	≥90 cm
China	Cooperative Task Force	≥85 cm	≥80 cm
Middle East, Mediterranean	IDF	≥94 cm	≥80 cm
Sub-Saharan African	IDF	≥94 cm	≥80 cm
Ethnic Central and South American	IDF	≥90 cm	≥80 cm

Source: Harmonizing the Metabolic Syndrome, 2009 (16)

Body Mass Index (BMI)

The primary classification of obesity is based on the measurement of BMI, calculated as weight in kilograms divided by height in meters squared (kg/m^2). Even if BMI does not separate fat mass from muscle mass, but nevertheless, is highly correlated with both adipose and muscle mass. This classification is designed to relate BMI to risk of disease. It should be noted that the relation between BMI and disease risk varies among individuals and among different populations. Therefore, the classification must be viewed as a broad generalization. Individuals who are very muscular may have a BMI placing them in an overweight category when they are not overly fat. Also, very short persons (under 5 feet) may have high BMIs that may not reflect overweight or fatness. In addition, susceptibility to risk factors at a given weight varies among individuals. Some individuals may have multiple risk factors with mild obesity, whereas others may have fewer risk factors with more severe obesity. It should also be noted that the risk levels shown for each increment in risk are relative risks; that is, relative to risk at normal weight. They should not be equated with absolute risk which is determined by a summation of risk factors (20).

In 1997, the WHO provided further authoritative refinements to the overweight terminology and BMI cutoffs, not only suggested BMI to classify normal weight and overweight but also added criteria for underweight, pre-obese, and class 1, 2, and 3 obese categories that are age independent and the same for both sexes (25). However, as these WHO criteria are based on data from Western population, it may underestimate obesity in Asians. Several epidemiologic studies in Asians population reported that at a given BMI, both the body fat content and the amount of visceral adipose tissue (central obesity) are apparently higher in Asian people compared with Western populations (151). Thus, the WHO expert consultation has proposed the standards for adult obesity in Asian population as BMI $\geq$ 23.0 kg/m^2 for overweight and BMI $\geq$ 25.0 kg/m^2 for obesity. (Table 2.5)

Table 2.5 Classification of underweight, overweight and obesity in adult Europeans and Asians according to BMI

Classification	BMI (kg/m^2)		Risk of co-morbidities
	Europeans	Asians	
Underweight	<18.5	<18.5	Low (but increased risk of other clinical problem)
Normal	18.5-24.9	18.5-22.9	Average
Overweight	≥ 25.0	≥ 23.0	
Pre-obese	25.0-29.9	23.0-24.9	Increase
Obese I	30.0-34.9	25.0-29.9	Moderate
Obese II	35.0-39.9	≥ 30.0	Severe
Obese III	≥40.0		Very Severe

Source: Modified from WHO, 2004 (25)

Cut-off points in different Asian groups

People of different racial and ethnic backgrounds have a distinct pattern of central fat deposition. Thus, cut-off points chosen vary considerably between ethnic groups. Most studies in Asian groups had suggested WC and BMI cut-off points lower than European groups cut-off points. The appropriate WC and BMI cut-off points for Asian groups are summarized in Table 2.6.

Table 2.6 Cut-off points of WC and BMI in various Asian populations

Ethnic groups	No. of subjects	WC (cm) Male	WC (cm) Female	BMI (kg/m^2)	Risk factors	References
Indian	2,050	90	80	25.0	BP, FBG, Lipid profile	Misra et al. (28)
Iranian	3,277	87	82		BP, FBG, Lipid profile	Sharifi et al. (152)
Chinese	111,411	85	80	24.0	BP, FBG, Lipid profile	Bei-Fan et al. (27)
Chinese	75,788	86.5	82.1	24.0	BP, FBG, Lipid profile	Wang et al. (153)
Chinese	16,711	87	80		BP, FBG, Lipid profile	Wang et al. (154)
Chinese	14,919	83.3	76.1	M=25.0 F=23.0	BP, FBG, Lipid profile	Ko GTC, Tang JSF (155)
Japanese	2,113	85	80		BP, FPG, Lipid profile	Nishimura et al. (156)
Japanese	361	82	73	M=24.0 F=23.0	BP, FPG, Lipid profile	Shiwaku et al. (157)
Korean	6,561	85	80		BP, FPG, Lipid profile	Lee et al. (158)
Korean	31,076	83	76		BP, FPG, Lipid profile	Kim, H. K., et al. (159)
Malaysian	32,703	81	80		BP, FPG, Lipid profile	Cheong et al. (160)
Thai	5,646	87.75	79.75	M=23.81 F=23.65	BP, FPG, Lipid profile	Worachartcheewan et al. (29)
Thai	5,305	82-85	82-85	23.0-25.0	BP, FPG, Lipid profile	Aekplakorn et al. (30)
Thai	998	84	80	23.0	BP, FPG, Lipid profile	Narksawat et al. (31)

CHAPTER III
MATERIALS AND METHODS

Research Design

This research was a cross-sectional study aimed to determine the optimal cut-off points of waist circumference and body mass index for identification of metabolic syndrome in Royal Thai Army personnel in Bangkok and suburban.

Study Population and Sample

The population of this study was Royal Thai Army personnel male and female in Bangkok and suburban who received annual health checkup at Armed Forces Research Institute of Medical Sciences (AFRIMS), Army Medical Department, Bangkok during 1st October, 2013 to 30th September, 2014. The following criteria were used for selecting the subjects of the study.

Inclusion Criteria

Male and female personnel aged 35-60 year old who received annual health checkup at Armed Forces Research Institute of Medical Sciences (AFRIMS).

Exclusion Criteria

1. The subjects who had not completed the annual health checkup data including personal general health information (age, body weight, body height, waist circumference and blood pressure) and laboratory data (glucose and lipid profile).
2. The female subjects who had pregnancy.
3. The subjects who informed in health survey form that they had the symptoms of abdominal mass or ascites; cirrhosis, kidney disease, abdominal aortic aneurysms and stomach cancer.

4. The subjects who informed in health survey form that they had any complication conditions or diseases that induce increase or decrease weight change; renal disease, liver disease, thyroid disease, cancer, post orthopedic operation with plate and screw.

Sample size

The sample size was calculated by the following formula: (161)

$$n = \frac{Z_{\alpha/2}^{2} PQ}{d^{2}}$$

n = The sample size

$Z_{\alpha/2}$ = The standard estimate under normal curve α=0.05, $Z_{\alpha/2}$ = 1.96

P = The sensitivity and specificity by ROC curve analysis of the WC cut-off points to identify metabolic syndrome in Thai male and female. This data were collected from annual medical checkup, Faculty of Medical Technology, Mahidol University 2008 (29).

Male: P_{sen} = 0.66, P_{spec} = 0.67

Female: P_{sen} = 0.73, P_{spec} = 0.69

Q = 1-P, Male: Q_{sen} = 1 - 0.66 = 0.34

Q_{spec} = 1 - 0.67 = 0.33

Female: Q_{sen} = 1 - 0.73 = 0.27

Q_{spec} = 1 - 0.69 = 0.31

d = Error between sample population

= 5% of P, Male: d_{sen} = 0.033, d_{spec} = 0.0335

Female: d_{sen} = 0.0365, d_{spec} = 0.0345

Calculation of formula:

Male: $$n_{sen} = \frac{(1.96)^2(0.66)(0.34)}{(0.033)^2} = 791.6$$

$$n_{\text{spec}} = \frac{(1.96)^2(0.67)(0.33)}{(0.0335)^2} = 756.8$$

Female:

$$n_{\text{sen}} = \frac{(1.96)^2(0.73)(0.27)}{(0.0365)^2} = 568.3$$

$$n_{\text{spec}} = \frac{(1.96)^2(0.69)(0.31)}{(0.0345)^2} = 690.3$$

Therefore, a minimum of 2,809 samples (1,549 males and 1,260 females) were necessary in this study.

Random Sampling

The sample of this study was random by simple random sampling technique using Microsoft excel.

Data collection

Using existing data during 1st October, 2013 to 30th September, 2014 from AFRIMS (Appendix). The following data were used for analysis.

1. General information: age, sex, rank and unit.
2. Health behavior information: smoking, alcohol consumption and exercise habits.
3. Physical examination: body weight, body height, body mass index, waist circumference and blood pressure.
4. Laboratory analysis: plasma glucose and serum total cholesterol, triglyceride, HDL-C and calculated LDL-C.

Note: The subjects who had triglyceride level more than 400 mg/dL will not be included in the analysis of LDL-C.

Type of Variables

1. Independent variables

- Waist circumference
- Body mass index
- Smoking
- Alcohol consumption
- Exercise

2. Dependent variables

- Metabolic syndrome: define as presence two or more of the following factors 1.Triglyceride 2.HDL-C 3.Blood pressure 4.Plasma glucose

Note: Waist circumference is not included in the definition of metabolic syndrome since it will be treated as an independent variable.

3. Controlled variables

- Sex
- Age

Statistical Analysis

The data were analyzed by the Statistical Package for the Social Sciences (SPSS) program version 18.0 for Windows

1. Descriptive statistic including frequency, percentage, mean, and standard deviation were used to describe a general characteristics, health characteristics and metabolic syndrome component of subjects.

2. Receiver operating characteristic curve (ROC) analysis

- Identify the cut-off points of WC with sensitivity and specificity for metabolic syndrome.
- Identify the cut-off points of BMI with sensitivity and specificity for metabolic syndrome.
- Identify the cut-off points of combine WC and BMI with sensitivity and specificity for metabolic syndrome.

The ROC curve was plotted using present at least two other components of the metabolic syndrome, excluding WC, as defined by the JIS criteria. The distance on the ROC curve for each WC and BMI value was calculated by plotting the true-positive rate (sensitivity) against the false positive rate (1− specificity). The sensitivity at least 80 percent was used for determining the appropriate WC and BMI cut-off points. The area under the curve (AUC) with 95% confidence interval (CI) was used as indicators of the diagnostic performance of WC and BMI for identifying metabolic syndrome.

3. Logistic regression analysis was used to determine the association between smoking, alcohol consumption, exercise and metabolic syndrome by crude and adjusted odds ratio (OR) with 95% confidence interval and p-values of less than 0.05 were considered statistically significant.

Ethical Issue

The research was conducted after the final approval was granted by the Human Research Protection Unit, Faculty of Medicine Siriraj Hospital, Mahidol University (COA no.Si164/2015) and Institutional Review Board, Royal Thai Army Medical Department (Q016h/58). The researcher was well aware of the research ethics. Therefore, the data collected from Armed Forces Research Institute of Medical Sciences would be considered confidential and used only for research purposes. All information obtained in this study cannot be referred back to the individual.

CHAPTER IV
RESULTS

This research aimed to determine the optimal cut-off points of waist circumference and body mass index for identification of metabolic syndrome in Royal Thai Army personnel in Bangkok and suburban. The results of the study were presented in four parts as follows:

Part 4.1 Description of characteristics of subjects

4.1.1 General characteristics

4.1.2 Health behavior characteristics

Part 4.2 Health status of the subjects

4.2.1 Anthropometric data

4.2.2 Blood pressure

4.2.3 Lipid profile

4.2.4 Plasma glucose

Part 4.3 The optimal cut-off points of waist circumference and body mass index for identification of metabolic syndrome

Part 4.4 Prevalence of metabolic syndrome

Part 4.5 Prevalence of high LDL cholesterol

Part 4.6 Odds ratio of association between smoking, alcohol consumption, exercise and metabolic syndrome

Part 4.1 Description of characteristics of subjects

4.1.1 General characteristics

General characteristics of 2,809 subjects (1,549 males and 1,260 females) in terms of age and rank were shown in Table 4.1. The age average of the subjects was 48.3 ± 6.9 years (48.1 ± 6.9 years for male and 48.4 ± 6.9 years for female). Most of male subjects were non-commissioned officer (50.5%) and female subjects were civilian employees (68.7%).

Table 4.1 The number and percentage distribution of general characteristics of subjects stratified by gender (n=2,809)

Characteristics	Male		Female		Total	
	n	**%**	**n**	**%**	**n**	**%**
Age (years)						
35-40	234	15.1	184	14.6	418	14.9
41-45	317	20.4	238	18.9	555	19.8
46-50	319	20.6	291	23.1	610	21.7
51-55	447	28.9	320	25.4	767	27.3
56-60	232	15.0	227	18.0	459	16.3
Mean ± SD	48.1 ± 6.9		48.4 ± 6.9		48.3 ± 6.9	
Min - Max	35 - 60		35 - 60		35 - 60	
Rank						
Commissioned officer	508	32.8	254	20.2	762	27.1
Non-commissioned officer	783	50.5	140	11.1	923	32.9
Civilian employees	258	16.7	866	68.7	1124	40.0
Total	1549	100.0	1260	100.0	2809	100.0

4.1.2 Health behavior characteristics

The data of health behavior characteristics of the subjects in terms of smoking habits, alcohol consumption and exercise habits were shown in Table 4.2.

More than 70 percent of subjects were no-smoked and only 16.7 percent who was currently smoking. In terms of alcohol consumption, it was most found in male. Among the male subjects who drinking alcohol, 54.1 percent occasional drinking and 12.5 percent regularly drinking. For exercise habits, more than 80 percent of the subjects exercised. Among the subjects who exercised, 63.1 percent exercised less than 3 times per week and 22.4 percent exercised at least 20 minutes at a time and 3 or more times per week.

Table 4.2 The number and percentage of smoking habits, alcohol consumption and exercise habits of subjects stratified by gender (n=2,809)

Characteristics	**Male**		**Female**		**Total**	
	n	**%**	**n**	**%**	**n**	**%**
Smoking habits						
No-smoked	786	50.7	1237	98.2	2023	72.0
Ex-smoked	301	19.4	15	1.2	316	11.2
Current smoking	462	29.8	8	0.6	470	16.7
Alcohol consumption						
No drinking	517	33.4	1051	83.4	1568	55.8
Occasional drinker	838	54.1	199	15.8	1037	36.9
Regular drinker	194	12.5	10	0.8	204	7.3
Exercise habits						
No exercise	102	6.6	305	24.2	407	14.5
Occasional exercise	988	63.8	784	62.2	1772	63.1
Regular exercise	459	29.6	171	13.6	630	22.4

Part 4.2 Health status of the subjects

4.2.1 Anthropometric data

Body weight and body height

Body weight and body height categories of the subjects were shown in Table 4.3. The results found that the average body weight was 71.7 ± 10.9 kg for male subjects (range from 44 kg to 135 kg) and 60.7 ± 10.8 kg for female subjects (range from 40 kg to 103 kg). In term of body height, the average body height was 169.1 ± 5.5 for male subjects. The minimum body height was 150 cm, while 190 cm was the maximum recorded body height. Most of them had a body height of 160 cm to 169 cm. For female, the average body height was 157.6 ± 5.4 cm and body height ranged from 143 cm for the minimum and 181 cm for the maximum. Most of them had a body height of 150 cm to 159 cm.

Table 4.3 The number and percentage of weight and height of subjects stratified by gender (n=2,809)

Variables	Male		Female		Total	
	n	%	n	%	n	%
Body weight (kg)						
40 - 49.9	11	0.7	163	12.9	174	6.2
50 - 59.9	160	10.4	476	37.8	636	22.7
60 - 69.9	524	33.8	378	30	902	32.1
70 - 79.9	493	31.8	159	12.6	652	23.2
80 - 89.9	267	17.2	62	4.9	329	11.7
90 - 99.9	73	4.7	20	1.6	93	3.3
≥ 100	21	1.4	2	0.2	23	0.8
Mean ± SD	71.7 ± 10.9		60.7 ± 10.8		66.8 ± 12.2	
Min-Max	44 - 135		40 - 103		40 - 135	

Table 4.3 The number and percentage of weight and height of subjects stratified by gender (n=2,809) (cont.)

Variables	Male		Female		Total	
	n	%	n	n	%	n
Body height (cm)						
< 150	0	0	22	1.7	22	0.8
150 - 159	28	1.8	777	61.7	805	28.6
160 - 169	811	52.4	434	34.4	1245	44.3
170 - 179	639	41.2	26	2.1	665	23.7
≥ 180	71	4.6	1	0.1	72	2.6
Mean ± SD	169.1 ± 5.5		157.6 ± 5.4		163.9 ± 7.9	
Min-Max	150 - 190		143 - 181		143 - 190	

Waist circumference

The results of waist circumference at the umbilicus level (WC-U) were shown in Table 4.4. In Asia-Pacific classification criteria, abdominal obesity was defined as WC values ≥ 90 cm and ≥ 80 cm for male and female respectively. The results was classified by Asia-Pacific criteria found 56.5 percent of the subjects who had WC values in normal group and 43.5 percent had WC values in abdominal obesity group. The majority of abdominal obesity was female (51.3%). The average WC was 87.2 ± 8.9 cm for male subjects. The minimum WC was 60 cm and 137 cm was the maximum WC. For female, the average WC was 80.2 ± 10.3 cm and WC ranged from 55 cm for the minimum and 118 cm for the maximum.

Table 4.4 The number and percentage of WC of subjects classified by Asia-Pacific criteria stratified by gender (n=2,809)

WC	Male		Female		Total	
	n	%	n	%	n	%
Asia-Pacific criteria						
Normal	973	62.8	613	48.7	1586	56.5
Abdominal obesity*	576	37.2	647	51.3	1223	43.5
Mean ± SD	87.2 ± 8.9		80.2 ± 10.3		84.0 ± 10.2	
Min - Max	60 - 137		55 - 118		55 - 137	

Note: *Waist circumference ≥ 90 cm for male and ≥ 80 cm for female.

Body mass index

An average of body mass index of the subjects was 24.8 ± 3.8 kg/m^2 (BMI 25.0 ± 3.5 kg/m^2 for male and 24.4 ± 4.1 kg/m^2 for female). The BMI categories of the subjects were classified by Asia-Pacific criteria (Table 4.5). The results found the most of the subjects were overweight group with BMI ≥ 23 kg/m^2 and the proportion of overweight in male was higher than in female. Among the subjects who had overweight, 25.1 percent were pre-obese (BMI 23.0 - 24.9 kg/m^2), 31.9 percent were obese level I (BMI 25.0 - 29.9 kg/m^2) and 9.3 percent were obese level II (BMI ≥30.0 kg/m^2).

Table 4.5 The number and percentage of BMI of subjects classified by Asia-Pacific criteria stratified by gender (n=2,809)

BMI	Male		Female		Total	
	n	%	n	%	n	%
Asia-Pacific criteria						
Underweight (<18.5)	24	1.5	34	2.7	58	2.1
Normal (18.5-22.9)	400	25.8	488	38.7	888	31.6
Overweight (≥ 23.0)	1125	72.7	738	58.6	1863	66.3
Pre-obese (23.0-24.9)	421	27.2	283	22.5	704	25.1
Obese I (25.0-29.9)	567	36.6	329	26.1	896	31.9
Obese II (≥ 30.0)	137	8.9	126	10.0	263	9.3
Mean ± SD	25.0 ± 3.5		24.4 ± 4.1		24.8 ± 3.8	
Min-Max	13.7 - 43.0		16.2 - 39.7		13.7 - 43.0	

4.2.2 Blood pressure

Systolic blood pressure

The systolic blood pressure of the subjects was classified by the Joint Interim Statement criteria (Table 4.6). The results found that 50.6 percent of the subjects had high SBP levels (≥130 mmHg) and 49.4 percent in normal levels (<130 mmHg). The proportion of high SBP levels in male was higher than in female. The average of SBP of the subjects was 130.2 ± 15.3 mmHg. The minimum SBP was 87 mmHg, while 204 mmHg was the maximum recorded SBP.

Diastolic blood pressure

The diastolic blood pressure of the subjects was classified by the Joint Interim Statement criteria (Table 4.6). The results found that more than 60 percent of the subjects had DBP in normal levels (<85 mmHg), while 30.8 percent high DBP (≥85 mmHg). The average of DBP of the subjects was 79.9 ± 10.7 mmHg and DBP ranged from 48 mmHg for the minimum and 126 mmHg for the maximum.

Table 4.6 The number and percentage of blood pressure of subjects classified by the Joint Interim Statement criteria stratified by gender (n=2,809)

Blood pressure	**Male**		**Female**		**Total**	
	n	**%**	**n**	**%**	**n**	**%**
SBP (mmHg)						
Normal	683	44.1	704	55.9	1387	49.4
High SBP (≥130 mmHg)	866	55.9	556	44.1	1422	50.6
Mean ± SD	132.2 ± 14.5		127.7 ± 15.9		130.2 ± 15.3	
Min - Max	94 - 204		87 - 201		87 - 204	
DBP (mmHg)						
Normal	983	63.5	962	76.3	1945	69.2
High DBP (≥85 mmHg)	566	36.5	298	23.7	864	30.8
Mean ± SD	81.8 ± 10.4		77.5 ± 10.7		79.9 ± 10.7	
Min - Max	48 - 126		50 - 115		48 - 126	

4.2.3 Lipid profile

Triglyceride (TG)

The subjects had average level of triglyceride at 143.7 ± 96.5 mg/dL with a minimum and maximum of 23 mg/dL and 1490 mg/dL respectively. When TG level of the subjects was classified by the Joint Interim Statement criteria, the results found that 65.9 percent of the subjects had TG values in optimal levels (<150 mg/dL) and 34.1 percent TG values in high risk levels (≥150 mg/dL). In addition, the percentage of male with TG in high risk levels was higher than those of female (43.6% and 22.5%) (Table 4.7).

High-density lipoprotein cholesterol (HDL-C)

The male and female subjects had average level of high-density lipoprotein cholesterol at 51.8 ± 14.5 mg/dL and 65.1 ± 17.3 mg/dL respectively. A minimum of HDL-C was 11 mg/dL in male and 23 mg/dL in female. The HDL-C of the subjects was classified by the Joint Interim Statement criteria, the results found that most of the subjects had optimal HDL-C levels and only 18.7 percent had a high risk HDL-C levels (Table 4.7).

Low-density lipoprotein cholesterol (LDL-C)

The average level of low-density lipoprotein cholesterol was 139.5 ± 41.5 mg/dL in male (range from 10 to 329 mg/dL) and 135.9 ± 39.0 mg/dL in female (range from 39 to 332 mg/dL). The LDL-C of the subjects was classified by AACE criteria, the results found that 42.2 percent of the subjects had LDL-C in optimal levels (<130 mg/dL), 28.5 percent LDL-C in borderline levels (130-159 mg/dL), 17.5 percent LDL-C in high risk levels (160-189 mg/dL) and 9.6 percent LDL-C in very high risk levels (≥ 190 mg/dL). In addition, the percentage of male with LDL-C in high risk and very high risk levels were higher than those of female (Table 4.7).

Total cholesterol (TC)

The subjects had average level of total cholesterol at 223.5 ± 43.8 mg/dL with a minimum and maximum of 66 mg/dL and 434 mg/dL respectively. The TC of the subjects was classified by AACE criteria, the results found that 29.2 percent of the subjects had TC in optimal levels (< 200 mg/dL), 37.4 percent TC in borderline levels (200-239 mg/dL) and 33.4 percent TC in high risk levels (≥ 240 mg/dL) (Table 4.7).

Table 4.7 The number and percentage of lipid profile of subjects stratified by gender (n=2,809)

Lipid profile	Male		Female		Total	
	n	%	n	%	n	%
Triglyceride (mg/dL)						
Optimal level (<150 mg/dL)	874	56.4	976	77.5	1850	65.9
High risk level (≥150 mg/dL)	675	43.6	284	22.5	959	34.1
Mean ± SD	165.1 ± 112.5		117.3 ± 62.8		143.7 ± 96.5	
Min - Max	23 - 1490		29 - 533		23 - 1490	
HDL-C (mg/dL)						
Optimal level (M; ≥ 40 mg/dL, F; ≥ 50 mg/dL)	1263	81.5	1022	81.1	2285	81.3
High risk level (M; < 40 mg/dL, F; < 50 mg/dL)	286	18.5	238	18.9	524	18.7
Mean ± SD	51.8 ± 14.5		65.1 ± 17.3		57.8 ± 17.1	
Min - Max	11 - 149		23 - 152		11 - 152	
LDL-C (mg/dL)*						
Optimal level (< 130 mg/dL)	604	39.0	581	46.1	1185	42.2
Borderline level (130-159 mg/dL)	437	28.2	363	28.8	800	28.5
High risk level (160-189 mg/dL)	297	19.2	196	15.6	493	17.5
Very high risk level (≥ 190 mg/dL)	159	10.3	111	8.8	270	9.6
Mean ± SD	139.5 ± 41.5		135.9 ± 39.0		137.8 ± 40.4	
Min - Max	10 - 329		39 - 332		10 - 332	
Total cholesterol (mg/dL)						
Optimal level (< 200 mg/dL)	458	29.6	362	28.7	820	29.2
Borderline level (200-239 mg/dL)	573	37.0	478	37.9	1051	37.4
High risk level (≥ 240 mg/dL)	518	33.4	420	33.4	938	33.4
Mean ± SD	222.9 ± 45.2		224.2 ± 42.0		223.5 ± 43.8	
Min - Max	66 - 415		95 - 434		66 - 434	

*Male = 1,497, Female = 1,251 and Total = 2,748.

4.2.4 Plasma glucose

The fasting plasma glucose of the subjects was classified by the Joint Interim Statement criteria (Table 4.8). The results found that more than 70 percent of the subjects had fasting plasma glucose in normal levels (<100 mg/dL), while 29.3 percent fasting plasma glucose in high levels (≥100 mg/dL). The average of fasting plasma glucose of the subjects was 99.5 ± 29.6 mg/dL. Minimum and maximum of fasting plasma glucose were 46 – 494 mg/dL.

Table 4.8 The number and percentage of fasting plasma glucose of subjects classified by the Joint Interim Statement criteria stratified by gender (n=2,809)

Plasma glucose	**Male**		**Female**		**Total**	
	n	**%**	**n**	**%**	**n**	**%**
Normal level (<100 mg/dL)	1005	64.9	982	77.9	1987	70.7
High level (≥100 mg/dL)	544	35.1	278	22.1	822	29.3
Mean ± SD	102.9 ± 34.5		95.4 ± 21.6		99.5 ± 29.6	
Min - Max	46 - 494		60 - 287		46 - 494	

Part 4.3 The optimal cut-off points of waist circumference and body mass index for identification of metabolic syndrome

4.3.1 The ROC curve for WC to predict the presence of two or more risk factors of metabolic syndrome, as defined by the JIS criteria

The Table 4.9 shows the result of ROC analysis to identify subjects with two or more risk factors of metabolic syndrome using the JIS criteria. In male, the optimal cut-off points of WC with the highest Youden's index was 85.5 cm (Youden's index = 0.267, sensitivity 70.0%, specificity 56.8%, positive predictive value (PPV) 46.6%, negative predictive value (NPV) 77.8% and accuracy 61.4%), while 82.5 cm was the optimal cut-off points of WC yielding at least 80% sensitivity (Youden's index = 0.252, sensitivity 81.9%, specificity 43.2%, PPV 43.7%, NPV 81.6% and accuracy 56.8%). These two cut-off points of WC were not significantly different in the Youden's index. For female, the optimal cut-off of WC yielding the highest Youden's index was 81.5 cm (Youden's index = 0.398, sensitivity 69.2%, specificity 70.6%, PPV

43.9%, NPV 87.3% and accuracy 70.2%), while 77.5 cm was the optimal cut-off points of WC yielding at least 80% sensitivity (Youden's index = 0.344, sensitivity 81.3%, specificity 53.1%, PPV 36.6%, NPV 89.5% and accuracy 60.4%). The ROC curve was plotted to compare with the cut off points of WC yielding the highest Youden's index and yielding at least 80% sensitivity (Figure 4.1).

Table 4.9 The WC cut-off points, sensitivity, specificity, positive predictive value, negative predictive value, accuracy and Youden's index to predict metabolic syndrome stratified by gender

	WC cut-off points (cm)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)	Youden's index
Male	81.50	85.7	39.0	43.0	83.5	55.3	0.246
	82.50	81.9	43.2	43.7	81.6	56.8	0.252
	83.50	77.7	47.1	44.2	79.7	57.8	0.248
	84.50	73.6	52.2	45.3	78.6	59.7	0.258
	85.50	70.0	56.8	46.6	77.8	61.4	0.267
	86.50	65.0	61.4	47.6	76.5	62.7	0.264
	87.50	58.4	67.1	48.8	74.9	64.0	0.254
	88.50	53.0	71.6	50.1	73.9	65.1	0.246
	89.50	49.4	75.9	52.5	73.6	66.6	0.253
	90.50	43.3	79.7	53.4	72.3	66.9	0.229

Table 4.9 The WC cut-off points, sensitivity, specificity, positive predictive value, negative predictive value, accuracy and Youden's index to predict metabolic syndrome stratified by gender (cont.)

	WC cut-off points (cm)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)	Youden's index
Female	75.50	86.8	45.1	34.5	91.1	55.9	0.319
	76.50	84.2	48.5	35.3	90.2	57.8	0.327
	77.50	81.3	53.1	36.6	89.5	60.4	0.344
	78.50	78.5	57.0	37.8	88.8	62.6	0.355
	79.50	75.9	59.5	38.4	88.1	63.8	0.354
	80.50	71.8	65.8	41.1	87.5	67.3	0.376
	81.50	69.2	70.6	43.9	87.3	70.2	0.398
	82.50	64.2	74.5	45.6	86.2	71.8	0.387
	83.50	60.1	76.7	46.2	85.2	72.4	0.368
	84.50	56.7	79.9	48.4	84.7	73.8	0.366

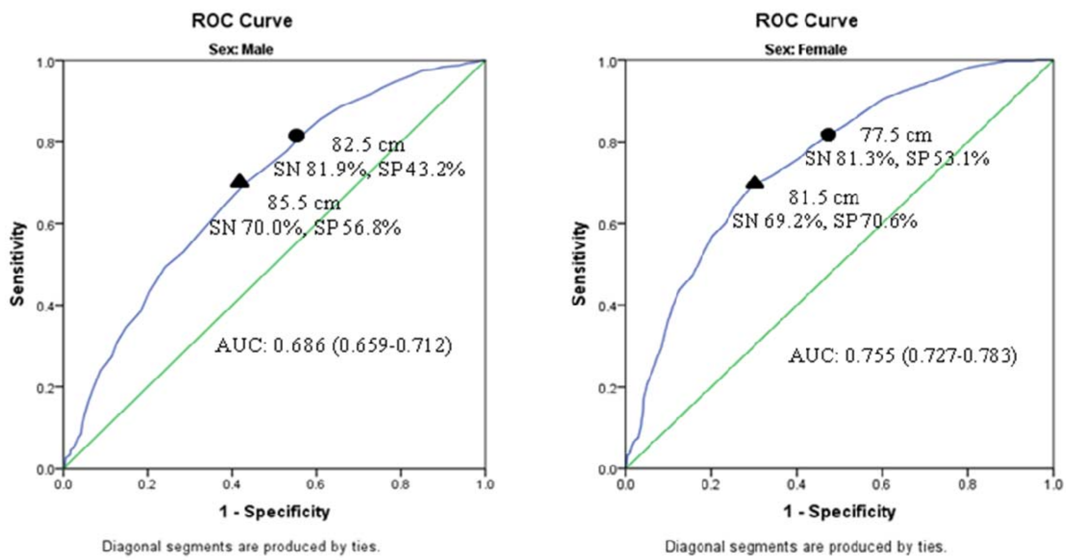

Figure 4.1 Receiver operating characteristic (ROC) curves of waist circumference (WC) to detect the metabolic syndrome in male (left) and female (right), based on having at least two of four the JIS criteria. ▲ Cut-off WC yielding the highest Youden's index, ● Cut-off WC yielding at least 80% sensitivity.

4.3.2 The ROC curve for WC to predict the presence of three or more risk factors of metabolic syndrome, as defined by the JIS criteria

The Table 4.10 shows the result of ROC analysis to identify subjects with three or more risk factors of metabolic syndrome using the JIS criteria. In male, the optimal cut-off points of WC with the highest Youden's index was 89.5 cm (Youden's index = 0.24, sensitivity 56.1%, specificity 67.9%, positive predictive value (PPV) 48.5%, negative predictive value (NPV) 74.2% and accuracy 63.8%), while 83.5 cm was the optimal cut-off points of WC yielding at least 80% sensitivity (Youden's index = 0.193, sensitivity 81.0%, specificity 38.3%, PPV 41.4%, NPV 78.9% and accuracy 53.3%). For female, the optimal cut-off of WC yielding the highest Youden's index was 82.5 cm (Youden's index = 0.439, sensitivity 75.6%, specificity 68.3%, PPV 44.3%, NPV 89.4% and accuracy 70.2%), while 80.5 cm was the optimal cut-off points of WC yielding at least 80% sensitivity (Youden's index = 0.407, sensitivity 81.1%, specificity 59.6%, PPV 40.1%, NPV 90.4% and accuracy 65.0%). The ROC curve was plotted to compare with the cut off points of WC yielding the highest Youden's index and yielding at least 80% sensitivity (Figure 4.2).

Table 4.10 The WC cut-off points, sensitivity, specificity, positive predictive value, negative predictive value, accuracy and Youden's index to predict metabolic syndrome stratified by gender

	WC cut-off points (cm)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)	Youden's index
Male	82.50	85.6	34.4	41.3	81.6	52.3	0.200
	83.50	81.0	38.3	41.4	78.9	53.3	0.193
	84.50	77.6	43.3	42.4	78.2	55.3	0.209
	85.50	74.2	47.5	43.2	77.4	56.9	0.217
	86.50	69.6	52.4	44.1	76.2	58.4	0.220
	87.50	63.2	58.5	45.0	74.7	60.1	0.217
	88.50	59.8	63.9	47.1	74.7	62.4	0.237
	89.50	56.1	67.9	48.5	74.2	63.8	0.240
	90.50	48.8	72.2	48.6	72.4	64.0	0.210

Table 4.10 The WC cut-off points, sensitivity, specificity, positive predictive value, negative predictive value, accuracy and Youden's index to predict metabolic syndrome stratified by gender (cont.)

	WC cut-off points (cm)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)	Youden's index
Female	77.50	88.4	47.2	35.8	92.4	57.5	0.356
	78.50	86.6	51.0	37.1	91.9	59.9	0.376
	79.50	86.0	53.8	38.3	92.0	61.9	0.398
	80.50	81.1	59.6	40.1	90.4	65.0	0.407
	81.50	78.7	64.0	42.1	90.0	67.6	0.426
	82.50	75.6	68.3	44.3	89.4	70.2	0.439
	83.50	70.1	70.7	44.4	87.7	70.6	0.408
	84.50	67.7	74.1	46.5	87.3	72.5	0.418
	85.50	62.2	76.6	46.9	85.9	73.0	0.387
	86.50	55.5	79.1	47.0	84.2	73.2	0.346

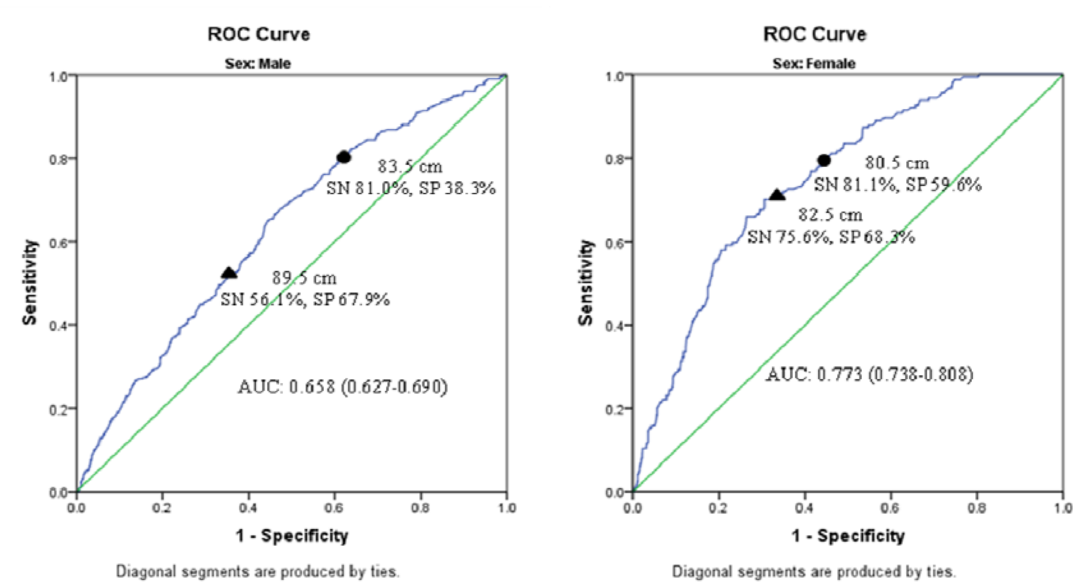

Figure 4.2 Receiver operating characteristic (ROC) curves of waist circumference (WC) to detect the metabolic syndrome in male (left) and female (right), based on having at least three of four the JIS criteria. ▲ Cut-off WC yielding the highest Youden's index, ● Cut-off WC yielding at least 80% sensitivity.

Table 4.11 shows the areas under the curve (AUC) and the proposed cut-off points of WC as defined metabolic syndrome using JIS criteria including high blood pressure, high triglyceride level, low HDL-C level, hyperglycemia, at least one of risk factors and clusters of two and three or more risk factors of metabolic syndrome. The selected cut-off WC yielding at least 80% sensitivity found WC cut-off points range was used for predicting the presence of multiple risk factors in male was 80.5-83.5 cm and in female was 73.5-80.5 cm. In male, the AUC for the presence of one or more risk factors was highest for WC (0.700), while female, the highest AUC was the presence of three or more risk factors (0.773). The AUC value range of WC in both male (AUC 0.609-0.700) and female (AUC 0.680-0.773) was acceptable.

Table 4.11 Areas under the curve (AUC) of waist circumference

		WC cut-off points[c] (cm)	Sensitivity (%)	Specificity (%)	AUC (95% CI)
Male	High blood pressure[a]	80.50	83.2	31.4	0.622 (0.594-0.651)
	Triglyceride ≥ 150 mg/dL	82.50	80.3	38.3	0.614 (0.587-0.642)
	HDL-C < 40 mg/dL	82.50	80.8	32.7	0.609 (0.574-0.644)
	Hyperglycemia[b]	82.50	83.1	37.4	0.664 (0.637-0.692)
	≥ 1 of the above	80.50	82.3	43.2	0.700 (0.667-0.734)
	≥ 2 of the above	82.50	81.9	43.2	0.686 (0.659-0.712)
	≥ 3 of the above	83.50	81.0	38.3	0.658 (0.627-0.690)
Female	High blood pressure[a]	74.50	80.0	40.7	0.680 (0.650-0.709)
	Triglyceride ≥ 150 mg/dL	76.50	81.0	44.2	0.698 (0.665-0.731)
	HDL-C < 50 mg/dL	75.50	84.0	39.8	0.686 (0.650-0.722)
	Hyperglycemia[b]	77.50	81.7	49.4	0.730 (0.698-0.763)
	≥ 1 of the above	73.50	82.4	42.3	0.731 (0.704-0.759)
	≥ 2 of the above	77.50	81.3	53.1	0.755 (0.727-0.783)
	≥ 3 of the above	80.50	81.1	59.6	0.773 (0.738-0.808)

[a] SBP ≥130 mmHg and/or DBP ≥85 mmHg, or use of antihypertensive drug treatment.

[b] FPG ≥ 100 mg/dL. [c] Selected cut-off WC yielding at least 80% sensitivity.

4.3.3 The ROC curve for BMI to predict the presence of two or more and three or more risk factors of metabolic syndrome, as defined by the JIS criteria

The Table 4.12 showed the results of ROC analysis to identify subjects with two or more and three or more risk factors of metabolic syndrome using the JIS criteria. For the presence of two or more risk factors, the optimal cut-off points of BMI to detect the metabolic syndrome with the highest Youden's index was 24.76 kg/m^2 (Youden's index = 0.283, sensitivity 60.5%, specificity 67.7%, positive predictive value (PPV) 44.6%, negative predictive value (NPV) 80.0% and accuracy 65.6%), while 23.14 kg/m^2 was the optimal cut-off points of BMI yielding at least 80% sensitivity (Youden's index = 0.268, sensitivity 80.0%, specificity 47.1%, PPV 39.2%, NPV 84.4% and accuracy 56.9%). For the presence of three or more risk factors, the optimal cut-off of BMI yielding the highest Youden's index was 24.60 kg/m^2 (Youden's index = 0.273, sensitivity 68.6%, specificity 58.7%, PPV 41.6%, NPV 81.3% and accuracy 61.7%), while 23.60 kg/m^2 was the optimal cut-off points of BMI yielding at least 80% sensitivity (Youden's index = 0.251, sensitivity 80.0%, specificity 45.1%, PPV 38.4%, NPV 84.0% and accuracy 55.6%). The ROC curve was plotted to compare with the cut off points of BMI yielding the highest Youden's index and yielding at least 80% sensitivity (Figure 4.3).

Table 4.12 The BMI cut-off points, sensitivity, specificity, positive predictive value, negative predictive value, accuracy and Youden's index to predict metabolic syndrome by the presence risk factors

	BMI cut-off points (kg/m^2)	**Sensitivity (%)**	**Specificity (%)**	**PPV (%)**	**NPV (%)**	**Accuracy (%)**	**Youden's index**
≥ 2 Risk factor	23.14	80.0	47.1	39.2	84.4	56.9	0.268
	23.51	76.7	51.2	40.2	83.7	58.8	0.279
	23.70	74.4	53.5	40.7	83.0	59.8	0.279
	24.00	69.5	57.4	41.1	81.5	61.0	0.269
	24.10	68.0	59.0	41.5	81.1	61.7	0.270
	24.35	64.9	62.6	42.6	80.6	63.3	0.275
	24.50	63.0	64.5	43.2	80.3	64.0	0.275

Table 4.12 The BMI cut-off points, sensitivity, specificity, positive predictive value, negative predictive value, accuracy and Youden's index to predict metabolic syndrome by the presence risk factors (cont.)

	BMI cut-off points (kg/m^2)	**Sensitivity (%)**	**Specificity (%)**	**PPV (%)**	**NPV (%)**	**Accuracy (%)**	**Youden's index**
≥ 2 Risk factor	24.55	62.7	65.0	43.5	80.3	64.3	0.277
	24.60	62.2	65.8	43.8	80.3	64.7	0.280
	24.76	60.5	67.7	44.6	80.0	65.6	0.283
	24.80	59.8	68.3	44.7	79.9	65.8	0.281
	24.85	58.6	68.8	44.6	79.5	65.8	0.274
	24.90	58.1	69.3	44.8	79.4	65.9	0.274
	24.95	57.6	69.6	44.8	79.3	66.0	0.272
	25.01	56.9	70.6	45.3	79.3	66.5	0.275
≥ 3 Risk factor	23.60	80.0	45.1	38.4	84.0	55.6	0.251
	23.70	79.2	46.1	38.6	83.8	56.0	0.253
	23.81	77.8	47.2	38.7	83.2	56.3	0.249
	23.91	75.5	49.7	39.2	82.6	57.5	0.252
	24.00	74.5	50.3	39.1	82.2	57.6	0.248
	24.10	73.7	52.0	39.7	82.2	58.5	0.257
	24.21	72.4	53.2	39.9	81.8	59.0	0.256
	24.31	71.0	55.2	40.4	81.6	59.9	0.262
	24.41	70.2	56.1	40.6	81.4	60.3	0.263
	24.50	69.4	57.5	41.2	81.4	61.1	0.269
	24.60	68.6	58.7	41.6	81.3	61.7	0.273
	24.71	67.1	60.0	41.9	81.0	62.2	0.272
	24.80	66.1	61.1	42.2	80.8	62.6	0.273
	24.90	63.9	62.3	42.0	80.1	62.8	0.261
	25.01	62.7	63.5	42.4	79.9	63.3	0.262

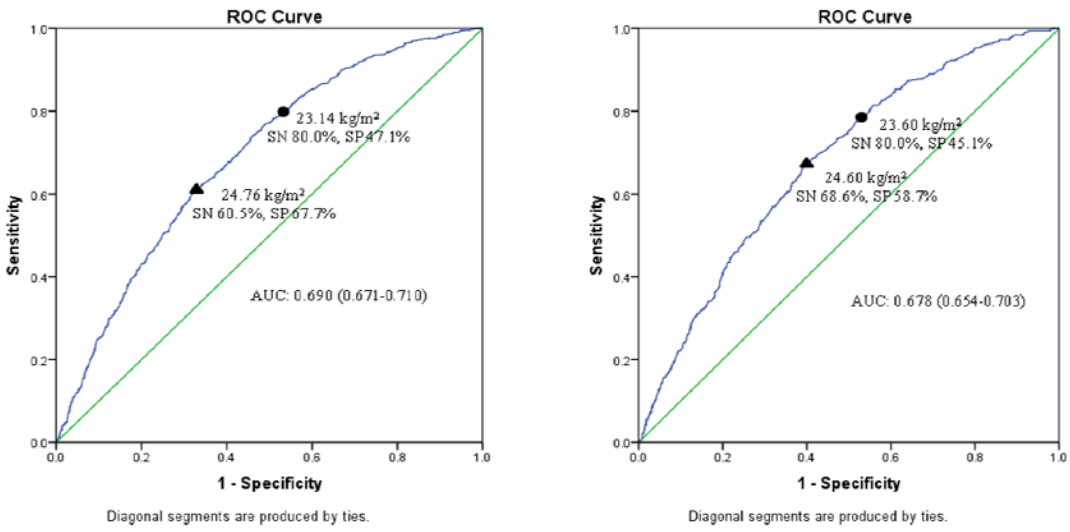

Figure 4.3 Receiver operating characteristic (ROC) curves of body mass index (BMI) to detect the metabolic syndrome, based on having at least two of four (left) and three of four (right) the JIS criteria. ▲ Cut-off BMI yielding the highest Youden's index, ● Cut-off BMI yielding at least 80% sensitivity.

4.3.4 The cut-off points of combine WC and BMI with sensitivity and specificity for prediction of metabolic syndrome

Using the optimal cut-off points of WC and BMI yielding at least 80% sensitivity for predict the metabolic syndrome by combined test. The optimal cut-off points of WC was 82.5 cm in male and 77.5 cm in female and the optimal cut-off points of BMI was 23.14 kg/m^2 in both male and female.

The Table 4.13 showed the results of combining both the optimal cut-off points of WC and BMI by parallel and series testings. For parallel testing, the sensitivity increased from 81.9% (using only WC), 80.0% (using only BMI) to 95.0% for male and 81.3% (using only WC), 80.0% (using only BMI) to 96.2% for female, while the specificity decreased from 43.2% (using only WC), 47.1% (using only BMI) to 30.0% for male and 53.1% (using only WC), 47.1% (using only BMI) to 43.3% for female. For series testing, the sensitivity decreased from 81.9% (using only WC), 80.0% (using only BMI) to 66.0% for male and 81.3% (using only WC), 80.0% (using only BMI) to 65.0% for female. On the other hand, the specificity improved from 43.2% (using only WC), 47.1% (using only BMI) to 70.0% for male and 53.1% (using only WC), 47.1% (using only BMI) to 75.0% for female.

Table 4.13 The sensitivity, specificity, positive predictive value, negative predictive value and accuracy to predict metabolic syndrome by combine test

	Combine test	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
All	Parallel	95.4	36.4	39.6	94.8	54.3
	Series	66.0	75.0	53.6	83.5	72.3
Male	Parallel	95.0	30.0	37.2	93.2	49.8
	Series	66.0	70.0	49.0	82.5	68.8
Female	Parallel	96.2	43.3	42.6	96.3	59.4
	Series	65.0	75.0	53.2	83.1	72.0

Part 4.4 Prevalence of metabolic syndrome

The prevalence of metabolic syndrome as defined by different criteria was shown in Table 4.14. The overall prevalence of MetS using the JIS criteria, the proposed WC and BMI cut-off, the proposed BMI cut-off, the combined parallel test and the combined series test were 30.4, 36.9, 36.6, 38.7 and 34.8%, respectively. Regarding gender, the prevalence of MetS in male is higher as compared to female by all criteria. The highest prevalence is 47.3% in male and 28.2% in female according to the combined parallel test criteria. With regard to age, the prevalence of MetS increased with the increasing age. Among male, the prevalence of MetS peaked in the oldest age group (56-60 years) according to JIS criteria, while the proposed criteria in the studied population had the highest age prevalence of MetS in 46-55 years. Among female, the prevalence of MetS peaked in the oldest age group (56-60 years) according to all criteria.

Table 4.14 The prevalence of metabolic syndrome by gender and age according JIS criteria, the proposed criteria in the studied population and combined test

	JIS criteria n (%)	Proposed WC cut-off[a] n (%)	Proposed BMI cut-off[b] n (%)	Combined parallel WC and BMI n (%)	Combined series WC and BMI n (%)
Total (n = 2809)	855 (30.4)	1037 (36.9)	1028 (36.6)	1087 (38.7)	978 (34.8)
Male (n = 1549)	539 (34.8)	704 (45.4)	692 (44.7)	732 (47.3)	664 (42.9)
35-40 (n = 234)	70 (29.9)	90 (38.5)	94 (40.2)	97 (41.5)	87 (37.2)
41-45 (n = 317)	104 (32.8)	138 (43.5)	138 (43.5)	142 (44.8)	134 (42.3)
46-50 (n = 319)	118 (37.0)	150 (47.0)	150 (47.0)	155 (48.6)	145 (45.5)
51-55 (n = 447)	160 (35.8)	215 (48.1)	208 (46.5)	223 (49.9)	200 (44.7)
56-60 (n = 232)	87 (37.5)	111 (47.8)	102 (44.0)	115 (49.6)	98 (42.2)
p-value*	0.327	0.126	0.482	0.207	0.321
Female (n = 1260)	316 (25.1)	333 (26.4)	336 (26.7)	355 (28.2)	314 (24.9)
35-40 (n = 184)	26 (14.1)	28 (15.2)	30 (16.3)	30 (16.3)	28 (15.2)
41-45 (n = 238)	49 (20.6)	54 (22.7)	58 (24.4)	60 (25.2)	52 (21.8)
46-50 (n = 291)	61 (21.0)	66 (22.7)	65 (22.3)	72 (24.7)	59 (20.3)
51-55 (n = 320)	99 (30.9)	101 (31.6)	102 (31.9)	105 (32.8)	98 (30.6)
56-60 (n = 227)	81 (35.7)	84 (37.0)	81 (35.7)	88 (38.8)	77 (33.9)
p-value*	<0.001	<0.001	<0.001	<0.001	<0.001

[a] The proposed WC cut-off to detect the metabolic syndrome was 82.5 cm in male and 77.5 cm in female, other criteria according to JIS criteria.

[b] The proposed BMI cut-off to detect the metabolic syndrome was 23.14 kg/m^2 in both male and female.

* For the statistical significance of the differences in age groups, *p*-value by χ^2-test.

Part 4.5 Prevalence of high LDL cholesterol

The LDL cholesterol was categorized by AACE guidelines. In Table 4.15 shows the prevalence of optimal LDL cholesterol level, borderline LDL cholesterol level and high risk LDL cholesterol level were 42.1, 28.5 and 27.2%, respectively. Regarding gender, Male has slightly higher the prevalence of high risk LDL cholesterol level than females, 29.4% and 24.4% respectively.

Table 4.15 The prevalence of high LDL cholesterol by gender according AACE

LDL-C (mg/dL)	**Prevalence (%)**		
	Male	**Female**	**Total**
Optimal level (< 130 mg/dL)	39.0	46.1	42.1
Borderline level (130-159 mg/dL)	28.2	28.8	28.5
High risk level $\geq$160 mg/dL	29.4	24.4	27.2

Note: The subjects who had TG level more than 400 mg/dL will not be included in the analysis of LDL-C, missing data 2.2%.

Part 4.6 Odds ratio of association between smoking, alcohol consumption, exercise and metabolic syndrome

Logistic regression analysis was used to determine the association between smoking, alcohol consumption, exercise and metabolic syndrome by crude and adjusted analyses for sex, age, smoking, alcohol consumption and exercise with 95% confidence interval and p-values of less than 0.05 were considered statistically significant.

Table 4.16 shows association between smoking, alcohol consumption, exercise and metabolic syndrome (defined according to the JIS criteria except WC cut-off using the proposed cut-off points at 82.5 cm in male and 77.5 cm in female). Smoking was categorized into no-smoked, ex-smoked and current smoking. Among the subjects who had metabolic syndrome, the percentage of no-smoked, ex-smoked and current smoking were 63.5, 15.6 and 20.9% respectively. In non-metabolic syndrome group, the percentage of no-smoked, ex-smoked and current smoking were 77.0, 8.7 and 14.3% respectively. The metabolic syndrome was significantly associated with ex-smoked (OR=2.15, 95% CI=1.69-2.73) and current smoking (OR=1.78, 95% CI=1.45-2.18). After adjustment for other behavior, sex and age, the metabolic syndrome was significantly associated only ex-smoked and adjusted OR decreased from 2.15 to 1.33 (95% CI=1.02-1.73). Alcohol consumption was categorized into no drinking, occasional drinker and regular drinker. Among the subjects who had metabolic syndrome, the percentage of no drinking, occasional drinker and regular drinker were 47.9, 42.0 and 10.1% respectively. In non-metabolic syndrome group, the percentage of no drinking, occasional drinker and regular drinker were 60.4, 34.0 and 5.6% respectively. The metabolic syndrome was significantly associated with occasional drinker (OR=1.56, 95% CI=1.32-1.83) and regular drinker (OR=2.29, 95% CI=1.70-3.07). After adjustment, the metabolic syndrome was significantly associated only regular drinker and adjusted OR decreased from 2.29 to 1.40 (95% CI=1.01-1.93). Exercise was categorized into no exercise, occasional exercise and regular exercise. Among the subjects who had metabolic syndrome, the percentage of no exercise, occasional exercise and regular exercise were 14.3, 65.8 and 19.9% respectively. In non-metabolic syndrome group, the percentage of no exercise, occasional exercise and regular exercise were 14.6, 61.5 and 23.9% respectively. The metabolic syndrome was significantly associated only occasional exercise (OR=1.29, 95% CI=1.06-1.56). While adjustment, the metabolic syndrome was significantly associated no exercise (OR=1.90, 95% CI=1.43-2.52) and occasional exercise adjusted OR increased from 1.29 to 1.48 (95% CI=1.22-1.81).

Table 4.17 shows association between smoking, alcohol consumption, exercise and metabolic syndrome (defined according to the JIS criteria). Smoking was categorized into no-smoked, ex-smoked and current smoking. Among the subjects who had metabolic syndrome, the percentage of no-smoked, ex-smoked and current smoking were 66.5, 14.4 and 19.1% respectively. In non-metabolic syndrome group, the percentage of no-smoked, ex-smoked and current smoking were 74.4, 9.9 and 15.7% respectively. The metabolic syndrome was significantly associated with ex-smoked (OR=1.63, 95% CI=1.27-2.08) and current smoking (OR=1.36, 95%

CI=1.10-1.68). On the other hand after adjustment, the metabolic syndrome was not significantly associated with any metabolic syndrome risk behaviors. Alcohol consumption was categorized into no drinking, occasional drinker and regular drinker. Among the subjects who had metabolic syndrome, the percentage of no drinking, occasional drinker and regular drinker were 50.9, 40.2 and 8.9% respectively. In non-metabolic syndrome group, the percentage of no drinking, occasional drinker and regular drinker were 58.0, 35.4 and 6.6% respectively. The metabolic syndrome was significantly associated with occasional drinker (OR=1.29, 95% CI=1.09-1.53) and regular drinker (OR=1.55, 95% CI=1.14-2.10). When adjustment, the metabolic syndrome was not significantly associated with any metabolic syndrome risk behaviors. Exercise was categorized into no exercise, occasional exercise and regular exercise. Among the subjects who had metabolic syndrome, the percentage of no exercise, occasional exercise and regular exercise were 15.3, 67.1 and 17.6% respectively. In non-metabolic syndrome group, the percentage of no exercise, occasional exercise and regular exercise were 14.1, 61.3 and 24.6% respectively. The metabolic syndrome was significantly associated with no exercise (OR=1.52, 95% CI=1.15-2.00) and occasional exercise (OR=1.53, 95% CI=1.25-1.89). After adjustment, the metabolic syndrome was significantly associated with no exercise and occasional exercise and adjusted OR increased from 1.52 to 2.03 (95% CI=1.51-2.72) and 1.53 to 1.67 (95% CI=1.35-2.07) respectively.

Table 4.16 Association between smoking, alcohol consumption, exercise and metabolic syndrome

Behavior	Metabolic syndrome[a] Yes n (%)	Metabolic syndrome[a] No n (%)	Crude OR (95% CI)	Adjusted OR** (95% CI)	*p*-value
Smoking habits					
No-smoked*	659 (32.6)	1364 (67.4)	1	1	
Ex-smoked	161 (50.9)	155 (49.1)	2.15 (1.69-2.73)	1.33 (1.02-1.73)	0.039
Current smoking	217 (46.2)	253 (53.8)	1.78 (1.45-2.18)	1.13 (0.89-1.43)	0.321
Alcohol consumption					
No drinking*	497 (31.7)	1071 (68.3)	1	1	
Occasional drinker	435 (41.9)	602 (58.1)	1.56 (1.32-1.83)	1.10 (0.91-1.33)	0.344
Regular drinker	105 (51.5)	99 (48.5)	2.29 (1.70-3.07)	1.40 (1.01-1.93)	0.044
Exercise habits					
No exercise	149 (36.6)	258 (63.4)	1.19 (0.92-1.54)	1.90 (1.43-2.52)	<0.001
Occasional exercise	682 (38.5)	1090 (61.5)	1.29 (1.06-1.56)	1.48 (1.22-1.81)	<0.001
Regular exercise*	206 (32.7)	424 (67.3)	1	1	

[a] Metabolic syndrome is defined according to the JIS criteria except WC cut-off using at 82.5 cm in male and 77.5 cm in female.

* Reference category.

** Adjusted for sex, age, smoking habits, alcohol consumption and exercise habits.

Table 4.17 Association between smoking, alcohol consumption, exercise and metabolic syndrome

Behavior	Metabolic syndrome[a]		Crude OR	Adjusted OR**	*p*-value
	Yes n (%)	No n (%)	(95% CI)	(95% CI)	
Smoking habits					
No-smoked*	569 (28.1)	1454 (71.9)	1	1	
Ex-smoked	123 (38.9)	193 (69.1)	1.63 (1.27-2.08)	1.20 (0.91-1.58)	0.187
Current smoking	163 (34.7)	307 (65.3)	1.36 (1.10-1.68)	1.05 (0.81-1.35)	0.703
Alcohol consumption					
No drinking*	435 (27.7)	1133 (72.3)	1	1	
Occasional drinker	344 (33.2)	693 (66.8)	1.29 (1.09-1.53)	1.08 (0.88-1.32)	0.456
Regular drinker	76 (37.3)	128 (62.7)	1.55 (1.14-2.10)	1.17 (0.83-1.63)	0.369
Exercise habits					
No exercise	131 (32.2)	276 (67.8)	1.52 (1.15-2.00)	2.03 (1.51-2.72)	<0.001
Occasional exercise	574 (32.4)	1198 (67.6)	1.53 (1.25-1.89)	1.67 (1.35-2.07)	<0.001
Regular exercise*	150 (23.8)	480 (76.2)	1	1	

[a] Metabolic syndrome is defined according to the JIS criteria.

* Reference category.

** Adjusted for sex, age, smoking habits, alcohol consumption and exercise habits.

CHAPTER V
DISCUSSION

This is a cross-sectional study with an aim to determine the optimal cut-off points of WC and BMI in order to identify the metabolic syndrome in Royal Thai Army personnels whose aged of 35-60 years in Bangkok and suburban area using existing annual health checkup data during 1st October, 2013 to 30th September, 2014 from Armed Forces Research Institute of Medical Sciences. To determine the sample size, the researcher used sensitivity and specificity based on the determination of the WC cut-off points for the identification of metabolic syndrome for Thai population. Sample size of this study at least contains of 2,809 persons (1,549 males and 1,260 females). Due to this study utilized secondary data, hence if it is found that any annual health checkup result of any RTA personnel is incomplete, whether it is basic physical check up, health behavior information, or laboratory result, the researcher excluded the records with missing data and sampling process was performed. The researcher used JIS criteria for diagnosis of the metabolic syndrome, as it is the most up-to-date criteria that have been agreed by many organizations using the same fundamental as IDF and NCEP. Only difference is the WC cut-off points that is differed by group of population and race. Based on the objective of this study, the result can be used in combination of JIS criteria to identify the metabolic syndrome in RTA personnel.

Design and Research methodology

Based on research question and objective of this study, the most suitable design is cross-sectional study. The researcher used the secondary data of the annual health checkup of RTA personnel in Bangkok and suburban in fiscal year 2014. All data is from questionnaire and laboratory test from AFRIMS. According to the Royal Thai Army's policy specifying that every RTA personnel must have an annual health checkup, therefore the response rate of the questionnaire is 100% and it can reduce selection bias. To make the RTA personnel in sample group to be a good representative of the RTA population in Bangkok and suburban, the researcher randomly select samples by using a computer program (Microsoft Excel) which is a convenient way with a same possibility that each sample will be equally selected. However, annual health checkup is only a basic screening for disease among RTA personnels, the limitation of the use of these data obtained from the questionnaire is that the questionnaire is not specially designed for this study. Data of topic that the researcher wishes to study is therefore not able to be acquired in detail and completely. The question concerning health behavior is responded by self-reported, therefore, it causes some information error and information bias which is considered as an error on false information. For example, information error might be from an RTA personnel who just stops smoking yesterday responds to the questionnaire that he is the one in the group of people who ever smoked. Sometimes, an RTA personnel cannot remember his alcohol consumption frequency which causes information bias. Some RTA personnel might be afraid that if he accepts that he drinks alcohol, health care providers might criticize about his drinking, so he just tells that he drinks only from time to time. In addition, RTA personnel's general information including height, and weight, may be filled in with estimation. WC is measured by the officer which can be an error based on the measuring position. All these bias lead to an error in classifying those with risk and those without risk. Deviation of information to be analyzed can be controlled by 1) create a standard in measuring the WC by determining the measuring position and using only one officer to measure in order to reduce the difference of the WC values, 2) the definition is defined and the factors to be examined are classified clearly and carefully, and 3) the factors to be examined may be questioned by interview instead of having the respondent fills in the answer. However, due to the researcher used secondary data, there might be some deviation. Thus, in order to obtain the most complete and accurate data, the researcher sets criteria for exclusion and inclusion of the sample group before analyzing the data. In addition, to determine relationship between the behavioral risk factors and metabolic syndrome, the researcher used the statistical method to control age and gender because they are factors that related to metabolic syndrome. For cross-sectional study which is a study that saves both time and expenses, it shows the prevalence of the metabolic syndrome and the health status of the RTA personnel at that moment. The study also identifies multiple risk factors and health status of the metabolic syndrome at the same time. This study design can demonstrate the behavioral risk factors that related to metabolic syndrome but cannot tell the sequence of events or rationality between risk factors and the metabolic syndrome. In addition, statistics that are used to determine the risk is simply the ratio of risk (Odds ratio, OR), which are not direct relative risks (Relative Risk, RR). However, the results from this cross-sectional study can be used as a fundamental information that contributes to the creation and test of hypotheses in other studies further.

General Characteristics

General characteristic of RTA personnel in the sample groups is that they are in the average age of 48.3 years old (± 6.9 years). Most of the male are non-concomissioned RTA personnel and most of the female are civilian employee. Average age of RTA personnel in the sample group is older than all RTA population in Bangkok and suburban (average age is 42.6 years, aged 18 - 60 years). Based on the result of physical examinaion, male and female personnel have average WC and BMI of 87.2 cm, 25.0 kg/m^2 and 80.2 cm, 24.4 kg/m^2, respectively. Average WC and BMI of the RTA personnel in this study is higher than in geneal Thai population (162), except for the BMI of female RTA personnel that equals to other general Thai females (Male: 79.9 cm., 23.1 kg/m^2 and female: 79.1 cm., 24.4 kg/m^2). The Asia-Pacific criteria (25) is used to consider the WC and to determine obesity. It reveals that most of male RTA personnel have normal WC while more than half of female RTA personnel have abdominal obesity. Regarding the prevalence of obesity (BMI ≥25.0 kg/m^2), male RTA personnel has higher prevelence of obesity than general Thai male population (45.5% and 28.3%). On the contrary, female RTA personnel have lower prevenlence than general Thai female population (36.1% and 40.7%). Moreover, health problem commonly found in the sample group is high total cholesterol level (70.8%) and high blood pressure (50.6%). Based on annual report of AFRIMS, 3 years retrospectively (36, 163, 164), number of the RTA personnel in RTA who have high total cholesterol level and high blood pressure tends to increase every year and the prevalence of high total cholesterol level and high blood pressure is higher than in general population

(50.9% and 21.4%, respectively (162). Therefore, RTA personnel tends to have higher risk factors of metabolic syndrome than general population. Based on data about health behavior, it is found that male RTA personnel have risky behaviors including smoking and drinking. It is found that most of female RTA personnel do not exercise or do exercise but not sufficient enough to reach standard recommendation of exercising. Pattern of health risk behaviors in the RTA personnel whose aged 35-60 years is very similar to general population whose aged of 15-59 years but the prevalence is different In general population, the prevalence of smoking is higher than RTA personnel (19.9% and 16.7%). On the contrary, the RTA personnel have a prevalence of insufficient exercise higher than normal population (63.1% and 18.5%). Both general population and RTA personnel have similar prevalence of alcohol drinking (45.3% and 44.2%) (162).

Use of Statistics to analyze the WC and BMI cut-off points

Metabolic syndrome is mainly caused by obesity, especially abdominal obesity. Popular tool used to classify groups of people who are overweight and abdominal obesity currently according to the recommendation of the WHO is measuring of WC and calculation of BMI. This tool can be used easily with no need for specific expertise and no side effects or harm to the person being tested. In addition, this tool can also be used in the community or to be used in the field as well. Thus, WC and BMI are therefore suitable to be used as a preliminary tool to screen the occurrence of the metabolic syndrome. However, the problem with both of these tools is the optimal cut-off point that gives accurate result in the diagnosis of metabolic syndrome. WC used the diagnosis the metabolic syndrome only apply to the cut-off points that recommended by organizations such as WHO, IDF and NCEP. According to several studies in Asia, it is suggested that the recommended criteria are not appropriate for the population in Asia. Even the study conducted in the same country, the results are also varied (153-159). This may be because of different demographic structure and physical behavior in everyday life. Thus, WC cut-off points used currently can be changed if there is any other cut-off points that is more suitable for any particular ethnic groups and race of population. For BMI cut-off points is not in the criteria to diagnosis the metabolic syndrome. Only the criteria of IDF recommended that if a person has BMI over 30 kg/m^2, central obesity can be assumed and WC does not need to be measured (15). Therefore, at present many countries continue to conduct study to determine appropriate cut-off points for groups and nationalities in order to identify the metabolic syndrome.

This study aims to find the appropriate WC and BMI cut-off points to be used as a screening tool for metabolic syndrome. The researcher analyzed the data separately for the presence of at least two of the four and at least three of the four risk factors of metabolic syndrome but in order to get the cut-off points that can be used in early detection of metabolic syndrome, the researcher, therefore, recommends the WC and BMI cut-off points that are analyzed from the RTA personnel to have factor of metabolic syndrome of at least two of the four (Table 4.9). The statistics used in this analysis is Receiver operating characteristic (ROC) curve analysis. It is used to plot graph between the sensitivity (true positive rate) and 1-specificity (false positive rate), using the diagnosis of the metabolic syndrome of JIS as the gold standard. There are many ways to select the optimal cut-off points such as select the point at the shortest distance on ROC curve, select the point that gives highest Youden's index, select the point with the same sensitivity and specificity or even select by using the sensitivity and specificity together with PPV and NPV (165). However, most of studies use the point that gives maximum Youden's index. Youden's index can be calculated with the formula [sensitivity + (specificity − 1)] with the value 0-1. The value closest to 1 is the best value to be used to indicate metabolic syndrome. The good point of this method is that the value will not vary according to the disease prevalence but the spectrum of disease has impact to this value (166). In this study, the researcher used the optimal cut-off points by using two methods and compares the value between these two methods which is the cut-off points with the maximum Youden's index and the sensitivity consideration. Once result from both methods are compared, it is found that the cut-off points with maximum Youden's index have lower sensitivity than specificity. The researcher considers that to choose the optimal cut-off points by using maximum Youden's index still cannot serve the right objective and the use in the RTA personnel because the study requires preliminary tool to screen the occurrence of the metabolic syndrome, if the metabolic syndrome is diagnosed since the begining, it will be able to reduce the incidence of CVD, stroke, as well as diabetes.

Therefore, the researcher select the optimal cut-off points by considering the sensivity. Previous study suggested that the WC cut-off points yielding at least 80% sensitivity is a good screening tool for metabolic syndrome even if the specificity would be lower and the false positive would be high. Thus, the proposed optimal WC cut-off points in this study is 82.5 cm for male RTA personnel (Sensitivity 81.9% and Specificity 43.2%) and 77.5 cm. for female RTA personnel (Sensitivity 81.3% and Specificity 53.1%). Result of this study gives the value that lower than the value recommended by WHO and IDF (90.0 cm for male and 80.0 cm for female) (15). After the analysis is considered, if the cut-off points of 90 cm is used in this study of male RTA personnels, the sensitivity will be lower than specificty (43.3% and 79.7% respectively). Regarding female RTA personnels, the cut-off points of 80 cm has a sensitivity that is lower than the cut-off points recommended to be used in this study but close to the cut-off points with maximum Youden's index.

When comparing to previous study on the WC cut-off points in Thai population, the result also give a lower value. The study conducted by Worachartcheewan et al. (29) on 5,646 Thai population who have an annual health checkup from the Faculty of Medical Technology, Mahidol University, the WC cut-off points for male is 87.75 cm and for female is 79.75 cm. The study of Narksawat et al. (31) 998 Thai people on the data from the Second Thai National Health Examination Survey shows the cut-off points of 84.0 cm for male and 80.0 cm for females. It is found that even the studies are conducted in that same nationality of people, the results are different. It may be because of the characteristic of population studied that are different. Samples in previous study are from people who came to have the health checkup (29). Thus they are a group of people who concern about good health and may have good health behavior. Another study uses the survey of the health of Thai people in general where both populations in Bangkok and in other provinces are included (31). These previous studies are different from this study where the population in RTA personnel only in Bangkok and suburban. In addition, the RTA personnel have working characteristic, lifestyle, and health behavior that are different for general people such as participation in military training in order to be ready to work at all time, or be on day or night duty, etc. Furthermore, the position to measure WC may lead to different cut-off points. There are 3 common positions usually used in studies: 1) the midpoint between the lowest rib and the iliac crest (WC-M), which is a position recommended by the WHO and IDF, 2) the iliac crest (WC-I) recommended by the NIH and NCEP (167) and 3) at the umbilicus level (WC-U) introduced by the Ministry of Public Health of Thailand. Although the WC-M and WC-I are the internationally recommended, there is also limitation to use these two positions because it may be more difficult to measure. A person who does the measurement must be knowledgeable about human anatomy. Thus, many studies usually use WC-U because of this position is more obvious than other positions and it is easier to measure, and does not require a lot of expertise. There are different suggestions from previous studies such as WC-M helps predict risk of CVD better than other positions, the position above the iliac crest is correlated with total body fat and the WC-U can identify obesity as well (168, 169). However, the study conducted by Hitze et al. (170) indicates that different positions of WC give the same relationship with risk factors of metabolic syndrome. In addition, Systemic review suggested that the WC at different positions has no substantial influence on the association between WC, all-cause and CVD mortality, CVD and diabetes (169). When compared the results with other studies in Asian countries, it is found that the results of this study is similar to the findings of Kim HK et al. (159), which studied 31,076 Korean people. The WC cut-off point for male is 83.0 cm and for female is 76.0 cm. Another study conducted by Ko and Tang (155) on 14,919 Chinese people reveals WC cut-off points for male of 83.3 cm and 76.1 cm for female.

Moreover, the researcher applies AUC to evaluate the performance of screening tools. The screening tool that provides AUC close to 1 indicates that the tool can be used to distinguish between those who have and do not have the disease whereas the AUC approaching 0.5 indicates that the tool cannot be used to distinguish between those who have and do not have the disease. Table 4.11 shows the AUC of the WC of each factor on the occurrence of the metabolic syndrome. WC cut-off points are larger when there are more risk of metabolic syndrome both in male and female. The cut-off points obtained from the analysis of data of male RTA personnel who have at least two out of four risk factors of metabolic syndrome, AUC at 0.686, is considered as effective cut-off points to be used as a screening tool to distinguish RTA personnel with and without metabolic syndrome. An effective cut-off point for female RTA personnel is AUC 0.755 which is better than male RTA personnel.

BMI is a significant indicator of obesity. Even BMI is not used as criteria to identify metabolic syndrome by various organizations, but IDF considers that BMI can be used instead of WC. If a person has BMI of 30 kg/m^2 or more, that person is diagnosed as having central obesity with no need to measure the WC (15). The study of Whitlock et al. (171) reveals that BMI was significantly associated with an abnormality of metabolism. In this study, the researchers use the rules to select the cut-off points of BMI as same as the cut-off points of WC. The proposed BMI cut-off points for the RTA personnel is 23.14 kg/m^2 (Table 4.12). When compared to previous studied conducted with Thai population, they are quite similar. Based on the study conducted by Worachartcheewan et al. (29), BMI for male is 23.81 kg/m^2 and for female is 23.65 kg/m^2. And study of Narksawat et al. (31) suggests the BMI of 23.0 kg/m2 as a cut-off point. The results are the same as the BMI recommended for Asian people from WHO where the BMI of 23.14 kg/m^2 is considered as pre-obese, which is the group of people whose health status should be monitored. These people should get recommendation to modify their lifestyle and eating habit in order to prevent abdominal obesity and metabolic syndrome.

In addition to analyzing the optimal cut-off points of WC and BMI, the researcher as well applies both screening tools together to maximize the effectiveness of screening tools. Based on this study, combining both tools together in parallel testing increases the sensitivity from 81.9% (using only WC), 80.0% (using only BMI) to 95.0% for male and 81.3% (using only WC), 80.0% (using only BMI) to 96.2% for female but with decreased specificity. When combine both tools together in series testing, the specificity is increased from 43.2% (using only WC), 47.1% (using only BMI) to 70.0% for male and 53.1% (using only WC), 47.1% (using only BMI) to 75.0% for female (Table 4.13). The suggest method to be used for RTA personnel is to combine the WC and BMI in parallel testing as the researcher would like to have tools that have the sensitivity of at least 80% with accepted reduced specificity. Consideration of the characteristics of metabolic syndrome that the tool with high false negative will be disadvantage for the RTA personnel than the tool with high false positive because metabolic syndrome is not a communicable disease, neither a disease that lead to rapid death, and false positive does not pose serious harm to personnel physical and mental health. Oppositely, it is likely to provide benefit to the RTA personnel. RTA personnel with false positive result may have higher concern on health and more tendency to change to even more healthy lifestyle which may cause no additional expenses with no complications. On the other hand, with false negative result the RTA personnel may ignore to maintain good health or keep having risky behavior. However, these RTA personnel still need to have regular health checkup according to the policy of the Royal Thai Army (35). Thus, RTA personnel in the group if false negative will be evaluated on the risk of metabolic syndrome every year. Based on this study, the parallel testing leads to false negative and false positive of 5.2% and 60.3% respectively. While, series testing leads to false negative and false positive of 16.6% and 46.4% respectively. Thus, parallel testing is more likely to be suitable for the health promotion campaign as a monitor and screen of the occurrence of metabolic syndrome in RTA personnel.

Prevalence of metabolic syndrome and Prevalence of high LDL cholesterol

Currently, the prevalence of metabolic syndrome is increasing worldwide. According to the study, both in Thailand and overseas, it is found that the trend of the prevalence of metabolic syndrome is following the trend of increasing prevalence of obesity and diabetes in both children and adults. The prevalence of metabolic syndrome in each study, although conducted in the same country may have different results depending on the criteria used for diagnosis, age and racial groups studied. For example, study on the prevalence of metabolic syndrome from the Third National Health and Nutrition Examination Survey, NHANES III in adults in the US found that the prevalence of metabolic syndrome are different based on race, prevalence of 16% in African-American and 37% in Hispanic population (12). Several studies have shown that in European countries, the prevalence of metabolic syndrome is about 20-40% (Table 2.1), and in Asia was approximately 10-30% (Table 2.2). Several years ago in Asia, the prevalence of metabolic syndrome is increased rapidly due to changes in the economy and society. The society becomes more industrialized, routine behavior of population has been changed, and more migration between urban and rural society occurs.

In Thailand, data from the Thai National Health Examination Survey, NHES IV in 2009 (162) reveals that Thai people aged of 15 and over have prevalence of metabolic syndrome of 21.7% using JIS criteria. The prevalence in females (24.5%) is higher than in males (18.8%) and the prevalence is increasing as age increased. In males, the age group with higher prevalence is group of 60-69 years. In females, the age group with highest prevalence is 70-79 years. When each region is considered, it is found that central region has the most prevalence, which is 25.4% (22.7% in males and 27.8% in females), followed by Bangkok with the prevalence of 24.2% (23.4% in males and 25.0% in females). In this study, the researcher has categorized the determination of prevalence of metabolic syndrome into 2 categories: using JIS criteria and using the criteria of WC cut-off points and BMI obtained from this study (Table 4.14). The prevalence of Mets in RTA personnel as determined by JIS criteria is 30.4% but with parallel test of WC and BMI, the prevalence is higher (38.7%). When considering the prevalence based on gender, male RTA personnel have higher prevalence than females in all diagnosis criteria. In males, the prevalence in each age group is not statistically different. The prevalence in male RTA personnel is highest in those with age of 56-60 years according to JIS criteria and 46-50 years according to the proposed cut-off points criteria. While the prevalence in each age group of female RTA personnel are significantly different. However, both criteria show the highest prevalence in female RTA personnel aged 56-60 years.

Compared with survey data from NHES IV in 2009, the prevalence of metabolic syndrome, according to JIS criteria, of female RTA personnel is close to general female population (25.1% and 24.5% respectively), but in male RTA personnel is higher than general male population (34.8% and 23.4% respectively) as male RTA personnel maybe have some risk factors for metabolic syndrome than general male population. Once comparing the prevalence according to JIS among population in Chiang Mai Province (76), it is found that total prevalence and gender prevalence are lower than this study (total prevalence of 16.1%, and 26.5% for males and 13.7% for females) as the prevalence in central region is higher than northern region. In addition, the study is conducted among health personnel in hospital who are likely to have more knowledge and understanding of maintaining good health than any other careers. In addition, the prevalence in Europe is higher than Asia (59, 64, 70), except for Malaysia that has higher prevalence (42.5%) than some countries in Europe and higher than Thailand. This may be because there are many races live in Malaysia such as Malay, Chinese and Indian (78). Even each study shows difference in prevalence but they are in the same direction, including this study, that the prevalence of metabolic syndrome is increased according to increased age and the highest prevalence in females is in the older age than in males. In addition, when each of risk factor of metabolic syndrome is concerned, the RTA personnel who are diagnosed to have metabolic syndrome and those who are normal have highest risk of hypertension. Therefore, the researcher considers that WC cut-off points, BMI cut-off points, and blood pressure measurement should be used together in screening of metabolic syndrome because these three tools can be used easily, rapid, and with less cost than laboratory check. They can also be used with the RTA personnel in the field setting.

Furthermore, the researcher also studies the prevalence of high level of LDL-C in blood because hyperlipidemia is related to the incidence of CVD, particularly high LDL-C. In clinical practice, LDL-C is the target to be reduced in order to effectively prevent CVD. In this study, the researcher uses the criteria of AACE for categorizing level of LDL-C (Table 4.15). RTA personnel with level of LDL-C less than 130 mg/dL are considered as “normal”, with the level of 130-159 mg/dL are considered as “surveillance”, and the level of higher than 160 mg/dL are considered as “high risk”. Study result reveals that the prevalence of high LDL-C in RTA personnel is 27.2%. Male RTA personnel have slightly higher prevalence than females, 29.4% and 24.4% respectively. There are 28.5% of the RTA personnel in a level of “surveillance”. Thus, there should be regular follow up for RTA personnel in the surveillance group and the recommendation to prevent of having too high level of LDL-C should be provided. However, level of LDL-C is obtained by using Friedewald formula which has a limitation where the LDL-C cannot be calculated if the level of triglycerides is more than 400 mg/dL (172). Hence, data of the level of LDL-C of some RTA personnel is missing which is accounted for 2.2%. However, LDL-C level that is obtained by the calculation is not as accurate as using the laboratory test. Calculation method is suitable to use with RTA personnel in this study because there are large number of RTA personnel to be screened in this study. It helps reduce the cost for laboratory test. Only RTA personnel with high risk based on continual health checkup are transferred to medical procedure.

Association between smoking, alcohol consumption, exercise and metabolic syndrome

Metabolic Syndrome is a cluster of disorders that is the risk for CVD. It also increases the risk of type 2 diabetes. Currently, it is believed that the cause of the occurrence of the metabolic syndrome is insulin resistance and obesity, in particular, the abdominal obesity which is also a cause of hypertension. The treatment of the metabolic syndrome focuses on lifestyle changes, reducing health risk behaviors such as smoking, drinking alcohol, stress, etc., as well as changing eating habits by reducing the energy from food intake and increasing exercise. In RTA personnel annual health checkup, 3 types of health information are collected, which are smoking behavior, drinking behavior and exercise behavior. Based on 3 years retrospective (36, 163, 164) of the annual report of AFRIMS, the prevalence of smoking, drinking, and no exercise plus exercising under standard criteria were 25-30%, 10-15%, and 55-65%, respectively.

Bases on such information, the researcher analyzed the association of health behavior and the metabolic syndrome in RTA. In this study, the researcher uses 2 diagnosis criteria of metabolic syndrome, which are JIS criteria and the proposed WC cut-off points obtained from this study (82.5 cm for males and 77.5 cm for females). The study reveals that when each individual factor is analyzed, all factors are associated with the metabolic syndrome with statically significance, when JIS criteria is applied. While using of the proposed WC cut-off points gives the result that no exercise is not associated with the metabolic syndrome. Multivariate analysis using these 3 behaviors together with age and gender in the model showed exercise behavior is associated with the metabolic syndrome with statistical significance and has high OR than other factors for the JIS criteria. RTA personnel with no exercise and occasional exercise are 2.03 and 1.67 times higher risk of metabolic syndrome compared to those who exercise regularly. Using the proposed WC cut-off points gives the same results as using JIS, but the difference is “ex-smoked” and “regular drinker” are still associated with the metabolic syndrome with statistical significance (Table 4.16 and 4.17). The ex-smoker RTA personnel are 1.33 times higher risk of metabolic syndrome than those who never smoked. RTA personnel who drink regularly are at 1.40 times higher risk of metabolic syndrome than those who do not drink. Regarding of smoking when age is controlled in multivariate analysis, it is found to be not associated. This may be because the RTA personnel in the sample group just smoked for a short period of time and the effect of smoking on metabolism might not occur yet. Therefore, question related to duration of smoking and number of cigarette smoked should be included in the further study.

Several previous studies reports in the same direction that smoking and exercise behavior are factors associated with metabolic syndrome. For example, health survey in USA (49) and health survey in Korea (173) show that those who currently smoke are at higher risk of metabolic syndrome than those who never smoked, both males and females (1.50, 1.80 times and 1.40, 1.60 time respectively). Study conducted by Chen et al. (133) in Taiwanese people indicates that current smoking are at risk of metabolic syndrome because of the effect of smoking on increased triglycerides and reduced HDL-C. In addition, number of cigarette smoked is also related to the metabolic syndrome. Those who smoke more than 20 pack-years are at higher risk (1.82 times). Studies in Japan, by Ishizaka et al. (174) and Nakanishi et al. (135) show that smokers and ex-smokers are at higher risk of metabolic syndrome compared to non-smokers. The risk is found in those who smoke 10 cigarettes and more per day for the duration of 10 years or more. In ex-smokers who had smoked for 10 years and more, even already stop smoking, are still at risk of metabolic syndrome. Smoking for a long period of time may cause reduction of plasma adiponectin which leads to insulin resistance, hyperglycemia, change of lipid profile (increase of triglycerides and reduction of HDL-C), etc. It is found that 35%-70% of those who stop smoking in the first year have weight gain (175) and smokers who had stop smoking within the past 10 years were significantly more likely than non-smokers to become overweight (odds ratios, 2.4 for male and 2.0 for female), body weight increases 5 kilograms on average in females and 4.4 kilograms in males (176).

In term of exercise and metabolic syndrome, there are both cross-sectional and intervention studies, i.e. health survey in USA (49) reveals that males with no exercise are at 1.4 times higher risk of metabolic syndrome than males who exercise. Study of Churilla and Zoeller (177) shows that those with no exercise are at 1.63 times higher risk of metabolic syndrome than those who exercise regularly (more than 150 minutes per week). Stewart et al. studied exercise program for a period of 6 months in elderly people who have hypertension and found significant weight reduction, decreased abdominal fat, increased body mass, decreased diastolic blood pressure, and increased HDL-C in experimental group. (147) The study of Johnson et al. (178) was conducted by having elderly people with obesity exercise according to given program and found that moderate intensity exercise program for a period of 30 minutes per day on every day can reduce risk of metabolic syndrome better than vigorous intensity exercise program. Moreover, some studies (179, 180) suggest that exercise for weight loss can reduce the risk of metabolic syndrome better than exercise for muscle strength.

Regarding relationship between alcohol consumption and the metabolic syndrome, positive relationship, negative relationship and even J-shaped relationship are reported. The difference in the study results depends on amount of alcohol intake, duration of alcohol drinking, and type of alcoholic beverage. However, most of studies found that drinking alcohol in low to moderate amount has health benefit by increasing HDL-C. The risk of metabolic syndrome is higher when drinking in high amount of alcohol. For example, health survey in USA (49) mentions that those who drink low to moderate amount of alcohol have low prevalence of metabolic syndrome. Low and moderate intake of alcohol have benefit on blood glucose and lipid similar to the study of Chen et al. (140). It is also found that different type of alcohol might affect the components of metabolic syndrome differently. However, type of alcohol is not related to the cause of metabolic syndrome. On the contrary, health survey in Korea (142) suggests that even alcohol intake gives benefits to level of HDL-C, it negatively affects to the other components of the metabolic syndrome. Fan et al. (143) found that drinking one or more times per week reduce the risk of metabolic syndrome without lowering HDL-C. While HDL-C of those who drink three or more times per week is not reduced, but it causes 2 times higher risk of hypertension than those who do not consume alcohol. In addition, there is a study on pattern of alcohol consumption of

Thai population by conducting a survey in household level in 2007 (181). This study found that males drink alcohol more than females and they usually drink at the bar, office, and friend's house. Most females drink at home or in the party. Pattern of alcohol consumption of in the UK Armed Forces and the RTA personnel is similar. That is to say RTA personnel drink alcohol more than general people (182, 183). Most of them drink after work and main reason of drinking is social relation, for fun, and celebration. In addition, it is also found that they usually smoke while drink alcohol. Same as in this study, the prevalence of smoking and drinking in male RTA personnel is higher than in female RTA personnel.

The result is compared by using two criteria to diagnosis metabolic syndrome, it reveals that a smaller WC cut-off point has higher health risk factors. When the criteria of WC cut-off points obtained from this study is used, it shows that the importance of not smoking, not drinking, and exercise regularly, as it can reduce the risk of metabolic syndrome. WHO recommends those whose age range is 18-64 years to have moderate-intensity aerobic exercise for least 150 minutes per week or vigorous-intensity aerobic exercise for at least 75 minutes per week (144). Furthermore, the results can be reported to supervisors to raise awareness of the health problems of the RTA personnel and support activities to promote health, which will make the RTA personnel have a healthier and more quality life.

Limitation of the study

1. This study conducted among the RTA personnel. The WC cut-off points obtained from the analysis of data of female RTA personnel may be extrapolated to represent female general Thai population as many of the participants are employees whose job functions are similar to those outside the RTA. While, the WC cut-off points obtained from male RTA personnel, prior to extrapolation may need to be adjusted after consideration of participant's life style and daily activity.

2. Information of WC that is analyzed in this study is the WC that is measured at the umbilicus level because this is a position that is easy to measure. In addition, many studies measure the WC at this position. However, measuring at the position of the umbilicus level is not an international standard. There is a study indicating that to measure WC at the midpoint between the lowest rib and the iliac crest (WHO and IDF), at the iliac crest (NCEP), and at the umbilicus level (Ministry of Health), give different result when samples have severe problem of abdominal obesity. To measure that the midpoint between the lowest rib and the iliac crest can be used as an indicator of the risk of metabolic syndrome better than any other position.

3. This study used secondary information with a limitation in detail of information. This study still lack of information about familial disease and medication history. For example, RTA personnel who take drug for hypertension may have normal blood pressure, therefore he/she would be categorized under the group of RTA personnel without hypertension condition. It also lack of data about health behavior such as quantity of cigarette and duration of smoking, amount and type of alcohol intake, duration of exercise, etc. Due to this result, the association of health behavior and metabolic syndrome can be analyzed only if there is any factor associated with the syndrome but not more in details.

4. This study is a cross-sectional study design because the exposure and outcome are simultaneously assessed, there is generally no evidence of a temporal relationship between exposure and outcome. That is, although the investigator may determine that there is an association between smoking behavior, drink behavior, exercise behavior and metabolic syndrome, the cause and effect relationship cannot be determined.

5. Based on the result, the researcher uses the cut-off points with high sensitivity. Therefore, if this result is used in practice, there will be a large number of false positive result making general RTA personnel being diagnosed as having metabolic syndrome. This may lead to further expense in laboratory test to confirm the diagnosis.

6. The limitations of BMI should be considered. BMI is a calculation of total body mass. Factors such as age, sex, ethnicity, and muscle mass can influence the relationship between BMI and body fat. Also, BMI does not distinguish between

excess fat, muscle, or bone mass. Thus, to use only this indicator as the only screening tool may not sufficient to identify the metabolic syndrome. In order to have more effective screening tools, BMI should be used together with WC in screening of metabolic syndrome.

CHAPTER VI
CONCLUSION AND RECOMMENDATIONS

The aim of the study was to determine the optimal cut-off points of waist circumference (WC) and body mass index (BMI) for identification of metabolic syndrome in Royal Thai Army personnel aged 35-60 years in Bangkok and suburban.

The design of this study was a cross sectional research conducted in 2,809 samples (1,549 males and 1,260 females). All of them received annual health checkup at Armed Forces Research Institute of Medical Sciences, Army Medical Department, Bangkok during 1st October, 2013 to 30th September, 2014.

Data collection by using existing data consists of general information, health behavior information, physical examination and laboratory analysis. Receiver operating characteristic (ROC) analysis was used for identifying the cut-off points of WC and BMI with sensitivity and specificity for screening of metabolic syndrome. The sensitivity of at least 80 percent was used for determining the appropriate WC and BMI cut-off points. The area under the curve (AUC) with 95% confidence interval (CI) was used as indicators of the diagnostic performance of WC and BMI for identifying metabolic syndrome. Logistic regression analysis was used to determine the association between smoking, alcohol consumption, exercise and metabolic syndrome.

Results from descriptive analysis showed that average age of the subjects was 48.3 ± 6.9 years (48.1 ± 6.9 years for male and 48.4 ± 6.9 years for female). Waist circumference was measured horizontally at the umbilicus level (WC-U). The average WC was 87.2 ± 8.9 cm for male and 80.2 ± 10.3 cm for female. The results were classified by Asia-Pacific criteria found that 56.5 percent of the subjects had WC values in normal group and 43.5 percent with WC values in abdominal obesity group. An average body mass index of the male subjects was 25.0 ± 3.5 kg/m^2 and female was 24.4 ± 4.1 kg/m^2. The results found that most of the subjects were in overweight group with BMI ≥ 23 kg/m^2 and the proportion of overweight in male was higher than in female (72.7% and 58.6% respectively). For the risk factors of metabolic syndrome, the average LDL-C and total cholesterol levels in both male and female were higher than normal levels, while means of systolic blood pressure, triglyceride and plasma glucose were higher than normal levels only in male. For health behavior, most of the subjects were non-smokers (72.0%) non-drinkers (55.8%) and exercised occasionally (63.1%). Regarding to sex, the percentage of smoking and drinking in male is higher than in female, while the percentage of no exercise in female is higher as compared to male.

The results from ROC analysis showed that the optimal cut-off points of WC for detection of the metabolic syndrome with yielding at least 80 percent sensitivity among male was 82.5 cm and among female was 77.5 cm. For the optimal cut-off points of BMI for detection of the metabolic syndrome with yielding at least 80 percent sensitivity was 23.14 kg/m^2. When using the optimal cut-off points of WC and BMI by combined test, parallel testing had increased sensitivity while series testing could improve specificity. In order to early detect of metabolic syndrome, parallel testing would be appropriate rather than series testing.

The prevalence of metabolic syndrome as defined by JIS criteria, the proposed WC cut-off, the proposed BMI cut-off, the combined parallel test and the combined series test were 30.4, 36.9, 36.6, 38.7 and 34.8%, respectively. Regarding to sex, the prevalence of metabolic syndrome in male is higher as compared to female by all criteria. With regard to age, the prevalence of metabolic syndrome is increased according to increased age and the highest prevalence in females is in the older age than in males. From univariate logistic regression analyses found that ex-smoked, current smoking, occasional drinking, regular drinking and occasional exercise significantly associated with metabolic syndrome (defined according to the JIS criteria except WC cut-off using the proposed WC cut-off at 82.5 cm in male and 77.5 cm in female). Multivariate analysis after adjusted for other behavior, sex and age, the metabolic syndrome was significantly associated with ex-smoked (OR=1.33, 95% CI=1.02-1.73), regular drinking (OR=1.40, 95% CI=1.01-1.93), no exercise (OR=1.90, 95% CI=1.43-2.52) and occasional exercise (OR=1.48, 95% CI=1.22-1.81).

Recommendations

1. WC and BMI are suitable screening tools for early metabolic syndrome detection. Especially in field setting, screening by using WC and BMI would be more convenient than laboratory test. In the present study, we proposed that an optimal cut-off point of WC for identification of metabolic syndrome in Royal Thai Army personnel in Bangkok and suburban of 82.5 cm for male and 77.5 cm for female. For optimal cut-off point of BMI we proposed it to be 23.14 kg/m^2 in both sexes.

2. The advantages of WC and BMI are effectiveness and simplicity. The combined test we proposed would be a powerful and cost-effective tool for initial screening for screening of metabolic syndrome. It may also increase the sensitivity of metabolic syndrome diagnosis.

3. In this study, the prevalence of metabolic syndrome in Royal Thai Army personnel was high. There should be a surveillance, continuous intervention programs and campaigns to reduce these risks to prevent disease and promote good health at all levels. Since almost a third of the Royal Thai Army personnel have metabolic syndrome, they should be continuously monitored for these health risk behaviors. Appropriate health measures for prevention and control should be implemented in order to reduce the occurrence of the metabolic syndrome complication and the resources for treatment of the diseases.

4. Study results showed high prevalence of high LDL cholesterol in the Royal Thai Army personnel, there should be regular follow up continuously with health checkup and recommendation to prevent of having too high level of LDL-C should be provided.

5. Royal Thai Army personnel should take care of their health by receiving annual health checkup every year and follow-up the results. Their WC can be self-measured and prevention of metabolic syndrome with lifestyle changes; weight loss, improved diet, and regular physical exercise should be performed.

Recommendations for further study

1. We suggest a study to compare the difference between optimal cut-off point of WC and BMI for identification of metabolic syndrome in Royal Thai Army personnel in urban and rural areas. This will lead to find optimal cut-off point of WC and BMI for application in Royal Thai Army population.

2. We suggest a study to determine optimal cut-off point of WC and BMI for identification of metabolic syndrome in Royal Thai Army personnel under 35 years in order to conduct surveillance and prevention for initial metabolic syndrome.

3. We suggest a study to compare WC measurements for prediction of risk factors of metabolic syndrome and for finding of standard of WC to be used in Royal Thai Army.

4. We suggest a study to conduct retrospective cohort to explore risk factors of cardiovascular disease and associations between metabolic syndrome and cardiovascular disease in Royal Thai Army personnel.

5. We suggest a study to develop screening tools for noncommunicable diseases to be initially used in health promotion program in Royal Thai Army.

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APPENDIX

HEALTH SURVEY AT ARMED FORCES RESEARCH INSTITUTE OF MEDICAL SCIENCES (AFRIMS)

Armed Forces Research Institute of Medical Sciences (AFRIMS) is responsibility of annual health checkup for the RTA personnel who worked in 60 RTA departments in Bangkok and suburban. Annual health checkup consist of 5 parts as following:

1. The self-administered questionnaires

The self-administered questionnaires for collecting RTA personal information consisted of 3 parts, as following:

Part I General information: name, rank, ID card number, sex, date of birth, age, unit and telephone number.

Part II General health information: result health checkup last year, medical history or medical problems, family history, body weight and body height.

Part III Health behavior information: smoking, alcohol consumption and exercise habits.

2. Measurement technique

2.1 Waist circumference was measured at the umbilical level (WC-U), with subjects standing, breathing normally and not to hold their breath in abdominal. A bendable and non-stretch tape was placed directly on the skin around the waist site in a horizontal plane, recorded the WC value by AFRIMS officers.

2.2 Blood pressure was measured with automatic digital blood pressure monitor in the sitting position on the left arm after at least 10 minutes rest period. Blood pressure of the RTA personal who has high blood pressure (SBP $\geq$140 mmHg and/or DBP $\geq$90 mmHg) would be measured again after at least 10 minutes of physical rest.

3. Physical examination by physician

4. Digital Chest X-ray by Phramongkutkloa Hospital mobile X-ray

5. Laboratory analysis by Biochemistry section, Analysis division, AFRIMS

Blood sample of 3-5 ml was collected from vein of the RTA personal into EDTA, NaF and clot tube in the morning after 10-12 hours fasting and at least 24 hours after alcohol drinking for analysis of serum/plasma level.

5.1 Blood chemical analysis

- Plasma levels of glucose and serum levels of total cholesterol, triglyceride, HDL-C, ALP, AST, ALT, Uric acid, BUN and Creatine were assayed by enzymatic colorimetric method test (Cobas integra 800, Roche).

- LDL-C was calculated by Freidewald's formula:

LDL-C (mg/dL) = TC - HDL - TG/5

5.2 Blood hematology analysis

Complete blood count test analyzed by automated hematology analyzer (Sysmex and Beckman coulter).

5.3 Urine analysis analyzed by dipstick chemical analysis (Uriscan).

BIOGRAPHY

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