

**Research Article****A gender-based study on the effects of hypertension, hyperglycemia, and hyperlipidemia on ten-year risk for cardiovascular disease****Tsan Yang<sup>1</sup>, Choo-Aun Neoh<sup>2</sup>, Wan-Wen Huang<sup>3</sup>, Shu-Chun Hsueh<sup>1</sup>, Wen-Li Hou<sup>4</sup>, Pi-Li Lin<sup>4</sup>, Yu-Kuei Liao<sup>5\*</sup>**<sup>1</sup>Department of Health Business Administration, Meiho University, Pingtung County, Taiwan.<sup>2</sup>Pingtung Christian Hospital, Pain Clinic, Pingtung County, Taiwan.<sup>3</sup>Department of Elderly Industry and Service, Kaomei Junior College of Health care & Management, Kaohsiung City, Taiwan.<sup>4</sup>Department of Nursing, Meiho University, Pingtung County, Taiwan.<sup>5</sup>Pingtung Christian Hospital, Nursing Department, Pingtung County, Taiwan.**\*Corresponding author**

Yu-Kuei Liao

Email: [x00002115@meiho.edu.tw](mailto:x00002115@meiho.edu.tw)

---

**Abstract:** Many studies have sought to determine factors for predicting cardiovascular diseases (CVD), and it is already known that metabolic syndrome increases the incidence and mortality rate of CVD. The purpose of this study was to investigate the correlation between the three highs, which are hypertension, hyperglycemia, and hyperlipidemia on ten-year risk of CVD for sex difference. A cross-sectional study design was adopted for the periods from August 2011 to December 2013. Subjects were people who participated in an adult health check at a regional hospital in Pingtung City in Southern Taiwan. The 10-year cardiovascular risk assessment of the Framingham Heart Study was used to calculate the risk, with  $\leq 10\%$  indicating low risk, 11~20% medium risk, and  $>20\%$  high risk. Multiple logistic regression analysis was used to evaluate the effect that the three highs have on the 10-year risk of patients with cardiovascular diseases. The results indicated that men aged 65 or older, smoke, drink, or chew betel nut had a significantly higher 10-year risk for CVD; those with metabolic syndrome and its components also had a significantly higher 10-year risk for CVD. Comparison of men and women found that those suffering from more of these conditions had a significantly higher 10-year risk of CVD. Logistic regression analysis for males indicated the 10-year risk of CVD increased as hypertension, hyperglycemia, and hyperlipidemia increased and the odds ratios were 3.44, 8.13, and 16.64, respectively. In conclusion, hypertension, hyperglycemia, and hyperlipidemia are risk factor affecting the 10-year risk for CVD for both men and women and men have a higher risk if they suffer from more than one of these conditions. Strict and proactive treatment and control is necessary to reduce the incidence of cardiovascular disease.

**Keywords:** Hypertension, hyperglycemia, hyperlipidemia, cardiovascular disease.

---

**INTRODUCTION**

Quick diagnosis and early treatment are important when facing cardiovascular disease (CVD), especially for patients who have had a myocardial infarction. Hypertension, hyperglycemia, hyperlipidemia, and metabolic syndrome are important factors impacting the occurrence of cardiovascular disease. Past research has noted that those with metabolic syndrome are twice as likely to have CVD and five times as likely to have type 2 diabetes. While it is uncertain whether they share the same pathophysiology, primary treatment is weight loss, increased exercise, and proper medication to prevent CVD [1, 2]. Metabolic syndrome is a combination of hypertension, hyperglycemia, and hyperlipidemia. Severe metabolic syndrome may develop into diabetes and patients with metabolic syndrome are over twice as at risk for atherosclerosis than the average population [3].

Hypertension, hyperglycemia, and hyperlipidemia are modern lifestyle diseases that occur due to individual physique (age, ethnicity and genetic factors), poor diet (high intake of oils and fats, cholesterol, calories, sodium, and sugar), poor habits (such as smoking and drinking), irregular sleep-wake cycles (staying awake all night, sleeping late, or excessive socialization), lack of exercise, and stress.

Previous studies have indicated that for rises in blood pressure from 115/75 to 185/115mmHg, every 20/10mmHg increase doubles the risk for CVD. Blood pressure should be maintained below 130/85mmHg; reducing blood pressure can lower the incidence rates for stroke 35-40%, for myocardial infarction 20-25%, and for heart failure over 50% [4]. Diabetes increases the burden on the heart as well as the risk of coronary

artery disease. Past literature has found that those with high cholesterol more likely suffer from coronary artery disease [5, 6].

The Taiwan 2010 health indicator white paper listed establishing a CVD prevention care system as a key measure. Recent studies rarely focus on how the number of conditions between hypertension, hyperglycemia, and hyperlipidemia affects the 10-year risk for CVD for both men and women. Therefore, this study investigated how hypertension, hyperglycemia, and hyperlipidemia influences the 10-year risk for CVD differently in middle-aged men and women in order to help early prevention and reduce deterioration of health.

## METHODS

This was a cross-sectional study that was conducted between August 2011 and December 2013 focusing on adults who had received a health examination at a regional hospital in Pingtung County, Taiwan. Data for this study, including basic information, physical examination data, and blood work, was collected after receipt of Institutional Review Board approval. Calculation of the 10-year risk for CVD was completed using data from the Framingham Heart Study [7]. All data, including age, gender, total cholesterol, high-density lipoprotein (HDL), smoking habit, systolic blood pressure, and current hypertension medication, was entered into a website and a computer was used to determine risk values. In this study,  $\leq 10\%$  was defined as low risk, 11-20% was defined as moderate risk, and  $>20\%$  was defined as high risk.

Metabolic syndrome status was defined according to the criteria set by the Health Promotion Administration, Ministry of Health and Welfare in 2007. Any three of the following five criteria were grounds for identifying metabolic syndrome:

(1) abdominal obesity: waist circumference (WC)  $\geq 90$  cm in men and  $\geq 80$  cm in women; (2) raised triglycerides (TG):  $\geq 150$  mg/dL; (3) reduced HDL-C: HDL-C  $<40$  mg/dL in men and  $<50$  mg/dL in women; (4) hypertension: blood pressure of at least 130/85mmHg or taking antihypertensive medication; and (5) raised fasting plasma glucose (FPG)  $\geq 100$  mg/dL and/or taking anti-glycemic medication.

The definitions for metabolic syndrome were used to determine hypertension (blood pressure over 130/85mmHg or current use of medication to reduce blood pressure), hyperglycemia (fasting blood sugar  $\geq 100$ mg/dL or current use of medication to reduce blood sugar), and hyperlipidemia (abnormal HDL (men:  $<40$ mg/dL; women:  $<50$ mg/dL) or triglycerides  $\geq 150$ mg/dL).

SPSS 17.0 software package was used for data processing and statistical analysis. Chi-square tests analyzed demographic characteristics, lifestyle habits, and metabolic syndrome and its components to examine

discrepancies in the 10-year risk for CVD between genders. Logistic regression analysis was also used to investigate the influence the number of conditions had on the 10-year risk for CVD.

## RESULTS

Data for 10,206 individuals were chosen from the 2011-2013 health examination databases. The effective sample was 8,957 after removing those who received multiple health checks and those with incomplete physiology, blood chemistry evaluations. Table 1 indicates that all variables reached statistical significant differences ( $p<.001$ ). The proportions of men at moderate risk for CVD (11-20%) and at high risk for CVD ( $>20\%$ ) were much higher than women (44.1% vs. 8.3% and 23.4% vs. 1.5%, respectively). Among the participants aged 65 or older, 39.5% were at moderate risk for CVD and 25.9% were at high risk for CVD; these were significantly higher than for those under the age of 65. Participants, who smoked, drank, or chewed betel nut had higher 10-year risk for CVD than those who did not. Participants with abnormal metabolic syndrome and its components (abdominal obesity, blood pressure, blood sugar, blood lipids, etc.) had higher 10-year risk for CVD ( $p<0.001$ ).

Table 2 divides the participants into those without hypertension, hyperglycemia, or hyperlipidemia and those with one, two, or all three of the conditions. Analysis of the 10-year risk for CVD found that for participants with CVD risk  $>20\%$ , their risk increased as the number of conditions increased (27.0% vs. 16.8% vs. 8.4% vs. 0.1%). Similar results were found when separating men and women; risk increased as the number of conditions increased (Table 3). The 10-year risk for CVD for women in this study tended to be lower; few participants had moderate or high risk. Therefore, great variation in logistic regression analysis results for women was seen when dividing the risk into low, moderate, and high. As such, this study only focused on men and defined 10-year risk for CVD  $\leq 10\%$  as low risk and  $>10\%$  as at risk. The number of conditions was held as a predictor for 10-year risk for CVD in regression analysis. After adjusting for age, smoking, drinking, and chewing betel nut, it was found that the 10-year risk for CVD odds ratios for participants with one, two, or three conditions were 3.44, 8.13, and 16.64 times higher, respectively, than for those who did not suffer from hypertension, hyperglycemia, or hyperlipidemia. It was clear that the 10-year risk for CVD increased as the number of conditions increased (Table-4).

## DISCUSSION

Past epidemiological studies have indicated that the prevalence of metabolic syndrome is increased for individuals who are men, in older age groups, obese, lack physical exercise, with low socio-economic status, and smoke in the US, Asia, Europe, and Mediterranean [8-13]. It has also been found that metabolic syndrome

is correlated to arteriosclerosis, CVD, type 2 diabetes, and mortality rate [14,15]. This study indicated that men, over the age of 65, smoke, drink, and chew betel nut have a higher 10-year risk for CVD. Participants with abnormal metabolic syndrome and its components (abdominal obesity, blood pressure, blood sugar, blood lipids, etc.) also had higher 10-year risk for CVD. A previous study on Americans with hypertension indicated that simultaneous control of blood pressure and low-density lipoprotein cholesterol (LDL-C) and HDL-C may prevent the majority of coronary heart disease events [16]. Hypertension and abnormal blood lipids have high prevalence rates in the US. Effective control can greatly reduce the future risk of cardiovascular events and mortality [7,17]. Previous research has also found that androgenic obesity increases the risk of CVD, hypertension, and diabetes mellitus [18,19]. Obesity is also an independent risk factor for CVD [20]. The research findings of this study were all similar to past studies.

Although the overall prevalence of coronary artery disease (CAD) is higher in men, clinical research is also gradually focusing on women with CAD [21-23]; CVD is also an important factor of morbidity and mortality for women [24, 25]. Therefore, results for the 10-year risk for CVD for women in this study are also worthy of note. Few studies have analyzed and compared the number of conditions and the 10-year risk for CVD. This study found that for both men and women, the 10-year risk for CVD increased as the number of conditions increased. It is worth noting that for women with 11-20% and >20% risk, 10-year risk for CVD clearly increased as the number of conditions increased.

However, as only 1.5% of the women in this study had a 10-year risk for CVD >20% and 90.2% were at low risk, this study only focused on predictors for 10-year risk for CVD in men. The results found that the 10-year risk for CVD odds ratios for participants with an increased number of conditions were higher than for those who did not suffer from hypertension, hyperglycemia, or hyperlipidemia.

Some past research have investigated how hypertension, hyperglycemia, and hyperlipidemia affect CVD independently, yet few have considered how multiple comorbid conditions influence the risk of CVD.

A Korean study pointed out that blood pressure has more impact on cardiovascular mortality than other factors [26]. It has been found that blood pressure also affects carotid atherosclerosis more so than other components of metabolic syndrome [27, 28]. A study on metabolic syndrome and heart structure and function in the Native American population indicated that hypertension and abdominal obesity were important

factors [29]. The cardiovascular mortality rate in the Asia-Pacific Region shows that 66% of CVD is due to hypertension [26]. Another study on stroke found that high blood pressure levels were associated with higher recurrent stroke risk over long-term follow-up [30].

Some longitudinal studies have indicated that CVD risk is correlated with fasting insulin and blood sugar concentrations [31-33]. Hyperglycemia can cause damage to lumen function of the blood vessels and quickens buildup of plaque and arteriosclerosis which narrows blood vessels. After years, chronic comorbidities of diabetes can lead to complications with small blood vessels (retinal arteries, nephropathy, peripheral circulation and neuropathies) and large blood vessels (coronary artery, cerebral arteries, and peripheral arteries). Thus, the American Heart Association has adopted coronary heart disease treatment standards in the treatment of diabetes; proper glycemic control and treatment for other risk factors (hypertension, hyperlipidemia, smoking, and weight) can reduce the risk for CVD [34].

High cholesterol, especially LDL-C, vessel lumen cell function breaks down and is damaged allowing more LDL-C into the lumen layer which causes a series of arteriosclerosis related reactions; macrophages repeatedly oxidized LDL-C until they turn into foam cells and later arteriosclerosis plaque [35]. If patients also have other risk factors, such as smoking, hypertension, diabetes, or old age (men >45 years, women >55 years), or have HDL-C levels <40 mg/dL, lumen cell function will deteriorate quicker, accelerating arteriosclerosis formation. Diabetes, obesity, and smoking further change cholesterol, lower HDL-C levels and cause hypertriglyceridemia, quicken the onset of arteriosclerosis [36].

These studies indicate that hypertension, hyperglycemia, and hyperlipidemia affect the risk for heart disease. This study further showed that a higher number of comorbid conditions increases the 10-year risk for CVD.

This study had several limitations. As the participants in this study were individuals aged 40 or older in a region of Pingtung County, Taiwan, these results cannot be generalized to other populations. Also, due to the nature of this cross-sectional study, information regarding some risk factors may be insufficient, thus limiting the inferences that can be made concerning the causal relationship. Continued follow-up in the future could provide more rigorous results. However, in terms of the increased CVD risk, the prevalence of hypertension, hyperglycemia, and hyperlipidemia are consistent with the results from other studies. Therefore, effective control of these conditions can help reduce the fatality risk of CVD.

**Table-1: Analysis of the effect of demographic characteristics, lifestyle habits, and metabolic syndrome and its components on the 10-year risk for CVD (n=8957)**

Variable	10-year risk for CVD			P* value
	≤10%	11-20%	>20%	
Gender				<.001
Male	1526 (32.6)	2064 (44.1)	1095 (23.4)	
Female	3852 (90.2)	354 (8.3)	66 (1.5)	
Age				<.001
<65	3973 (82.1)	775 (16.0)	93 (1.9)	
≥65	1405 (34.1)	1643 (39.9)	1068 (25.9)	
Smoking				<.001
No	5142 (64.1)	1909 (23.8)	977 (12.2)	
Yes	236 (25.4)	509 (54.8)	184 (19.8)	
Drinking				<.001
No	5271 (60.5)	2317 (26.6)	1126 (12.9)	
Yes	107 (44.0)	101 (41.6)	35 (14.4)	
Chewing betel nut				<.001
No	5327 (60.3)	2367 (26.8)	1138 (12.9)	
Yes	51 (40.8)	51 (40.8)	23 (18.4)	
Waist measurement				<.001
Normal	3119 (62.6)	1325 (26.6)	541 (10.9)	
Abnormal	2259 (56.9)	1093 (27.5)	620 (15.6)	
Obese				<.001
18.5 ≤ BMI < 26.9 Kg/m <sup>2</sup>	4114 (61.2)	1778 (26.4)	834 (12.4)	
BMI ≥ 27kg/m <sup>2</sup>	1264 (56.7)	640 (28.7)	327 (14.7)	
Blood pressure (mmHg) <sup>a</sup>				<.001
Normal	2629 (78.5)	655 (19.6)	64 (1.9)	
Abnormal (≥130/85mmHg)	2749 (49.0)	1763 (31.4)	1097 (19.6)	
Blood sugar (mg/dL) <sup>b</sup>				<.001
Normal	3322 (66.3)	1191 (23.8)	499 (10.0)	
Abnormal (≥100mg/dL)	2056 (52.1)	1227 (31.1)	662 (16.8)	
HDL-C (mg/dL)				<.001
Normal	3862 (62.3)	1729 (27.9)	608 (9.8)	
Abnormal	1516 (55.0)	689 (25.0)	553 (20.1)	
Triglycerides (mg/dL)				<.001
Normal	4148 (63.0)	1683 (25.6)	748 (11.4)	
Abnormal (≥150mg/dL)	1230 (51.7)	735 (30.9)	413 (17.4)	
Metabolic syndrome				<.001
No (<3 abnormal)	3735 (66.6)	1413 (25.2)	461 (8.2)	
Yes (≥3 abnormal)	1643 (49.1)	1005 (30.0)	700 (20.9)	

<sup>a</sup> Abnormal blood pressure is defined as ≥130/85mmHg or current use of medication to reduce blood pressure

<sup>b</sup> Abnormal blood sugar is defined as ≥100mg/dL or current use of medication to reduce blood sugar

**Table-2: Analysis of the effect the number of conditions among hypertension, hyperglycemia, and hyperlipidemia on the 10-year risk for CHD**

Variable	10-year risk for CHD			P* value
	≤10% (n=5378)	11-20% (n=2418)	>20% (n=1161)	
Hypertension, hyperglycemia, and hyperlipidemia				<.001
Normal	1283 (85.0)	224 (14.8)	2 (0.1)	
Abnormal (one condition)	1892 (64.8)	780 (26.7)	246 (8.4)	
Abnormal (two conditions)	1576 (51.8)	955 (31.4)	511 (16.8)	
Abnormal (three conditions)	627 (42.1)	459 (30.8)	402 (27.0)	

Note

1. Abnormal blood pressure was defined as blood pressure over 130/85mmHg or current use of medication to reduce blood pressure.

2. Abnormal blood sugar was defined as fasting blood sugar  $\geq 100$ mg/dL or current use of medication to reduce blood sugar.
3. Hyperlipidemia was defined as abnormal HDL (men:  $<40$ mg/dL; women:  $<50$ mg/dL) or triglycerides  $\geq 150$ mg/dL.

**Table 3 Analysis of the differences in effect the number of conditions among hypertension, hyperglycemia, and hyperlipidemia on the 10-year risk for CVD between men and women**

Variable	Men (n=4685) 10-year risk for CVD				Women (n=4272) 10-year risk for CVD			
	$\leq 10\%$ (n=1526)	11-20% (n=2064)	$>20\%$ (1095)	<i>P</i> * <i>value</i>	$\leq 10\%$ (n=3852)	11-20% (n=354)	$>20\%$ (n=66)	<i>P</i> * <i>value</i>
Hypertension, hyperglycemia, and hyperlipidemia				$<.001$				$<.001$
Normal	383 (62.9)	224 (36.8)	2 (0.3)		900 (100.0)	0 (0)	0 (0)	
Abnormal (one condition)	565 (36.8)	726 (47.3)	245 (16.0)		1327 (96.0)	54 (3.9)	1 (0.1)	
Abnormal (two conditions)	430 (24.9)	806 (46.7)	489 (28.3)		1146 (87.0)	149 (11.3)	22 (1.7)	
Abnormal (three conditions)	148 (18.2)	308 (37.8)	359 (44.0)		479 (71.2)	151 (22.4)	43 (6.4)	

Note:

1. Abnormal blood pressure was defined as blood pressure over 130/85mmHg or current use of medication to reduce blood pressure.
2. Abnormal blood sugar was defined as fasting blood sugar  $\geq 100$ mg/dL or current use of medication to reduce blood sugar.
3. Hyperlipidemia was defined as abnormal HDL (men:  $<40$ mg/dL; women:  $<50$ mg/dL) or triglycerides  $\geq 150$ mg/dL.

**Table-4: Analysis of the effect the number of conditions among hypertension, hyperglycemia, and hyperlipidemia on the 10-year risk for CVD in men (n=4685)**

Variable	$\beta$	wald	OR (95% CI)	p value
Constant	-2.92	404.54		$<.001$
1	1.23	71.78	3.44 (2.58-4.57)	$<.001$
2	2.10	189.77	8.13 (6.04-10.96)	$<.001$
3	2.81	245.23	16.64 (11.70-23.66)	$<.001$

Note 1: Dependent variables: Using the low-risk  $\leq 10\%$  group as the reference group. Note 2: The variables included in logistic regression analysis were age, smoking, drinking, chewing betel nut, and (hypertension, hyperglycemia, and hyperlipidemia (participants with none were the reference group; those with one condition were labeled 1, those with two conditions were labeled 2, and those with three conditions were labeled 3)

## REFERENCES

1. Eckel RH, Grundy SM, Zimmet PZ; The metabolic syndrome. The Lancet, 2005; 365(9468): 1415-1428.
2. Cornier MA, Dabelea D, Hernandez TL, Lindstrom RC, Steig AJ, Stob NR, Eckel RH, et al.; The metabolic syndrome. Endocrine reviews, 2008; 29(7): 777-822.
3. Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, Franklin BA, Costa F; Diagnosis and management of the metabolic syndrome an American Heart Association/National Heart, Lung, and Blood Institute scientific statement. Circulation, 2005; 112(17): 2735-2752.
4. Ministry of Health and Welfare Top ten causes of death in Taiwan, 2004.
5. Wilson PWF, D'Agostino RB, Levy D, Belanger AM, Silbershatz H, Kannel WB; Prediction of coronary heart disease using risk factor categories. Circulation, 1998; 97:1837-1847.
6. Stamler J, Wentworth D, Neaton JD; for the MRFIT Research Group. Is relationship between serum cholesterol and risk of premature death from coronary heart disease continuous and graded? Findings in 356 222 primary screenees of the Multiple Risk Factor Intervention Trial (MRFIT). JAMA, 1986; 256 :2823-2828.
7. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive Summary of the Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). JAMA. 2001 May, 16; 285(19): 2486-2497.

8. Buckland G, Salas-Salvadó J, Roure E, Bulló M, Serra-Majem L; Sociodemographic risk factors associated with metabolic syndrome in a Mediterranean population. *Public Health Nutr*, 2008;11(12):1372-1378.
9. Kuzuya M, Ando F, Iguchi A, Shimokata H; Age-specific change of prevalence of metabolic syndrome: longitudinal observation of large Japanese cohort. *Atherosclerosis*, 2006; 191: 305-312.
10. Hillier TA, Fagot-Campagna A, Eschwege E, Vol S, Cailleau M, Balkau B; the DESIR Study Group (2006) Weight change and changes in the metabolic syndrome as the French population moves towards overweight: The DESIR cohort. *Int J Epidemiol*, 2006; 35: 190-196.
11. Ford ES, Giles WH, Dietz WH; Prevalence of the metabolic syndrome among US adults: findings from the Third National Health and Nutrition Examination Survey. *JAMA*, 2002; 287: 356-359.
12. Brouwer B, Visseren F, van der Graaf Y, Group SS; The effect of leisure-time physical activity on the presence of metabolic syndrome in patients with manifest arterial disease. The SMART study. *Am Heart J*, 2007; 154: 1146-1152.
13. Masulli M, Riccardi G, Galasso R, Vaccaro O; Relationship between smoking habits and the features of the metabolic syndrome in a non-diabetic population. *Nutr Metab Cardiovasc Dis*, 2006; 16: 364-370.
14. Ford E; The metabolic syndrome and mortality from cardiovascular disease and all-causes: findings from the National Health and Nutrition Examination Survey II Mortality Study. *Atherosclerosis*, 2004; 173: 309-314.
15. Gami AS, Witt BJ, Howard DE, Erwin PJ, Gami LA, Somers VK, Montori VM; Metabolic syndrome and risk of incident cardiovascular events and death: a systematic review and meta-analysis of longitudinal studies. *J Am Coll Cardiol*, 2007; 49: 403-414.
16. Lopez VA, Franklin SS, Tang S, Wong ND; Coronary heart disease events preventable by control of blood pressure and lipids in US adults with hypertension. *J Clin Hypertens (Greenwich)*, 2007;9(6) :436-443.
17. The Seventh Report of the Joint National Committee on Prevention, Detection, valuation, and Treatment of High Blood Pressure: the JNC 7 report. *JAMA*, 2003; 289: 2560-2572.
18. Lee CMY, Huxley RR, Wildman RP, Woodward M; Indices of abdominal obesity are better discriminators of cardiovascular risk factors than BMI: a meta-analysis. *J Clin Epidemiol*, 2008; 61(7): 646-53.
19. Costa EC, Soares EMM, Lemos TMAM, Maranhão TMO, Azevedo GD; Índices de Obesidade Central e Fatores de Risco Cardiovascular na Síndrome dos Ovários Policísticos. *Arq Bras Cardiol*, 2010; 94(5): 633-638.
20. Cabrera MA; Relationship between body mass index, waist circumference, and waist-to-hip ratio and mortality in elderly women: a 5-year follow-up study. *Cad Saúde Pública*, 2005; 21(3):71-73.
21. Healy B; The yentl syndrome. *The New England Journal of Medicine*. 1991; 325:274-276. [PubMed: 2057027]
22. Vaccarino V; Ischemic Heart Disease in Women: Many Questions, Few Facts. *Circulation: Cardiovascular Quality and Outcomes*; 2010; 3: 111-115.
23. Izadnegahdar M, Norris C, Kaul P, Pilote L, Humphries KH; Basis for Sex-Dependent Outcomes in Acute Coronary Syndrome. *Canadian Journal of Cardiology*, 2014:1-8.
24. Manuel DG, Leung M, Nguyen K, Tanuseputro P, Johansen H; Burden of cardiovascular disease in Canada. *Canadian Journal of Cardiology*, 2003; 19: 997-1004.
25. Roger VL, Go AS, Lloyd-Jones DM, Benjamin EJ, Berry JD, Borden WB; Writing Group Members; on behalf of the American Heart Association Statistics Committee and Stroke Statistics Subcommittee, On behalf of the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Heart Disease and Stroke Statistics--2012 Update: A Report from the American Heart Association*. *Circulation*; 2012; 125:e2-e220.
26. Martiniuk AL, Lee CM, Lawes CM, Ueshima H, Suh I, Lam TH; Asia-Pacific Cohort Studies Collaboration. Hypertension: its prevalence and population-attributable fraction for mortality from cardiovascular disease in the Asia-Pacific region. *Journal of hypertension*, 2007; 25(1):73-79.
27. Irace C, Cortese C, Fiaschi E, Carallo C, Sesti G, Farinaro E, Gnasso A; Components of the Metabolic Syndrome and Carotid Atherosclerosis Role of Elevated Blood Pressure. *Hypertension*, 2005; 45(4): 597-601.
28. Su TC, Jeng JS, Chien KL, Sung FC, Hsu HC, Lee YT; Hypertension status is the major determinant of carotid atherosclerosis: a community-based study in Taiwan. *Stroke*, 2001; 32: 2265-2271.
29. Chinali M, Devereux RB, Howard BV, Roman MJ, Bella JN, Liu JE, de Simone G, et al.; Comparison of cardiac structure and function in American Indians with and without the metabolic syndrome (the Strong Heart Study). *The American journal of cardiology*, 2004; 93(1): 40-44.
30. Kaplan RC, Tirschwell DL, Longstreth WT Jr., Manolio TA, Heckbert SR, LeValley AJ et al.; Blood pressure level and outcomes in adults

- aged 65 and older with prior ischemic stroke , 2006; 54(9): 1309-1316.
31. Hanley AJ, Williams K, Stern MP, Haffner SM; Homeostasis model assessment of insulin resistance in relation to the incidence of cardiovascular disease: the San Antonio Heart Study. *Diabetes Care*, 2002; 25:1177–1184.
  32. Hedblad B, Nilsson P, Engstrom G, Berglund G, Janzon L; Insulin resistance in non-diabetic subjects is associated with increased incidence of myocardial infarction and death. *Diabet Med*, 2002; 19: 470–475.
  33. Robins SJ, Rubins HB, Faas FH, Schaefer EJ, Elam MB, Anderson JW, Collins D; Insulin resistance and cardiovascular events with low HDL cholesterol: the Veterans Affairs HDL Intervention Trial (VA-HIT). *Diabetes Care*, 2003; 26:1513–1517.
  34. Alberti KGMM, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, et al.; Harmonizing the Metabolic Syndrome 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. *Circulation*, 2009; 120(16): 1640-1645.
  35. Diaz MN, Frei B, Vita JA, Keaney JF Jr. Antioxidants and atherosclerotic heart disease. *N Engl J Med*, 1997; 337:408-416.
  36. Faxon DP, Fuster V, Libby P, Beckman JA, Hiatt WR, Thompson RW, et al.; Atherosclerotic Vascular Disease Conference Writing Group III: Pathophysiology. *Circulation*, 2004; 109: 2617-2625.