Korean J Clin Lab Sci. 2019;51(4):484-494

https://doi.org/10.15324/kjcls.2019.51.4.484

Korean Society for Clinical Laboratory Science

Korean Journal of CLINICAL LABORATORY SCIENCE

ORIGINAL ARTICLE

Relationship of Riboflavin and Niacin with Cardiovascular Disease

Ji Yeong Ahn[1,†], In Sik Kim[1,2,†], Ji-Sook Lee[3]

[1]Department of Biomedical Laboratory Science, School of Medicine, Eulji University, Daejeon, Korea
[2]Department of Senior Healthcare, BK21 Plus Program, Graduate School, Eulji University, Dajeon, Korea
[3]Department of Clinical Laboratory Science, Wonkwang Health Science University, Iksan, Korea

심혈관 질환과 리보플라빈 및 나이아신과의 상관성 연구

안지영[1,†], 김인식[1,2,†], 이지숙[3]

[1]을지대학교 대전캠퍼스 임상병리학과, [2]을지대학교 대전캠퍼스 BK21 플러스 프로그램 시니어헬스케어학과, [3]원광보건대학교 임상병리과

ARTICLE INFO

Received September 24, 2019
Revised 1st October 18, 2019
Revised 2nd October 31, 2019
Accepted November 3, 2019

Key words
Riboflavin
Niacin
Cardiovascular disease

ABSTRACT

Cardiovascular disease is caused by different factors. These factors include innateness factors such as aging, biological factors such as high blood pressure, and environmental factors such as stress. This study examined the factors associated with cardiovascular disease and the ways to reduce its prevalence by analyzing the data within the Korean National Health and Nutrition Examination Reports from 2013 to 2017, and particularly the survey and examination data for people over 50 years old. The study population was divided into two groups: members of the first group consumed riboflavin and niacin at the recommended rate while those in the second group did not. Riboflavin intake was correlated with hypertension, hyperglycemia, and a low HDL-cholesterol level, whereas niacin intake was correlated with hypertension, hyperglycemia, waist size, and a low HDL-cholesterol level. The combination of niacin and riboflavin intakes was correlated with hypertension, hyperglycemia, waist size, and a low HDL-cholesterol level ($P<0.05$). The combined intake of the recommended levels of riboflavin and niacin reduced the average physiological factor abnormality rate to 80%. Taken together, the beneficial effects of riboflavin and niacin can reduce the prevalence of cardiovascular disease.

INTRODUCTION

Cardiovascular disease encompasses a vast range of diseases of the heart and blood vessels. Cardiovascular disease is one of the three main causes of death in Korea, according to the National Statistical Office reports in 2017. According to the report, the cause of death due to three major disease is 46.4%, and the cause of death from heart disease takes 10.8%. The types of cardiovascular disease in this research are ischemic cardiovascular disease such as angina pectoris and myocardial infarction. In particular, the older people have a high death rate of circulatory system disease, the rate accelerates after age 70 [1-3]. One disease of the circulatory system, cardiovascular disease is caused by coronary artery contraction, which can be caused by smoking, hypertension, hyperlipidemia, diabetes, obesity, advanced age, and family history [4-6].

The core function of riboflavin is that of coenzyme

* Corresponding author: Ji-Sook Lee
Department of Clinical Laboratory Science, Wonkwang Health Science University, 501 Iksan-daero, Iksan 54538, Korea
E-mail: jslee1216@wu.ac.kr
* ORCID: https://orcid.org/0000-0001-5397-9142
†These authors contributed equally to this work.

pISSN 1738-3544 eISSN 2288-1662

for metabolism, and riboflavin is closely related to fat metabolism. Deficiency of riboflavin lowers fat acid oxidation and accumulates triglycerides [7-9]. Niacin contributes to reducing the cholesterol rate and to decreasing the incidence of cardiovascular disease of the coronary artery [10-12]. In particular, one-third of Korean adults showed inadequate riboflavin status [13]. On the basis of these functions, checked that the two nutrients are related to cardiovascular disease.

This research aims to confirm the correlation between physiological factors such as hypertension and cholesterol rate with cardiovascular disease from results of Korean National Health and Nutrition Examination reports (2013~2017) and to further explore other physiological factors and their correlation. In addition, the study also investigates the influence of riboflavin and niacin intake and relevance to reducing prevalence of cardiovascular disease.

MATERIALS AND METHODS

1. Subjects

The Korean National Health and Nutrition Examination is a nation-wide nutrition and health examination based on Section 16 of the National Health Promotion Act that was issued in 1995 [14]. It combines the former separately conducted studies: National Nutrition Examination and National Health Examination. The National Health Examination covers public health, behaviors concerning health, and food and nutrition intake on a national scale with city-unit significance. It is both a survey and health examination that has both validity and reliability. This study quotes the 11,958 men and women who were over 50 years old and who did not answer “unaware” or “no reply” to the 2013~2017 (sixth and seventh) Korean National Health and Nutrition Examination reports (2013-07CON-03-4C and 2013-12EXP-03-5C).

2. Measurement items

The content includes age, sex, cardiovascular disease including myocardial infarction or angina), hypertension, hyperglycemia, waist size, triglyceride, HDL, LDL, total cholesterol and other contents such as riboflavin, and niacin consumption. Intake of riboflavin and niacin from individual dish consumed by each subject was calculated. Among them, LDL was excluded due to unknown value. Myocardial infarction and angina were measured with a doctor’s diagnosis. Total cholesterol was measured with normal rate, with >200 mg/dL indicated as abnormal (Diagnostic criteria of dyslipidemia The Korean Society of Lipid and Atherosclerosis). As for hypertension, hyperglycemia, waist size, hypertriglyceridemia, low HDL-cholesterol are an important factor in metabolic syndrome. Thus, table of metabolic syndrome was used as indicators. If the rate was higher than 130/85 mmHg, “hypertension” was indicated; if the fasting blood sugar level was above 100 mg/dL or taking diabetic medication, “hyperglycemia” was indicated; As for waist size, men above 90 cm and women above 85 cm were indicated as “abnormal”, the triglyceride rate above 150 mg/dL was marked as “hypertriglyceridemia”, and a low HDL-cholesterol level of below 40 mg/dL for men, and 50 mg/dL for women was indicated [15]. Intake standard of riboflavin and niacin was based on 2015 dietary reference intakes for Koreans: riboflavin intake for men of 1.5 mg/day, for women of 1.2 mg/day, and niacin intake for men of 16 mg NE/day, and for women 14 mg NE/day. If the intake was above the standard level, it was indicated as being “satisfactory,” and if below, the level was indicated as “unsatisfactory” [16].

3. Statistical analysis

Correlation was confirmed by cross-analysis on cardiovascular disease and physiological factors. Hazard ration estimation was detected by logistic regression analysis. People with cardiovascular disease have a higher population of older people, and to control the study, the survey target was set to age 50 and above because there is few people with the disease below age 50. Other physiological factors and nutritional research cross-examination and logistic regression analysis were methods to identify the most closely related nutrition. Finally, the correlation between riboflavin and niacin intake and cardiovascular disease was determined with cross-analysis and then checked prevalence rate and risks with logistic regression analysis. This study was conducted with SPSS Statistics 25 with a significance level of P<0.05.

RESULTS

1. General characteristics of research subjects

The variables and frequency analysis for this study is shown in Table 1. The survey was conducted on 11,958 people: 5,099 men (47.4%) and 6,859 women (52.6%). The subjects were over 50 years old: 48.3% were in their 50s, 28% were in their 60s, and 23.7% were in their 70s and older. Riboflavin and niacin were divided into two categories—whether consumed or not. Riboflavin's intake amounted to 38.8%; the non-takers were 61.2%. Niacin's intake amounted to 38.5%; the non-takers were 61.5%. For both riboflavin and niacin, 26.1% consumed both, 25.1% took only one, and non-takers were 48.8%. For cardiovascular disease, the prevalence rate was 5%, and normal was 95%. Answers to questions on hypertension, hyperglycemia, hypertriglyceridemia, and low HDL-cholesterol were divided into yes and no based on the metabolic rate. For hypertension, 39.7% responded yes, and 60.3% responded no. For hyperglycemia, 46.7% responded yes, while 53.3% responded no. For hypertriglyceridemia, 33.6% responded yes, and 66.4% responded no. For low HDL-cholesterol, 39% responded yes, and 61% responded no. For waist size and total cholesterol level, the two categories were normal and abnormal, and for waist size, 32% of respondents were abnormal, while 68% were normal. For total cholesterol, 41.4% were abnormal, and 58.6% were normal.

Table 1. General characteristics of research subjects

Variables		N (%)
Sex	Men	5,099 (47.4)
	Women	6,859 (52.6)
Age group	50s	4,345 (48.3)
	60s	4,035 (28.0)
	70s or older	3,578 (23.7)
Riboflavin RI (<1.5 mg/day, men; <1.2 mg/day, women)	Yes	4,356 (38.8)
	No	7,602 (61.2)
Niacin RI (<16 mg/day, men; <14 mg/day, women)	Yes	4,242 (38.5)
	No	7,716 (61.5)
Riboflavin+Niacin RI	Both	2,842 (26.1)
	One	2,914 (25.1)
	None	6,202 (48.8)
Cardiovascular disease	Yes	599 (5)
	No	11,359 (95)
Hypertension (>130/85 mmHg)	Yes	4,852 (39.7)
	No	7,106 (60.3)
Hyperglycemia (>100 mg/mL)	Yes	5,577 (46.7)
	No	6,381 (53.3)
Total cholesterol (>200 mg/mL)	Abnormal	4,816 (41.4)
	Normal	7,142 (58.6)
Hypertriglyceridemia (>150 mg/mL)	Yes	3,921 (33.6)
	No	8,037 (66.4)
Low HDL cholesterol (<40 mg/mL)	Yes	4,896 (39)
	No	7,062 (61)
Waist measurement (>90 cm, men; >85 cm, women)	Abnormal	4,004 (32)
	Normal	7,954 (68)
Total		11,958 (100.0)

Abbreviations: RI, Recommended intake; HDL, High density lipoprotein.

2. Relationship of physiological factors with cardiovascular disease

1) Comparison of cardiovascular disease according to physiological factors

As for the prevalence rate, among 11,958 respondents, 599 people (5%) responded yes, while 11,359 people (95%) responded no. After a careful examination on the relationship between cardiovascular disease and numerous physiological factors with statistical analysis, hypertension, hyperglycemia, waist size, and low HDL-cholesterol showed a meaningful difference (P<0.001).

Assumed to be the most closely related, hypertriglyceridemia did not show a significant difference, and total cholesterol had shown a meaningful result (Table 2).

2) Effects of physiological factors on cardiovascular disease

To investigate the correlation between prevalence rate of cardiovascular disease and physiological

Table 2. Comparison of cardiovascular disease according to physiological factors

		Cardiovascular disease		Total	P
		Yes	No		
Hypertension	Yes	264 (4.7)	4,588 (95.3)	4,852 (100.0)	<0.001
	No	335 (4.1)	6,771 (95.9)	7,106 (100.0)	
Hyperglycemia	Yes	356 (5.5)	5,221 (94.5)	5,577 (100.0)	<0.001
	No	243 (3.3)	6,138 (96.7)	6,381 (100.0)	
Total cholesterol	Abnormal	114 (2.0)	4,702 (98.0)	4,816 (100.0)	<0.001
	Normal	485 (6.0)	6,657 (94.0)	7,142 (100.0)	
Hypertriglyceridemia	Yes	208 (4.6)	3,713 (95.4)	3,921 (100.0)	0.341
	No	391 (4.2)	7,646 (95.8)	8,037 (100.0)	
Low HDL cholesterol	Yes	290 (5.4)	4,606 (94.6)	4,896 (100.0)	<0.001
	No	309 (3.7)	6,753 (96.3)	7,062 (100.0)	
Waist measurement	Abnormal	264 (5.8)	3,740 (94.2)	4,004 (100.0)	<0.001
	Normal	335 (3.6)	7,619 (96.4)	7,954 (100.0)	
Total		599 (5)	11,359 (95)	11,958 (100.0)	

Abbreviations: See Table 1.

Table 3. Effects of physiological factors on cardiovascular disease

			OR	95% CI		P
				LLCI	ULCI	
Cardio vascular disease	Hypertension	Yes	1.164	0.956	1.417	0.130
		No	(reference)			
	Hyperglycemia	Yes	1.615	1.340	1.947	<0.001
		No	(reference)			
	Total cholesterol	Abnormal	0.331	0.264	0.416	<0.001
		Normal	(reference)			
	Hypertriglyceridemia	Yes	1.058	0.867	1.290	0.580
		No	(reference)			
	Low HDL cholesterol	Yes	1.602	1.329	1.930	<0.001
		No	(reference)			
	Waist measurement	Abnormal	1.663	1.340	1.947	<0.001
		Normal	(reference)			

Abbreviations: See Table 1.

factors, an odds ratio was used, and as a result, hyperglycemia, waist size and low HDL-cholesterol showed a meaningful difference (P<0.001). People with hypertension were 1.2 times more likely to suffer from cardiovascular disease than those who did not, and this did not and showed a significant gap (OR=1.164, P>0.05). People with hyperglycemia were 1.6 times more likely than those who did not and showed a meaningful rate (OR=1.615, P<0.001). Those who had abnormal waist size had a 1.7 times higher prevalence rate and showed an important difference (OR=1.663, P<0.001). People with hypertriglyceridemia did not show a meaningful difference (OR=1.058, P> 0.05). Those with low HDL-cholesterol were 1.6 times more likely to suffer from cardiovascular disease than those who did not and show an important difference (OR=1.602, P<0.001). Total cholesterol had shown important results but also had the opposite result from expectation abnormal people had a 0.3 times lower prevalence rate of cardiovascular disease (OR=0.331, P<0.001) (Table 3).

3. Relationship of riboflavin and niacin with physiological factors

1) Comparison of physiological factors according to recommended intake of riboflavin

Among the 11,958 respondents, 4,356 people consumed riboflavin above the standard level, and

7,602 did not. The correlation between intake of standard riboflavin and other physiological factors showed an important difference for hypertension, hyperglycemia and low HDL-cholesterol (P<0.05). Waist size and hypertriglyceridemia did not indicate an important difference, and total cholesterol showed an important level (Table 4).

2) Comparison of physiological factors according to recommended intake of niacin

Among the 11,958 respondents, 4,242 people consumed niacin above the standard level, and 7,716 did not. The correlation between intake of standard niacin and other physiological factors showed an important difference for hypertension, hyperglycemia, waist size and low HDL-cholesterol (P<0.05). Hyper-triglyceridemia and total cholesterol did not yield meaningful results (Table 5).

3) Comparison of physiological factors according to recommended intake of riboflavin and niacin

Among the 11,958 respondents, 2,842 people consumed both riboflavin and niacin above the standard level, while 2,914 people consumed either nutrient, and 6,202 people consumed neither. The correlation between intake of standard riboflavin and

Table 4. Comparison of physiological factors according to recommended intake of riboflavin

		Riboflavin RI		Total	*P*
		Yes	No		
Hypertension	Yes	1,620 (33.3)	3,232 (66.7)	4,852 (100.0)	<0.001
	No	2,736 (38.5)	4,370 (61.5)	7,106 (100.0)	
Hyperglycemia	Yes	1,949 (34.9)	3,628 (65.1)	5,577 (100.0)	0.007
	No	2,407 (37.7)	3,974 (62.3)	6,381 (100.0)	
Total cholesterol	Abnormal	1,899 (39.4)	2,917 (60.6)	4,816 (100.0)	<0.001
	Normal	2,457 (34.4)	4,685 (65.6)	7,142 (100.0)	
Hypertriglyceridemia	Yes	1,385 (35.3)	2,536 (64.6)	3,921 (100.0)	0.646
	No	2,971 (37)	5,066 (63)	8,037 (100.0)	
Low HDL cholesterol	Yes	1,648 (33.7)	3,248 (66.3)	4,896 (100.0)	<0.001
	No	2,708 (38.3)	4,354 (59.3)	7,062 (100.0)	
Waist measurement	Abnormal	1,384 (34.6)	2,620 (65.4)	4,004 (100.0)	0.078
	Normal	2,972 (37.4)	4,982 (62.6)	7,954 (100.0)	
Total		4,356 (36.4)	7,602 (63.6)	11,958 (100.0)	

Abbreviations: See Table 1.

Table 5. Comparison of physiological factors according to recommended intake of niacin

		Niacin RI		Total	*P*
		Yes	No		
Hypertension	Yes	1,605 (33.1)	3,247 (66.9)	4,852 (100.0)	0.017
	No	2,637 (37.1)	4,469 (62.9)	7,106 (100.0)	
Hyperglycemia	Yes	1,907 (34.2)	3,670 (65.8)	5,577 (100.0)	0.040
	No	2,335 (36.6)	4,046 (63.4)	6,381 (100.0)	
Total cholesterol	Abnormal	1,721 (35.7)	3,095 (64.3)	4,816 (100.0)	0.679
	normal	2,521 (35.3)	4,621 (64.7)	7,142 (100.0)	
Hypertriglyceridemia	Yes	1,336 (34.1)	2,585 (65.9)	3,921 (100.0)	0.519
	No	2,906 (36.2)	5,131 (63.8)	8,037 (100.0)	
Low HDL cholesterol	Yes	1,557 (31.8)	3,339 (68.2)	4,896 (100.0)	<0.001
	No	2,685 (38)	4,377 (62)	7,062 (100.0)	
Waist measurement	Abnormal	1,302 (32.5)	2,702 (67.5)	4,004 (100.0)	0.001
	Normal	2,940 (37)	5,014 (63)	7,954 (100.0)	
Total		4,242 (35.5)	7,716 (64.5)	11,958 (100.0)	

Abbreviations: See Table 1.

niacin and other physiological factors showed an important difference for hypertension, hyperglycemia, waist size and low HDL-cholesterol (P<0.05). Hypertriglyceridemia and total cholesterol did not yield meaningful results (Table 6).

4) Effects of riboflavin and niacin on physiological factors

To investigate the contributing effect of standard-level intake of riboflavin and niacin on normal and abnormal results of physiological factors, an odds ratio was used. Hypertension, hyperglycemia, and low HDL-cholesterol showed important differences (P<0.01). On riboflavin's effect alone, hypertension was reduced to 80% (OR=0.808, P<0.001), hyperglycemia was reduced to 88% (OR=0.881, P<0.01), and low HDL-cholesterol was reduced to 84% and showed significant results (OR=0.840, P<0.001). Total cholesterol showed an important difference but increased to 120% (OR=1.212, P<0.001). On niacin's effect alone, hypertension was reduced to 88% (OR=0.879, P<0.01), hyperglycemia was reduced to 85% (OR=0.848, P<0.001), abnormal waist size was reduced to 88% (OR=0.879, P<0.01), and low HDL-cholesterol was reduced to 84%, showing an important difference (OR=0.839, P<0.001). Hypertriglyceridemia (OR=0.971, P>0.05) and total cholesterol (OR=1.046, P>0.05) did not show important difference. On both riboflavin and niacin's effect, when both nutrients were consumed on a standard level, hypertension was reduced to 79% (OR=0.792, P<0.001), hyperglycemia was diminished to 81% (OR=0.813, P<0.001), and abnormal waist size was reduced to 84% (OR=0.844, P<0.01), and low HDL-cholesterol was reduced to 80% and showed a meaningful difference (OR=0.799, P<0.001). Hypertriglyceridemia did not show a meaningful difference (OR=0.920, P>0.05). Total cholesterol showed significant results, but the abnormal rate increased (OR=1.168, P<0.01) (Table 7).

4. Relationship of riboflavin and niacin with cardiovascular disease

1) Comparison of cardiovascular disease according to recommended intake of riboflavin and niacin

Among the 11,958 respondents, 599 people (5%) responded yes on cardiovascular disease diagnosis, while 11,359 (95%) did not. Among those 599 people, 174 people (3.3%) consumed riboflavin, and 425 people (5%) did not. Within the prevalent 599 people, 168 people (3.3%) consumed niacin, and 431 people (4.9%) did not. If we explore both nutrients, 97 people (2.7%) consumed both nutrients, while 148 people (4.5%) consumed either of the nutrients, and 354 people (5.1%) consumed neither of the nutrients. The correlation between intake of standard riboflavin and niacin and

Table 6. Comparison of physiologic factors according to recommended intake of riboflavin and niacin

		Riboflavin and Niacin RI			Total	P
		Both	One	None		
Hyper tension	Yes	1,035 (21.3)	1,155 (23.8)	2,662 (54.9)	4,852 (100.0)	<0.001
	No	1,807 (25.4)	1,759 (24.8)	3,540 (49.8)	7,106 (100.0)	
Hyper glycemia	Yes	1,249 (22.4)	1,358 (24.3)	2,970 (53.3)	5,577 (100.0)	0.010
	No	1,593 (25)	1,556 (24.4)	3,232 (50.6)	6,381 (100.0)	
Total Cholesterol	Abnormal	1,210 (25.1)	1,200 (24.9)	2,406 (50)	4,816 (100.0)	0.079
	Normal	1,632 (22.8)	1,714 (24)	3,796 (53.2)	7,142 (100.0)	
Hypertriglyceridemia	Yes	887 (22.6)	947 (24.2)	2,087 (53.2)	3,921 (100.0)	0.815
	No	1,955 (24.3)	1,967 (24.5)	4,115 (51.2)	8,037 (100.0)	
Low HDL cholesterol	Yes	1,046 (21.4)	1,113 (22.7)	2,737 (55.9)	4,896 (100.0)	<0.001
	No	1,796 (25.4)	1,801 (25.5)	3,465 (49.1)	7,062 (100.0)	
Waist measurement	Abnormal	852 (21.3)	982 (24.5)	2,170 (54.2)	4,004 (100.0)	0.006
	Normal	1,990 (25)	1,932 (24.3)	4,032 (50.7)	7,954 (100.0)	
Total		2,842 (23.8)	2,914 (24.4)	6,202 (51.8)	11,958 (100.0)	

Abbreviations: See Table 1.

Table 7. Effects of riboflavin and niacin on physiological factors

DV	IV		OR	95% CI		P
				LLCI	ULCI	
Hypertension	Riboflavin RI	Yes	0.808	0.738	0.884	<0.001
		No	(reference)			
	Niacin RI	Yes	0.879	0.803	0.962	0.005
		No	(reference)			
	Riboflavin+Niacin RI	Both	0.792	0.711	0.882	<0.001
		One	0.889	0.799	0.989	0.030
		None	(reference)			
Hyperglycemia	Riboflavin RI	Yes	0.881	0.808	0.961	0.004
		No	(reference)			
	Niacin RI	Yes	0.848	0.774	0.929	<0.001
		No	(reference)			
	Riboflavin+Niacin RI	Both	0.813	0.731	0.905	<0.001
		One	0.954	0.862	1.057	0.372
		None	(reference)			
Total Cholesterol	Riboflavin RI	Yes	1.212	1.110	1.323	<0.001
		No	(reference)			
	Niacin RI	Yes	1.046	0.954	1.148	0.337
		No	(reference)			
	Riboflavin+Niacin RI	Both	1.168	1.050	1.300	0.004
		One	1.129	1.016	1.253	0.024
		None	(reference)			
Hypertriglyceridemia	Riboflavin RI	Yes	0.971	0.880	1.071	0.552
		No	(reference)			
	Niacin RI	Yes	0.909	0.825	1.002	0.054
		No	(reference)			
	Riboflavin+Niacin RI	Both	0.920	0.819	1.033	0.158
		One	0.952	0.848	1.069	0.407
		None	(reference)			
Low HDL cholesterol	Riboflavin RI	Yes	0.840	0.766	0.921	<0.001
		No	(reference)			
	Niacin RI	Yes	0.839	0.767	0.918	<0.001
		No	(reference)			
	Riboflavin+Niacin RI	Both	0.799	0.715	0.892	<0.001
		One	0.832	0.751	0.921	<0.001
		None	(reference)			
Waist measurement	Riboflavin RI	Yes	0.918	0.832	1.012	0.084
		No	(reference)			
	Niacin RI	Yes	0.879	0.862	0.785	0.002
		No	(reference)			
	Riboflavin+Niacin RI	Both	0.844	0.754	0.944	0.003
		One	0.974	0.871	1.090	0.650
		None	(reference)			

Abbreviations: See Table 1.

cardiovascular disease showed an important difference (P<0.001) (Table 8).

2) Effects of riboflavin and niacin on cardiovascular disease

To study the contributing effect of riboflavin and niacin's standard-level intake on prevalence rate of cardiovascular disease, an odds ratio was conducted, which showed a significant difference (P<0.001). If those who did not take a standard level of riboflavin and niacin has a 100% likely get cardiovascular disease. On riboflavin's effect alone, prevalence rate of cardio-vascular disease was reduced to 64% (OR=0.641, P<0.001). When niacin was consumed on a standard level,

Table 8. Comparison of cardiovascular disease according to recommended intake of riboflavin and niacin

		Cardiovascular disease		Total	*P*
		Yes	No		
Riboflavin RI	Yes	174 (3.3)	4,182 (96.7)	4,356 (100.0)	<0.001
	No	425 (5.0)	7,177 (95.0)	7,602 (100.0)	
Niacin RI	Yes	168 (3.3)	4,074 (96.7)	4,242 (100.0)	<0.001
	No	431 (4.9)	7,285 (95.1)	7,716 (100.0)	
Riboflavin+Niacin RI	Both	97 (2.7)	2,745 (97.3)	2,842 (100.0)	<0.001
	One	148 (4.5)	2,766 (95.5)	2,914 (100.0)	
	No	354 (5.1)	5,848 (94.9)	6,202 (100.0)	
Total		599 (5)	11,359 (95)	11,958 (100.0)	

Abbreviations: See Table 1.

Table 9. Effects of riboflavin and niacin on cardiovascular disease

DV	IV		OR	95% CI		*P*
				LLCI	ULCI	
Cardio vascular disease	Riboflavin RI	Yes	0.641	0.522	0.786	<0.001
		No	(reference)			
	Niacin RI	Yes	0.634	0.513	0.785	<0.001
		No	(reference)			
	Riboflavin+Niacin RI	Both	0.508	0.391	0.660	<0.001
		One	0.857	0.684	1.073	0.178
		None	(reference)			

Abbreviations: See Table 1.

prevalence rate of cardiovascular disease was reduced to 63% (OR=0.634, P<0.001). If the contributing effect of both the riboflavin and niacin is combined, while intake of one nutrient drops the prevalence rate to 85%, consuming both nutrients reduces the prevalence rate of cardiovascular disease to 50% (OR=0.508, P<0.001) (Table 9).

DISCUSSION

The causes of cardiovascular disease can be of different types: innate factors such as aging, family history, and sex; biological factors such as hypertension and cholesterol level; as well as environmental factors such as smoking, eating, and stress [17, 18]. The major precedence diseases to cardiovascular disease are dyslipidemia, hypertension, and diabetes [19], and to reduce the incidence, many studies are being conducted on correlation between precedence diseases and cardiovascular disease [20-22].

At first, the analysis was conducted on adults 19 years of age or older. As a result, except for the age element, there was no significant result. The reason for such result was the 0% prevalence rate of cardiovascular disease among 19 to 39 years old individuals. On the basis of such trials, the study was reexamined with subjects over 50 years old. It was able to analyze it more accurately than before, excluding the influence of age. For lipid level, the variables were total cholesterol, hypertriglyceridemia, low HDL-cholesterol, and high LDL-cholesterol, but through analysis, LDL had a high missing value and was excluded from the variables. Before executing this study, the physiological factor most correlated to cardiovascular disease was expected to be lipid level [23-25]. However, through cross-analysis, hypertriglyceridemia does not display a high correlation, and total cholesterol had an opposite result from the hypothesis. According to P value, the result of total cholesterol are significant; however, the prevalence rate of the normal people was higher than the abnormal people. Variables on glucose and waist size showed a significant result as expected. As for total cholesterol level, it is a well-known fact that the higher the rate, the higher the likelihood of death from cardiovascular disease [26, 27], and the same is true of hypertriglyceridemia level and low HDL-cholesterol [28, 29]. Thus, the statistical results in this study raised questions about numerous articles that had been published to date. In addition, this study also checked clinical trial reports on the South Korean population. An observational study on patients hospitalized for myocardial infarction during 1993 reported that higher total cholesterol and triglyceride levels were found in the patient group (186.2 mg/dL and 131.8 mg/dL, respectively) than in the control group (145.2 mg/dL and 104.7 mg/dL, respectively) [30]. Another study on patients from 20 hospitals in South Korea showed that the risk of cardiovascular diseases increased when total cholesterol and triglyceride levels increased [31]. However, the risk of cardiovascular disease was not proportional to the gradual increase in cholesterol level in a prediction model for onset of ischemic heart disease among South Korean patients. Moreover, while the risk of cardiovascular disease increased gradually when the triglyceride level was between 100 and 299 mg/dL, the risk decreased when the triglyceride level was ≥300 mg/dL. The age of the study population was ≥50 years, whereas the age in clinical trials was mostly <60 years, while the average total cholesterol and triglyceride levels were higher than the levels reported in the Korean National Health and Nutrition Examination Survey (KNHANES) [32]. Physiologically, triglyceride levels fluctuate widely, and thus it is difficult to use a single measurement as an indicator [33]. Most studies in South Korea have the limitations of targeting clinical patients, being limited to specific communities, or not analyzing patterns of change based on long-term observation within the same population [34, 35]. Because KNHANES data are based on a questionnaire survey conducted mostly on healthy subjects, data may contain errors due to failure to check the diagnosis of each individual. Compared to clinical trials, this study divided the results simply by normal versus abnormal for comparison and included cardiovascular disease including myocardial infarction or angina. In addition, the results may differ from actual clinical results, and the results may also be based on the prediction model explained earlier. It is believed that cohort studies on cardiovascular disease associated with lipid levels among older age groups are needed in the future.

On the basis of relationship between riboflavin and niacin [7-9], the study further investigates the correlation between physiological variables and riboflavin or niacin. Total cholesterol and triglyceride, which had an unexpected correlation to cardiovascular disease, interestingly, also showed the same relationship with riboflavin and niacin. D'Andrea et al. demonstrated that cumulative evidence showed no preventive relation of niacin to therapeutic effects of cardiovascular disease in secondary prevention. It has been suggested that niacin may be useful in lipid control for secondary prevention as monotherapy [36]. Although niacin is recognized to reduce the cholesterol rate, the correlation results with total cholesterol had low significance. Finally, a study on riboflavin and niacin consumption of a standard level and the correlation to cardiovascular disease found that consuming both on a recommended level reduced the prevalence rate to 50%. Our research demonstrated that intake of riboflavin or niacin can prevent the prevalence rate of cardiovascular disease by inhibiting low HDL-cholesterol and hyperglycemia (Table 7).

Sex was another variable to conduct a frequency analysis, but was excluded from the actual research. Men averaged higher cardiovascular disease risk than women at most ages, but after age 75, the rate becomes similar [37, 38]; the body component changes over time, for both men and women as time goes by; the level of subcutaneous fat reduces; and visceral fat increases. As aging takes place, hormones that suppress fat decrease, resulting in visceral fat accumulation. On the

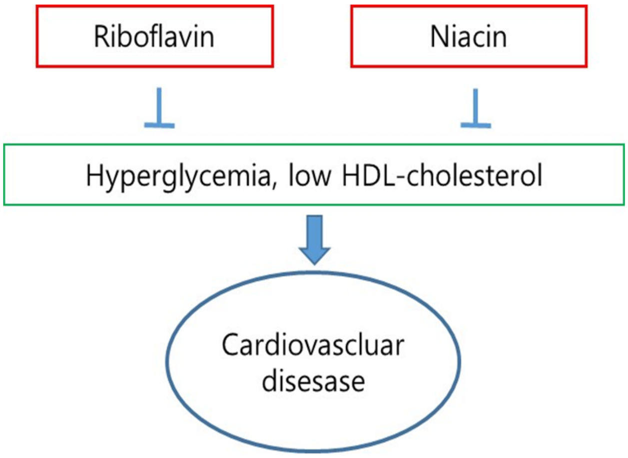

Figure 1. Schematic diagram of the effect of riboflavin and niacin on cardiovascular disease.

basis of statistics from the Korean National Health and Nutrition Examination, among a total of 11,958 subjects, 5,099 were men (47.4%), and 6,859 were women (52.6%). There were more women in a payment data of national health insurance corporation. Up to age 50, there is a higher percentage of men, but after age 60, the trend reverses, and after age 80, the percentage of women is 2.66 times higher than that of men [39]. As people grow older, the prevalence rate for women increased, and in this study, the respondents were also over 50 years old, yielding similar results. However, sex as a variable does not show great statistical difference and was excluded.

In conclusion, all the results from this research show the highest prevalence rate of cardiovascular diseases from physiological factors: hypertension, waist size, low HDL-cholesterol, and the nutrients that were related to the abnormal rate of physiological factors were riboflavin and niacin. Finally, riboflavin and niacin had a high correlation to prevalence rate of cardiovascular diseases (Figure 1). These observations indicate that riboflavin and niacin may be effective in prevention of cardiovascular disease.

요 약

심혈관 질환의 위험 요인은 선천적으로 노화, 당 대사의 문제, 가 족력과 성별이 있으며 생리학적 요인으로 고혈압, 혈청 콜레스테롤이 있다. 그 외 환경적 요인으로 흡연, 섭식, 스트레스 등이 있다. 본 연구는 최근 2013~2017년 국민건강영양조사 내용을 바탕으로 50세이상 남녀를 대상으로 한 건강설문조사와 검진조사를 이용하여 심혈관 질환의 위험 요인 및 유병률을 낮출 수 있는 방법을 연구하고자 하였다. 생리학적 요소와 영양성분 권장섭취 여부와의 상관성을 보기 위해 리보플라빈과 나이아신의 권장량을 확인하여 권장섭취군과 비권장섭취군으로 나눈 후 생리학적 요소변수와 분석하였다. 리보플라빈은 고혈압, 고혈당, 낮은 HDL-콜레스테롤에서, 나이아신은 고혈압, 고혈당, 허리둘레, 낮은 HDL-콜레스테롤에서, 둘을 복합적으로 보았을 때는 고혈압, 고혈당, 허리 둘레, 낮은 HDL-콜레스테롤에서 상관성이 있는 것으로 나타났다 (P<0.05). 결론적으로 리보플라빈, 나이아신의 권장섭취는 고혈당, 허리 둘레, HDL-콜레스테롤 등의 생리학적 요소에 영향을 줄 수 있으며, 이를 통해 심혈관 질환의 유병률을 낮출 수 있다. 이는 심혈관 질환의 위험율을 낮출 수 있는 가치 있는 연구로서 의의가 있다고 사료된다.

Acknowledgements: This paper was supported by Wonkwang Health Science University in 2019.

Conflict of interest: None

Author's information (Position): Ahn JY[1], Researcher; Kim IS[1,2], Professor; Lee JS[3], Professor.

REFERENCES

1. Ko HJ, Youn CH. The association between serum gamma-glutamyl transferase within normal range and risk factors of cardiovascular diseases: Based on the framingham risk score. Korean J Obes. 2013;22:261-263.
2. Youn SI, Moun JS, Sin C, Park HY, Lee JB, Jo IH. SNP study of the endothelial NO Synthase as risk factor for cardiovascular diseases in Koreans. Report of National Institute of Health. 2000;37:400-404.
3. Lee SW, Kim HC, Suh HS, Suh I. Thirty-year trends in mortality from cardiovascular diseases in Korea. Korean Circ J. 2015;45:202-209.
4. Xu L, Ryu S, Goong H. Gender differences in predictors of health behaviors modification among patients with cardiovascular disease. JKCA. 2015;15:280-289.
5. Cho JJ, Kim JY, Byun JS. Occupational stress on risk factors for cardiovascular diseases and metabolic syndrome. Ann Occup Environ Med. 2006;18:209-220.
6. Jee SH, Song JW, Cho HK, Kim S, Jang YS, Kim JH. Development of the individualized health risk appraisal model of ischemic heart disease risk in Korea. J Lipid Atheroscler. 2004;14:153-168.

7. Hoppel C, Dimarco JP, Tandler B. Riboflavin and rat hepatic cell structure and function, mitochondrial oxidative metabolism in deficiency states. J Biol chem. 1979;254:4164-4170.
8. Sugioka G, Porta EA, Corey PN, Hartoft WS. The liver of rats fed riboflav in-deficient diet at two levels of protein. Am J Pathol. 1969;54:1-19.
9. Mielgo-Ayuso J, Aparicio-Ugarriza R, Otza J, Aranceta-Bartrina J, Gil A,Ortega RM. et al. Dietary intake and food sources of niacin, riboflavin, thiamin and vitamin B6 in a representative sample of the Spanish population. The ANIBES Study. Nutrients. 2018;10:846.
10. Zhang LH, Kamanna VS, Zhang MC, Kashyap ML. Niacin inhibits surface expression of ATP synthase β chain in HepG2 cells: implications for raising HDL. J Lipid Res. 2008;49:1195-1201.
11. Braun MM, Stevens WA, Barstow CH. Stable coronary artery disease: treatment. Am Fam Physician. 2018;97:376-384.
12. Pisarik P. Evidence supporting niacin therapy is more nuanced than article states. Am Fam Physician. 2018;98:630-631.
13. Choi JY, Kim YN, Cho YO. Evaluation of riboflavin intakes and status of 20-64-year-old adults in South Korea. Nutrients. 2015;7:253-264.
14. Kweon S, Kim Y, Jang MJ, Kim Y, Kim K, Choi S, et al. Data resource profile: the Korea National Health and Nutrition Examination Survey (KNHANES). Int J Epidemiol. 2014;43:69-77.
15. Korea Centers for Disease Control and Prevention. Metabolic syndrome [Internet] Cheongju: Korea Centers for Disease Control and Prevention; 2016 [cited by 2019 Oct 10]. Available from: http://health.cdc.go.kr/health/HealthInfoArea/HealthInfo/View.do?idx=490&page=1&sortType=date&dept=&category_code=&category=1&searchField=titleAndSummary&searchWord=&dateSelect=1&fromDate=&toDate=.
16. Ministry of Health. Dietary reference intakes for Koreans [Internet] Sejong: Ministry of Health; 2019 [cited by 2019 Ocyt 10]. Available from: http://www.mohw.go.kr/react/jb/sjb030301vw.jsp? PAR_MENU_ID=03&MENU_ID=032901&CONT_SEQ=337356.
17. Mendis S, Puska P, Norrving B. Global atlas on cardiovascular disease. Prevention and control. The World Health Organization in collaboration with the World Heart Federation and the World Stroke Organization. Geneva, Switzerland. 2011;1:1-153.
18. Kim JS, Kim SS, Jung JK, Kim YD, Youn SJ, Kim JY, et al. Association of abdominal aortic calcification with lifestyle and risk factors of cardiovascular disease. Korean J Fam Med. 2013;34:213-220.
19. Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, et al. Heart disease and stroke statistics-2015 update a report from the American heart association. Circulation. 2015;131:E29-322.
20. Abramson BL, Melvin RG. Cardiovascular risk in women: focus on hypertension. Can J Cardiol. 2014;30:553-559.
21. Peter SA, Huxley RR, Woodward M. Diabetes as a risk factor for stroke in women compared with men: a systematic review and meta-analysis of 64 cohorts, including 775,385 individuals and 12,539 strokes. Lancet. 2014;383:1973-1980.
22. Bae YH, Lee KW. Risk factors for cardiovascular disease in adults aged 30 years and older. Journal of The Korean Society of Integrative Medicine. 2016;4:97-107.
23. Toth PP, Barter PJ, Rosenson RS, Boden WE, Chapman MJ, Cuchel M, et al. High-density lipoproteins: A consensus statement from the national lipid association. J Clin Lipidol. 2013;7:484-525.
24. Goff DC, Lloyd-Jones DM, Bennett G, Coady S, D'Agostino RB, Gibbons SR, et al. 2013 ACC /AHA guideline on the assessment of cardiovascular risk: A report of the American college of cardiology/American heart association task force on practice guidelines. J Am Coll Cardiol. 2014;1:2935-2959.
25. Ridker PM. LDL cholesterol: controversies and future therapeutic directions. Lancet. 2014;16:607-617.
26. Huxley R, Lewington S, Clarke R. Cholesterol, coronary heart disease and stroke: a review of published evidence from observational studies and randomized controlled trials. Semin Vasc Med. 2002;2:315-323.
27. Ragland DR, Brand RJ. Coronary heart disease mortality in the western collaborative group study, follow-up experience of 22 years. Am J Epidemiol. 1988;127:462-475.
28. Jeppesen J, Hein HO, Suadicani P, Gyntelberg F. Triglyceride concentration and ischemic heart disease: an eight-year follow-up in the copenhagen male study. Circulation. 1998;97:1029-1036.
29. Patel A, Barzi F, Jamrozik K, Lam TH, Ueshima H, Whitlock G, et al. Serum triglycerides as a risk factor for cardiovascular diseases in the Asia-Pacific region. Circulation. 2004;110:2078-2086.
30. Park JK, Kim HJ, Park KS, Lee SS, Chang SJ, Shin KC, et al. The case-control study on the risk factors of cerebrovascular diseases and coronary heart diseases. J Prev Med Public Health. 1996;29:639-655.
31. Sin SH, Lee TY. Associations of serum lipid profiles with incidence of ischemic heart diseases in Korean adults: Retrospective Cohort Study. Journal of Korea Academia-Industrial cooperation Society. 2012;13:2219-2231.
32. Jee SH, Song JW, Cho HK, Kim S, Jang YS, Kim JH. Development of the individualized health risk appraisal model of ischemic heart disease risk in Korea. J Lipid Atheroscler. 2004;14:153-168.
33. National Heart, Lung, and Blood Institute (NHLBI). Epidemiology and prevention of cardiovascular disease. Bethesda. 1994.
34. Choi MC, Song YH, Rhee SY, Woo JT. Frammingham risk scores by occupational group based on the 3rd Korean National Health and Nutrition Examination Survey. Ann Occup Environ Med. 2009;21:63-75.
35. Cho EY, Bae SJ, Cho HK, Ko YG, Park HY, Lee JH, et al. Association of cholesteryl ester transfer protein gene polymorphism with serum lipid concentration and coronary artery disease in Korean men. Korean Circ J. 2004;34:565-573.
36. D'Andrea E, Hey SP, Ramirez CL, Kesselheim AS. Assessment of the role of niacin in managing cardiovascular disease outcomes: a systematic review and meta-analysis. JAMA Netw Open. 2019;2:E192224.
37. Carretero OA, Oparil S. Essential hypertension, part 1: definition and etiology. Circulation. 2000;101:329-335.
38. Cutler JA. High blood pressure and end-organ damage. J Hypertens Suppl. 1996;14:3-6.
39. National Health Insurance Corporation. Payment data of health insurance Korea 2006~2011 [Internet]. Wonju: National Health Insurance Corporation; 2019 [cited 2019 Oct 10]. Available from: https://www.nhis.or.kr/retrieveHomeMain.xx.