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Association between Depression and Anemia with Physical activity by Isotemporal Substitution Analysis

빈혈과 우울증의 관계와 신체활동의 등시간대체 분석법

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이 논문을 보건학석사 학위논문으로 제출함
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남희경의 석사 학위논문을 인준함
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Abstract

Introduction: Depression is one of the important cause of Years Lived with Disability(YLD) for female in 2017. In Korea, prevalence of depression in 2014 was 6.7% for total population. Also, it is one of the main causes of death regarding to suicide. Anemia is prevalent worldwide with the 32.9% of prevalence in 2010. In Korea, about 7.4% people are affected by the disease, anemia. Physical activity is beneficial not only physically but also socially and psychologically. Especially team-based activities work as a role of social integration compare to sedentary activities such as watching television while seated. Many studies presented that physical activity has a protective effect on the depression. In addition, association of the depression and anemia has been studied by several studies. In spite of the association of the three keywords, association of depression, anemia and physical activities has not been studied. The purpose of this study is first, to observe different effect of the physical activity(effect modification) on depression related to anemia. Second, to measure the time substitution effect on depression according to types of the physical activities.

Methods: This study is a cross-sectional study with the Korean National Health and Nutrition Examination Survey(KNHANES) data. Depression examination had been conducted by Patient Health Questionnaire-9(PHQ-9), physical activity has been measured by Global Physical Assessment Questionnaire(GPAQ) and for the

anemia, hemoglobin status was considered. For all the analysis, SAS 9.4 has been utilized.

Result: Effects of the physical activity were different between anemic patients and non-anemic patients. In anemia group, more than ten minutes of moderate physical activity(OR: 0.526, CI:0.296 - 0.937), moderate to vigorous physical activity(OR: 0.543, CI: 0.326 - 0.905) and walking(OR: 0.670, CI: 0.457 - 0.982) had statistically significant protective effect on depression compare to those with less than ten minutes of exercise when adjusted. In non-anemic group, more than ten minutes of moderate physical activity(OR: 0.746, CI: 0.0644 - 0.864), moderate to vigorous physical activity(OR: 0.749, CI: 0.655 - 0.856), walking(OR: 0.733, CI: 0.641 - 0.838) and muscle training(OR: 0.825, CI: 0.723 - 0.940) were statistically significant compare to those who exercised less than ten minutes when adjusted. According to the time substitution analysis, isotemporal substitution model was not significant in anemic patients, however, substitution of sedentary behaviors to walking(OR: 0.985, CI: 0.976 - 0.995) and to moderate to vigorous physical activity(OR: 0.958, CI: 0.929 - 0.987) showed significant protective effect on depression in non-anemic participants. As shown in partition model, moderate to vigorous physical activity(OR:0.580, 0.346 - 0.971) presented the significant protective effect for the anemic group. For the non-anemic group, walking(OR: 0.767, CI: 0.671 - 0.876) and moderate to vigorous physical activity(OR: 0.783, CI:0.684 - 0.896) revealed to have the protective effect on depression.

Conclusion: Physical activity had a certain protective effect on depression, however it was different by anemia status. For the anemia patients, moderate to vigorous physical had an association of lower risk of depression. In other hands, for the non-anemic patients, walking and moderate to vigorous physical activity had significant association related to lower risk of depression. Regarding to time-replacement approach by isotemporal substitution analysis, walking and moderate to vigorous physical activities showed significant protective effect on depression when it substituted by sedentary behaviors only in non-anemic group.

Keyword : depression, anemia, physical activity, sedentary behavior, effect modification, isotemporal substitution analysis

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Chapter 1. Introduction

1.1 Background

Depression still matters. In 2010 alone, estimated deaths from depression were more than 2.2 million worldwide[1]. In 2017, in female, depressive disorders were one of the important cause of Years Lived with Disability(YLD) globally[2]. In Korea, prevalence of depression was 6.7% in 2014, and there was a gender difference. For male, prevalence was 4.2% and prevalence for female was 9.1%[3]. Notably, with the Organization for Economic Cooperation and Development(OECD) population data, Korea revealed to the country with the most suicide rates[4].

According to the study, people dying from suicide, about nine out of ten people were suffering from mental illness at the time of their deaths[5]. Depression with low economic status and with unemployment has association of higher risk of suicidal ideation[6]. Causes of the depression is various, therefore, active research is being conducted through joint research by experts in each field. Generally, determinants of depression are various such as female gender, low socioeconomic status, food insecurity and ages in whole life-course contexts for example[6].

Dealing with depression at individual level is not easy due to its complex mechanism. For adult mental disorders, physical activity and relaxation therapy, prompt diagnosis and proper treatment have been

suggested as a self-care[7]. Nevertheless, since depression is entangled with lots of factors, a thorough view is needed to see through the depression, the social and chronic disease. Therefore, great deal of efforts have been made organically worldwide such as Mental Health Gap Action Program(mhGAP) by WHO[8]. In addition, when considering the various causation of the disease, association of depression and other chronic diseases need more research.

Anemia prevalence was 32.9% in 2010 worldwide, causing 68.36 million YLD[9]. It affects more than one fourth of the global population and Iron Deficiency Anemia(IDA) is the most prevalent type of the anemia[10]. In addition, dietary iron deficiency revealed to fourth highest cause of YLD for female in 2017 globally [2]. In Korea, total prevalence of anemia in 2010 was 7.4% for the subjects aged more than 10, with 2.4 % for male and with 12.6% for female. Under the situation, individual who affects from anemia is more likely to be called a population.

Risk factor for anemia varies such as female gender, aging, malnutrition and infectious disease[11-15]. In addition, elderly, women, women with pregnant and children are generally considered to be a risk groups of the disease. With the severe current circumstances, actions to lessen the prevalence of anemia have been continued. Still these days, however, anemia has been thought as a by-product of other disease instead of a chronic disease itself[9].

Benefits of the physical activity is well known. In addition, physical activity is also beneficial in social contexts. This algorithm about social benefits of physical activity such as social integration and social changes has been widely studied[42]. One research recommended team-based sports since it has more positive association with improved psychological health compare to individual-based activities[43]. On the other hand, too much time spent doing sedentary behaviors might lead to lack of physical activity. According to one study, subjects who spent more time on sedentary behaviors tended to exercise less[16]. Sedentary behaviors were also related to higher cardiovascular mortality[17] and increased risk of type 2 diabetes[18].

Furthermore, physical activity plays an important role as a protective factor of depression. Some research suggested exercising as a self-care method for reducing depression[7]. In addition, physical activity on a regular basis is helpful reducing depressive symptoms. Interestingly, not only aerobic training but also flexibility and strength training indicated equal effectiveness on depression treatment[19]. Still, study of extent and types regarding to physical activity needs more research.

What more interesting is, with the positive relationship of depression and physical activity, association of depression and anemia has suggested by previous study. A study indicated that anemia had association of increased risk of depression in adult[20].

This study aims at the novel approach of depression and anemia with the physical activity intervention. In other words, people with anemia related to higher risk of depression have studied through previous research, however, a modification effect of the physical activity on anemia and depression has not been studied.

1.2 Literature review

Depression and anemia links have been mentioned in prior studies. According to previous study, anemia and depression has a significant association in elderly[21]. A population-based investigation in Japan also suggested that self-reported anemic participants had a higher risk of depression[22]. Moreover, a recent systematic review and meta-analysis literature suggested that anemia is related to increased risks of depression in adults, and the relationship was stronger in age 65 and older group[23]. What's more, the higher the depression severity, the more proportion of anemic subjects has been observed[24]. In this process, several mechanisms have been assumed. First, anemia could lead to depression by worsening the functional impairment such as fatigue and cognitive impairment. Secondly, depression may lead to poor health behavior including malnutrition, consequently it might be a driving factor of anemia[24].

Relationship of anemia and physical activity is complex. For instance, fatigue, one of the main symptoms of anemia[25] may related to declined physical ability. Therefore, when exercise, due to

low iron in blood which carrying less oxygen, people with anemia easily become tired and would like to have short breath. Also in general, for anemia patients, having short breaks while exercising and be cautious on their trial is recommended[26]. On the other hand, one research added that moderate intensity activity had positive effect on reducing the symptom of the anemia[27].

About the anemia and physical activity link, when exercised, blood volume; sum of erythrocyte volume and plasma volume change. In a circumstance of intensive exercise, plasma volume is able to expand rapidly in a few hours or several days, however, expansion of the erythrocyte volume occurs slowly during weeks to months. Therefore, with the intensive physical activity, increasing plasma volume exceeds the erythrocyte volume which in other words, sports anemia or athletes pseudoanemia could appeared[28]. However, according to one study, hematological variables are more likely to change according to the types of the physical activity than by the physical activity itself. Also in another perspective, physical activity might increase hemoglobin by concerning erythropoiesis, however it also depends on exercise types[29].

In addition, one research studied children and adolescents suffering from sickle cell anemia. They measured the different levels of physical activities and sedentary behavior. According to the study result, sickle cell anemia patients resulted into lower exercise trends than those of healthy participants[30]. Another research studied

non-anemic iron deficiency effects on physical activities in COPD patients. Following the study, compare to controlled group whom without non-anemic iron deficiency, trial group revealed to spend more time sitting. Also, physical activities rates on moderate to vigorous and daily physical activities were lower than with controls[31].

In terms of physical activity and depression, association might be different by types of physical activities such as vigorous physical activity(VPA), moderate physical activities(MPA) and sedentary behavior(SB). In this regard, depression with physical activity have been widely investigated by previous studies. One Asian study found that lower VPA has an significant association with the higher diagnosed rates of depression[32]. According to European study, when considering frequency of PA, group of participants with MPA and VPA at least once a week had a lower risk of depression than less than once a week group[33].

Especially, to observe the different effects of each physical activities, and to suggest the proper health behavior replacement, time substitution method has been applied. Baseline assumption of this method is that time is finite, therefore time spent on one activity may decrease the time engaged in other activity, since it is limited. This, isotemporal substitution model(ISM) has been first introduced in 2009[34]. In the early model, weight changes by activity types including SB has been investigated. The model then applicated by lots

of researchers with various subject. For instance, substitution effect of physical activities related to depression[16] and cardiometabolic risk[35] have been researched. ISM has been used in Korean study as well, for example one studied a reallocation effect of physical activity related to participants' subjective health and stress in Korean adult group[36].

Ahead of this research, our main keywords were 'Depression[MeSH]', 'Anemia[MeSH]' and 'Exercise[MeSH] OR Physical activity'. Then by three databases, 'Pubmed, 'Scopus' and 'Cochrane library', keywords have been searched. As a result, none of the literature has shown.

1.3 Objectives

The aim of the study is to investigate the role of the physical activity on the pathway of depression and anemia. Also, with the methodological trial, substitution effect of different types of physical activities will be investigated according to anemia status. Hypothesis of this study is as follows. First, depression and anemia would have significant association with physical activity, individually. Second, modification effect of physical activity would different by anemic status(anemic group/ non-anemic group). Lastly, modification effect of the physical activity would be substitutional with SB.

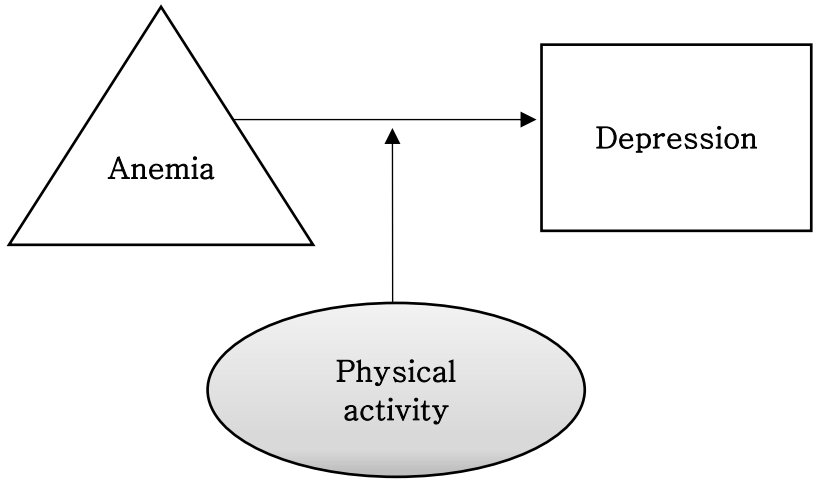

Figure 1 Association of the key variables

Chapter 2. Methods

2.1 Data sources and Study participants

This study used the sixth (2014) and seventh (2016, 2018) Korean National Health and Nutrition Examination Survey (KNHANES) [37, 38], which conducted by Korea Center for Disease Control (KCDC). KNHANES is a nationwide cross-sectional investigation, first established in 1998. This health surveillance survey monitors health related trends and risk factors every year[39]. It designed to measure the health behavior, condition, and nutritional status of Koreans[40]. To represent the Korean population, complex survey has been designed and sample weights were constructed according to the stratification[39]. In addition, to represent the sample 17 cities, provinces, dongs, towns, and villages are selected as the survey

areas and consequently, in consideration of housing types, 25 households in 192 areas are selected by KCDC. All members of the designated household aged 1 or older, which is 4,800 households, about 10,000 people each year will be the final survey subjects of KNHANES[41].

For this study, participants who surveyed two questionnaire, Patient Health Questionnaire -9(PHQ-9)[42] and Global Physical Assessment Questionnaire(GPAQ)[43] were utilized. Blood sampling test was also conducted, for this study Hemoglobin status has been considered.

Among total participants(N=23,692) of three selected years (2014, 2016, 2018), age less than 19(N=4,845) and missing value / No response / not included(N=3,489) were excluded. Consequently, respondents who participated all the three examination; PHQ-9, GPAQ and blood sampling test were considered for the analysis(N=15,358). The study was approved by the Institutional Review Board(IRB) from Seoul National University(IRB No. IRB No. E2009/003-013)

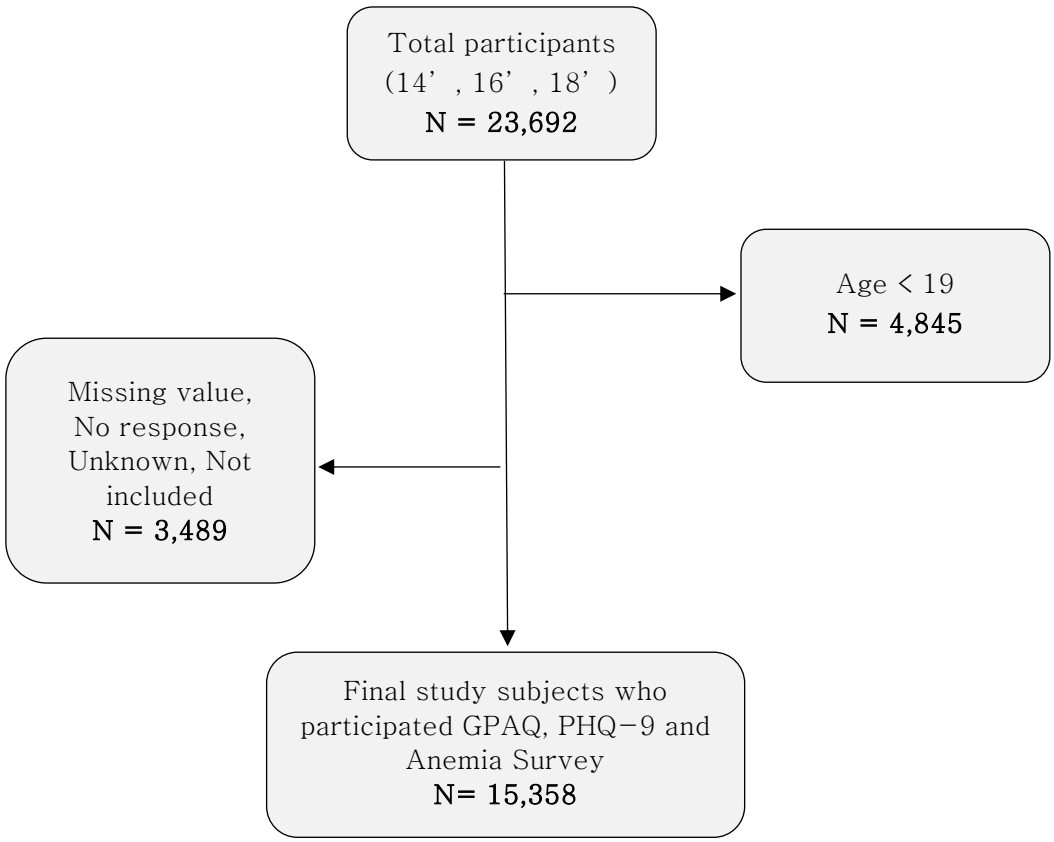

Figure 2. Schematic flow of the study population

2.2 Measurement

2.2.1 Depression

Assessment of depression status has been exanimated by PHQ-9, only for the participants age over 19. PHQ-9 is consisted of nine questions and each question has four answering options, ‘not at all’, ‘several days’, ‘more than half the days’ and ‘nearly every day’. Then, by sum of the answer, depression level is classified into five groups, ‘minimal(0-4)’, ‘mild(5-9)’, ‘moderate(10-14)’, ‘moderately severe(15-19)’ and ‘severe(20-27)’ [42].

For this study, whom with over mild depression have been considered as depressive participants, which then changed to binominal outcome variable. PHQ-9 has been evaluated for individual participants by trained worker.

2.2.2 Anemia

Anemia was defined by hemoglobin level, considering sex and age. Male participants age over 15 with hemoglobin less than 13 were considered anemic participants. Female who pregnant and age over 15 with HB less than 11, and non – pregnant female age over 15 with HB less than 12 have been classified into anemic participants. Several standard is being used, however KNHANES followed the WHO criteria[44]. For Anemia evaluation, blood sampling has been conducted by trained health personnel.

2.2.3 Physical activity

Physical activity variables were surveyed by GPAQ and original question of KNHANES which regarding to walk and muscle training. Participants age over 19 has been selected for the study. GPAQ is composed of four sections, 'Activity at work', 'Travel to and from places', 'Recreational activities' and 'Sedentary behavior', asking how much time and day has been spent doing different types of physical activities.[43] To analysis a physical activity effect in terms of free time, only two variables, recreational activities and sedentary behavior has been used for this study.

For recreational activities, Vigorous Physical Activity(VPA) and Moderate Physical Activity(MPA) have been assessed. VPA is defined as the activity which increases largely in breathing or heart rate, for example running, climbing mountain, basketball, swimming, playing badminton or jumping ropes. MPA is limited to the activity causing a small increase in breathing or heart rate such as brisk walking, jogging, playing golf, dance sports, weight training, or Pilates. VPA and MPA are calculated in case if it has been continued for at least 10 minutes. Sedentary Behavior (SB), in other hands, asks how much time has been spent sitting or reclining a day, for example sitting at a desk, sitting with friends, travelling in car, bus, train, reading, playing cards or watching television, however, time spent sleeping was excluded. All the time units of the variables have been recalculated into minutes for instinctive interpretation and analysis convenience.

Table 1. Recreational Activities in detail

	Activity Types	Definition	Examples
Recreational Activity	VPA	At least 10 minutes of activity will large increases in breathing or heart rate changes	running, climbing mountain, basketball, swimming, playing badminton or jumping ropes
	MPA	At least 10 minutes of activity with small increases in breathing or heart rate changes	brisk walking, jogging, playing golf, dance sports, weight training, or Pilates

	SB	Time spent while seated doing sedentary activity	sitting at a desk, sitting with friends, travelling in car, bus, train, reading, playing cards or watching television
	Walking	At least 10 minutes of walking at once	

(VPA: vigorous physical activity, MPA: moderate to vigorous physical activity, SB: sedentary behavior)

2.2.4 Covariates

Socioeconomic variables for the analysis have been described by gender and some of the variables have been adjusted for statistical models. Gender was divided into male and female according to the participants' response. Age was classified as five categories, '19-29', 30-39', '40-49', '50-59' and '60 or more'. Marital status was divided into 'ever married' including separated, divorced and widowed, and 'never married'. Education was categorized into four groups, 'less than elementary school graduate', 'middle school graduate', 'high school graduate' and 'more than university graduate'. Income level was grouped as four, 'low', 'low to medium', 'medium to high' and 'high'. Each standard was followed by Korean income distribution.

Occupation was separated into four groups by its similarity of work's characteristic, which is white color; manager and experts, pink color; service or sale workers, blue color; agriculture and fishery worker or simple laborer, and grey color; housewife, unemployed or students. Smoking status was divided into 'current smoker', 'former smoker' and 'non-smoker'. BMI was categorized into three groups, 'normal', 'low-weight'

and ’ over-weight’.

KNHANES includes walking and muscle training variable therefore, those were also considered, which assess how much time has been used a day as an hour/minute unit for a walking variable and asks muscle training status(yes/no).

2.3 Statistical analysis

For the analysis, first, the study considered a gender difference to observe the general distribution of the variables using chi-square test. Then the data were separated according to main variables(anemia and depression) using domain function in SAS. By univariate phrase function, time spent on physical activities have been presented in detail. To analyze the association of anemia and depression by physical activities status, logistic regression has been utilized to both adjusted and unadjusted models. Finally, ISM has been additionally analyzed. All analyses were conducted by SAS 9.4.

ISM generally suggested by three different multiple linear regression models. First, substitution model is related to time replacement concept. This model is presented with all the physical activity variables including total variable, which is the sum of physical activity variables. Purpose of the model is to estimating the effect when one physical activity is substituted by another physical activity. By eliminating one physical variable in turns, estimates of the remained variables represent the effect of time replaced. This

approach is essential since the time is limited in our daily life.

Next, partition model is to observe different effect of one physical activity while fixing other activities remained. This model does not signify time replacement effect, in other words isotemporal, since the total time of the physical activity has not been considered. Lastly, single model is presented as one physical activity each with covariates. This model has several limitations. The result of this model has not controlled by other physical activities, therefore, considering the result of this model alone might be insufficient to apply into physical activity prescription.

Table 2. Model explanation

<table>
<tr><td colspan="4">Physical activities = A, B, C, D
Total activity = (A + B + C+ D) = E
Covariates = F</td></tr>
<tr><td rowspan="4">Models</td><td>Types</td><td>Coefficients</td><td>Interpretation</td></tr>
<tr><td>ISM</td><td>Y = A+ C+ D+ E +F –> B
Y = A+ B+ D+ E +F –> C
Y = A+ B+ C+ E +F –> D
Y = A+ B+ C+ D +F –> E</td><td>Substituted effect of each variables when eliminate bold variable</td></tr>
<tr><td>Partition</td><td>Y = A+ B+ C+ D + F</td><td>Effect of each variable on outcome when others held constant</td></tr>
<tr><td>Single</td><td>Y = A+ F
Y = B+ F
Y = C+ F
Y = D+ F</td><td>Effect of one variable each when others are not considered</td></tr>
</table>

(ISM: isotemporal substitution model)

3. Results

3.1.1. Descriptive characteristic of participants I

General characteristic of study participants by gender has shown in table 3.1. All the subjects are age over 19 and have participated in anemia and depression assessments. Total number of study population was 15,358, while 6,678 for male and 8,680 for female. Socioeconomic variables were presented as age, marital status, education, income and occupation. Regarding age, male and female revealed similar distribution. Marital status, however, showed difference by gender, female(45.51%) had higher proportion of get married than male(35.95%) and less percentage(9.39%) of not get married than male(14.15%). About education, male showed significantly higher education level contrast to female in high school(19.49%; male and 17.97%; female)and university graduate(21.98; male and 18.15; female). Similarly, those difference were observed when it comes to income variable. The higher the income, the higher proportion of male was presented in middle state(15.88%; male and 16.40%; female) and middle to high level(16.40%; male and 14.92%; female). Regarding occupation, most answered job for female was grey color(22.83%) which includes housewife, unemployed and students, whereas white(16.36%) and blue(16.01%) color for male.

Table 3.1. Descriptive characteristic of participants by gender Ⅰ

		Male (N=6,678)	Female (N=8,680)	Total (N=15,358)	*P-value*
Age					
	19-29	831(9.85)	1,040(8.69)	1,871(18.54)	<.0001
	30-39	1,149(9.72)	1,485(9.15)	2,634(18.87)	
	40-49	1,221(10.53)	1,668(10.45)	2,889(20.98)	
	50-59	1,234(10.07)	1,760(10.15)	2,994(20.22)	
	60+	2,243(9.94)	2,727(11.46)	4,970(21.39)	
Marital status					
	Yes	5,343(35.95)	7,464(40.51)	12,807(76.46)	<.0001
	No	1,335(14.15)	1,216(9.39)	2,551(23.54)	
Education					
	Elementary	924(4.52)	2,039(9.05)	2,963(13.56)	<.0001
	Middle school	697(4.12)	903(4.73)	1,600(8.85)	
	High school	2,354(19.49)	2,810(17.97)	5,164(37.46)	
	University	2,703(21.98)	2,928(18.15)	5,631(40.13)	
Income					
	Low	1042(6.09)	1,586(7.93)	2,628(14.03)	<.0001
	Low-Middle	1,618(11.72)	2,175(12.37)	3,793(24.10)	
	Middle	1,979(15.88)	2,433(14.67)	4,412(30.55)	
	Middle-High	2,039(16.40)	2,486(14.92)	4,525(31.32)	
Occupation					
	White	1,973(16.36)	1,838(11.54)	3,811(27.90)	<.0001
	Pink	717(6.12)	1,380(8.52)	2,097(14.65)	
	Blue	2,240(16.01)	1,335(7.01)	3,575(23.02)	
	Grey	1,748(11.60)	4,127(22.83)	5,875(34.44)	

3.1.2. Descriptive characteristic of participants Ⅱ

Moreover as shown in table 3.2, smoking status showed clear difference in gender, current-smoker group had dominant percentage in male (19.59%) than in female(3.04%), especially about never-smoker(12.70%; male and 43.84%; female). For BMI, in low-

weight group, female(2.98%) showed higher percentage than that of male(1.31), however, in over-weight group male(20.49%) presented higher percentage than that of female(13.60%).

Main variable of the study, anemia showed predominant prevalence, 5.70% in female group whereas 1.38% in male group. Also, outcome variable of the study, depression presented significant difference by gender. Depression prevalence of male was 7.25%, whereas 12.25% for female. For physical activity variables, walking showed no difference in both male and female, however when it comes to muscle training, male(17.06%) is more likely to exercise compare to that of female(8.50%).

Table 3.2. Descriptive characteristic of participants by gender Ⅱ

		Male (N=6,678)	Female (N=8,680)	Total (N=15,363)	*P-value*
Smoking status					
	Never	1,532(12.70)	7,725(43.84)	9,257(56.54)	<.0001
	Former smoker	2,713(17.81)	489(3.02)	3,202(20.83)	
	Current smoker	2,433(19.59)	466(3.04)	2,899(22.63)	
BMI					
	<18.5	165(1.31)	455(2.98)	620(4.30)	<.0001
	18.5 – 25	3,829(28.30)	5,704(33.32)	9,533(61.62)	
	25+	2,684(20.49)	2,521(13.60)	5,205(34.08)	
Anemia					
	Yes	287(1.38)	990(5.70)	1,277(7.08)	<.0001
	No	6,391(48.72)	7,690(44.20)	14,081(92.92)	
Depression					
	Yes	946(7.25)	2,049(12.25)	14,507(94.76)	<.0001

	No	5,732(42.86)	6,631(37.64)	851(5.24)	
Walking					
	Yes	5,409(41.45)	7,146(41.83)	5,958(40.00)	0.1091
	No	1,269(8.65)	1,534(8.07)	9,405(60.00)	
Muscle training					
	Yes	2,168(17.06)	1,434(8.50)	3,602(25.57)	<.0001
	No	4,510(33.04)	7,246(41.40)	11,756(74.43)	

3.2.1. Descriptive characteristic of respondents by key variables Ⅰ

In Table 4.1, descriptive characteristic has been presented according to anemia and depression status. Overall anemia prevalence was 7.08% and subjects with depression were 19.50 %. Year domain shows clear association of anemia and depression. Total participants with depression in anemic group and non-anemic group were 23% and 19.24% respectively. Regarding sex, anemia prevalence was differed, 19.48% for male and 80.52% for female. Depression prevalence presented the same trends, 10.46% for male subjects whereas 31.78% for female subjects. Age group distributed slightly different by anemia status, respondents with anemia and depression were highest in age group over 60, however, respondents only with depression were highest in age group 19- 29. In anemic group, whom answered to yes to marital status had 18.88% depression prevalence, in contrast 13.33 % in those of non -anemia group.

Table 4.1. Descriptive characteristic of participants by anemia and depression I

		Anemia					
		Yes(N=1,277)			No(N=14,081)		
		Depression			Depression		
		Yes	No	Total	Yes	No	Total
		n(%)	n(%)	n(%)	n(%)	n(%)	n(%)
All		294(1.63)	983(5.45)	1,277(7.08)	2,701(17.87)	11,380(75.05)	14,081(92.92)
Year							
	2014	79(6.72)	244(19.28)	323(26.00)	845(6.24)	3,175(23.49)	4,020(29.73)
	2016	109(8.20)	381(28.95)	490(37.15)	988(6.81)	3,923(27.44)	4,911(34.24)
	2018	106(8.08)	358(28.77)	464(36.85)	868(6.19)	4,282(29.84)	5,150(36.03)
Sex							
	Male	50(2.88)	237(16.61)	287(19.48)	896(7.58)	5,495(44.86)	6391(52.43)
	Female	244(20.13)	746(60.38)	990(80.52)	1,805(11.65)	5,885(35.91)	7,690(47.57)
Age							
	19-29	22(3.13)	55(6.21)	77(9.34)	462(4.73)	1,332(14.50)	1,794(19.24)
	30-39	45(3.78)	151(12.87)	196(16.65)	508(4.06)	1,930(14.98)	2,438(19.04)
	40-49	49(4.49)	265(24.28)	314(28.77)	439(3.46)	2,136(16.92)	2,575(20.39)
	50-59	30(2.71)	108(9.14)	138(11.84)	489(3.39)	2,367(17.47)	2,856(20.86)
	60+	148(8.90)	404(24.49)	552(33.40)	803(3.59)	3,615(16.89)	4,418(20.48)
Marital status							
	Yes	260(18.88)	899(68.53)	1,159(87.41)	2,091(13.33)	9,557(62.30)	11,648(75.63)
	No	34(4.12)	84(8.46)	118(12.59)	610(5.91)	1,823(18.47)	2,433(24.37)

3.2.2 Descriptive characteristic of respondents by key variables Ⅱ

According to table 4.2, regarding education variable, higher percentage of elementary graduate subjects have observed in anemic group(21.13%) than in non-anemic group(12.99%). Income level and occupation presented similar trends in both by anemia and by depression status. In smoking variable, participants whom answered

to never-smoker was 77.76% in anemic group, whereas those of participants were 54.92% in non-anemic group. Also, current smoker in non-anemic group(23.84%) was higher than that of anemic group(6.76%). Lastly, for BMI, higher proportion of low-weigh participants were observed in anemic group(68.90%) than in non-anemic group(61.06%).

Table 4.2. Descriptive characteristic of participants by anemia and depression Ⅱ

		Anemia					
		Yes(N=1,277)			No(N=14,081)		
		Depression			Depression		
		Yes N(%)	No N(%)	Total N(%)	Yes N(%)	No N(%)	Total N(%)
Education							
	Elementary	117(7.47)	227(13.66)	344(21.13)	612(3.10)	2,007(9.88)	2,619(12.99)
	Middle	29(2.12)	92(6.34)	121(8.46)	282(1.68)	1,197(7.20)	1,479(8.88)
	High	79(6.90)	308(27.45)	387(34.34)	908(7.23)	3,869(30.47)	4,777(37.70)
	University	69(6.52)	356(29.54)	425(36.06)	899(7.22)	4,307(33.22)	5,206(33.22)
Income							
	Low	109(7.36)	198(13.08)	307(20.44)	637(3.80)	1,684(9.74)	2,321(13.54)
	Low-Middle	71(5.33)	259(20.35)	330(25.69)	721(5.19)	2,742(18.78)	3,463(23.97)
	Middle	69(5.69)	279(22.49)	348(28.18)	715(5.40)	3,349(25.33)	4,064(30.74)
	Middle-High	45(4.62)	247(21.07)	292(25.69)	628(4.84)	3,605(26.92)	4,233(31.75)
Occupation							
	White	46(4.57)	218(19.18)	264(23.75)	557(4.43)	2,990(23.79)	3,547(28.21)
	Pink	33(3.16)	121(10.57)	154(13.74)	398(3.15)	1,545(11.57)	1,943(14.72)
	Blue	45(3.28)	169(12.54)	214(15.81)	504(3.54)	2,857(20.02)	3,361(23.57)
	Grey	170(12.00)	475(34.69)	645(46.69)	1,242(8.11)	3,988(25.39)	5,230(33.50)
Smoking status							
	Never	220(17.81)	746(59.95)	966(77.76)	1,623(10.77)	6,668(44.15)	8,291(54.92)
	Former smoker	43(3.03)	177(12.45)	220(15.48)	450(3.12)	2,532(18.12)	2,982(21.24)
	Current	31(2.17)	60(4.59)	91(6.76)	628(5.34)	2,180(18.50)	2,808(23.84)

	smoker						
BMI							
	<18.5	192(15.19)	682(53.71)	874(68.90)	1,634(11.51)	7,025(49.55)	8,659(61.06)
	18.5 – 25	21(1.72)	61(4.92)	82(6.64)	172(1.33)	366(2.79)	538(4.12)
	25+	81(6.10)	240(18.36)	321(24.46)	895(6.39)	3,989(28.43)	4,884(34.82)

3.3 Physical activity status by key variables

Table 5 suggests a detail value of participating in physical activity by time units(minutes). Participants who exercised more than ten minutes have been regarded to did exercise whereas less than ten minutes group have been regarded to not did not exercise. The table, then presented the minimum, maximum, mean, median and standard deviation of each domains. Since, ten minutes have been suggested as a standard between yes and no to exercise status, minimum value of more than ten minutes of exercise has the same value, ten minutes.

VPA showed low participation rates in both anemic group and non-anemic group. In non-anemic group, subjects without depression(10.35%) presented higher percentage than that of subjects with depression(7.72%). For MPA, mean value was higher when the participants did not have the depression. In anemic group, mean value of the MPA was 32.5 minutes for whom without depression and 28.9 minutes for whom with depression. In non-anemic group, mean value of the MPA was 32.0 minutes for whom without depression and 30.9 minutes for whom with depression. About the standard deviation for anemic group without depression was highest by 31.4 minutes.

Mean of the MVPA in anemic group was 32.4 minutes and 35.0 minutes for with depression and without depression each and 37.5 minutes and 37.2 minutes for non-anemic group. Most of the respondents have answered to yes to walk more than 10 minutes a day. The mean value of walking was different by depression and by anemia status. In anemia group, participants with depression walked 56.4 minutes and participants without depression worked 57.6 minutes. In non-anemic group, participants with depression walked 59.5 minutes whereas participants without depression walked 62.1 minutes.

All the participants were spent at least more than ten minutes on sedentary behaviors. Especially, referencing mean value, subjects with depression presented higher time spent than whom without depression in both anemic(506.8 minutes) and non-anemic group(500.6 minutes).

Table 5. Physical activities status by key variable

		Anemia			
		Yes(N=1,277)		No(N=14,081)	
		Depression		Depression	
		Yes(n=294)	No(n=983)	Yes(N=2,701)	No(N=11,380)
VPA (Mins)	Less than 10	285(95.67)	934(93.66)	2,543(92.28)	10,427(89.65)
	10 or more	9(4.33)	49(6.34)	158(7.72)	953(10.35)
	Min	10.7	11.4	10.0	10.0
	Max	102.9	77.1	308.6	300.0
	Mean	28.3	26.1	35.0	31.0
	Median	17.1	21.4	25.7	25.7

	Std	29.5	13.8	34.0	24.2
MPA (Mins)	Less than 10	271(89.72)	840(83.23)	2,324(83.91)	9,134(78.87)
	10 or more	23(10.28)	143(16.77)	377(16.09)	2,246(21.13)
	Min	11.4	10.0	10.0	10.0
	Max	100.0	300.0	180.0	308.6
	Mean	28.9	32.5	30.9	32.0
	Median	21.4	25.7	25.7	25.7
	Std	22.8	31.4	22.1	25.7
MVPA (Mins)	Less than 10	264(87.39)	810(79.95)	2,228(79.33)	8,573(72.84)
	10 or more	30(12.61)	173(20.05)	473(20.67)	2,807(27.16)
	Min	10.7	10.0	10.0	10.0
	Max	102.9	300.0	317.1	308.6
	Mean	32.4	35.0	37.5	37.2
	Median	25.7	25.7	25.7	28.6
	Std	25.6	30.5	30.4	28.2
Walk (Mins)	Less than 10	78(22.31)	192(17.67)	586(19.46)	1,947(15.87)
	10 or more	216(77.69)	791(82.33)	2,115(80.54)	9,433(84.13)
	Min	10.0	10.0	10.0	10.0
	Max	420.0	600.0	900.0	900.0
	Mean	56.4	57.6	59.5	62.1
	Median	40.0	40.0	40.0	40.0
	Std	57.5	54.2	61.7	62.0
SB (Mins)	Less than 10	0	0	0	0
	10 or more	294(100)	983(100)	2,701(100)	11,380(100)
	Min	20.0	60.0	30.0	30.0
	Max	1140.0	1140.0	1260.0	1200.0
	Mean	506.8	469.4	500.6	464.8
	Median	480.0	480.0	480.0	480.0
	Std	239.9	210.8	227.1	211.0

(VPA: vigorous physical activity, MPA: moderate to vigorous physical activity, MVPA: moderate to vigorous physical activity, SB: sedentary behavior)

3.4 Association with depression and anemia with physical activity status

As shown in table 7, both anemic group and non-anemic group showed protection trends when the participants take part in physical activity. SB were inadequate for odds ratio calculation, since the only one reference exists. For anemic patients, MPA, MVPA and walking variable were statistically significant. MPA(OR: 0.526, CI: 0.296 – 0.937) and MVPA(OR: 0.543, CI: 0.326 – 0.905) showed protective correlation on the outcome variable, depression, when the other variable were adjusted. Also, walking presented a statistical significance(OR: 0.670, CI: 0.457 – 0.982). VPA and muscle training tends to have a protective effect on depression, however, they were not statistically significant.

When it comes to non-anemic participants, all the variable except VPA were statistically significant when the other variables were adjusted. Walking showed the most negative correlation with depression(OR:0.733, CI:0.641 –0.838). Respondents who answered to yes on MPA(OR:0.746, CI: 0.644 – 0.864)and MVPA(OR: 0.749, CI: 0.655 – 0.856) are expected to have protective effect on their depression than those who answered to no. Muscle training also suggested the protective effect on the depression with statistical significance when they adjusted.

Due to the use of different dataset, it is difficult to compare the

groups directly; anemic and non-anemic group. What we are able to know about the relationship of the two distinguished group is whether their results are significantly different or not. When analyze them as a one united dataset, the *p-value* for interaction between anemia and physical activities were not significant.

Table 6. Correlation of the variables

	VPA	MPA	Walking	Total time	SB
VPA	1	0.16866 <.0001	0.05024 <.0001	0.04057 <.0001	−0.03588 <.0001
MPA	0.16866 <.0001	1	0.09997 <.0001	0.07217 <.0001	−0.0362 <.0001
Walking	0.05024 <.0001	0.09997 <.0001	1	0.20125 <.0001	−0.08591 <.0001
Total time	0.04057 <.0001	0.07217 <.0001	0.20125 <.0001	1	0.95418 <.0001
SB	−0.03588 <.0001	−0.0362 <.0001	−0.08591 <.0001	0.95418 <.0001	1

(VPA: vigorous physical activity, MPA: moderate to vigorous physical activity, SB: sedentary behavior)

Table 7. Difference of physical activity effects on depression by anemia status

		Anemic participants N=1,277			*P− value***	Non− Anemic participants N=14,081		
	(Minutes)	N(%)	Unadjusted	Adjusted*	Adjusted*	N(%)	Unadjusted	Adjusted*
VPA	Less than 10	1,219(94.12)	1	1	0.4963	12,970(90.16)	1	1
	10 or more	58(5.87)	0.669 (0.239 − 1.870)	0.650 (0.253 − 1.667)		1,111(9.84)	**0.725 (0.588 − 0.895)**	0.811 (0.651 − 1.010)
MPA	Less than 10	1,111(84.72)	1	1	0.1085	11,458(79.84)	1	1
	10 or more	166(15.28)	0.569 (0.317 − 1.022)	**0.526 (0.296 − 0.937)**		2,623(20.16)	**0.716 (0.620 − 0.826)**	**0.746 (0.644 − 0.864)**
MVPA	Less than 10	1,074(81.66)	1	1	0.0918	10,804(74.09)	1	1
	10 or more	203(18.34)	**0.575 (0.343 − 0.965)**	**0.543 (0.326 − 0.905)**		3,281(25.91)	**0.699 (0.612 − 0.798)**	**0.749 (0.655 − 0.856)**
Walking	Less than 10	270(18.74)	1	1	0.8682	2,533(16.56)	1	1
	10 or more	1,007(81.26)	0.747 (0.519 − 1.076)	**0.670 (0.457 − 0.982)**		11,548(83.44)	**0.781 (0.685 − 0.891)**	**0.733 (0.641 − 0.838)**
Muscle training	Less than 10	1070(82.81)	1	1	0.5421	10,686(73.80)	1	1
	10 or more	207(17.19)	0.726 (0.424 − 1.245)	0.743 (0.449 − 1.230)		3,395(26.20)	**0.737 (0.648 − 0.838)**	**0.825 (0.723 − 0.940)**
SB	Less than 10	0	.	.	0.2309	0	.	.
	10 or more	1,277(100.00)	.	.		14,081(100.00)	.	.

*Adjusted by sex, marital status, smoking status, occupation, BMI and sleep.

** *P-value* for interaction between anemia status and physical activities.

(VPA: vigorous physical activity, MPA: moderate to vigorous physical activity, MVPA: moderate to vigorous physical activity, SB: sedentary behavior)

3.6 Various models by different MVPA options

As shown in Table 8, different options have been applied for the models. In model 1, MVPA was calculated by ten minutes a day and regarded as a continuous variable. In model 2, MVPA was calculated by ten minutes of MVPA a day and regarded as a continuous variable. In this model however, outliers have been eliminated after considering the distribution. With deletion of outliers, MVPA as a continuous variable was significantly associated with decreased risk of depression(OR: 0.794, CI: 0.660 - 0.957).

For the model 3, MVPA was considered as a categorical variable which measured by total physical activity time of ten minutes a week. As a result, MVPA likely to has an association of decreased risk on depression with OR: 0.592 and CI: 0.375−0.936. In terms of the model 4, MVPA was applied as a categorical variable with the standard of ten minutes a day. This model was also statistically significant with OR: 0.564 and CI: 0.338 - 0.940.

Table 8. Models for MVPA by different options

Models	Type	Standard	Main results
1	Continuous	10 minutes a day	0.892(0.756 – 1.051)
2	Continuous without outliers	10 minutes a day	**0.794(0.660 – 0.957)**
3	Categorical	10 minutes a week	**0.592(0.375 – 0.936)**
4	Categorical	10 minutes a day	**0.564(0.338 – 0.940)**

3.6.1 Model 1 – MVPA as a continuous variable

As shown in table 9, MVPA was not statistically significant. Other variables, however presented significant effects on depression. Female gender was associated with higher risk of depression by OR: 2.869 and CI: 1.605 - 5.129. Next, current smoker also significantly associated with higher risk of depression(OR: 2.593, CI: 1.299 - 5.175). About the occupation, grey color worker was related to higher risk of depression. Lastly, sleeping was statistically significant related to risk of depression.

Table 9. 10 minutes of MVPA a day as a continuous variable

		Odds ratio	Confidence Interval(95%)
Sex	Male		Reference
	Female	2.869	**1.605 – 5.129**
Smoking status	Never		Reference
	Former smoker	1.536	0.870 – 2.713
	Current smoker	2.593	**1.299 – 5.175**
Occupation	White		Reference
	Pink	1.538	0.820 – 2.884
	Blue	1.555	0.848 – 2.852
	Grey	1.759	**1.122 – 2.757**
Marital status	Yes		Reference
	No	1.887	**1.064 – 3.346**
Sleep		0.997	**0.995 – 0.999**
Walking		1.001	0.970 – 1.032
MVPA		0.892	0.756 – 1.051
SB		1.008	1.000 – 1.016

(MVPA: moderate to vigorous physical activity, SB: sedentary behavior)

3.6.2 Model 2 – MVPA as a continuous variable without outliers

In Model 2, MVPA was significantly associated with decreased risks of depression. According to table 10, female gender is likely to have a significant association with higher risks of depression compare to those of male. Current smoker (OR: 2.639, CI: 1.306 - 5.333), grey color of an occupation(OR: 1.658, CI: 1.064 - 2.538) and SB(OR: 1.009, CI: 1.001 - 1.017) were related to a higher risk of depression. Sleep however, showed protective effect on depression(OR: 0.997, CI: 0.995 0 0.999).

Table 10. 10 minutes of MVPA a day as a continuous variable without outliers

		Odds ratio	Confidence Interval(95%)
Sex	Male		Reference
	Female	2.833	**1.562 – 5.138**
Smoking status	Never		Reference
	Former smoker	1.532	0.863 – 2.718
	Current smoker	2.639	**1.306 – 5.333**
Occupation	White		Reference
	Pink	1.56	0.828 – 2.938
	Blue	1.507	0.821 – 2.764
	Grey	1.658	**1.064 – 2.583**
Marital status	Yes		Reference
	No	1.887	**1.064 – 3.346**
Sleep		0.997	**0.995 – 0.999**
Walking		0.998	0.967 – 1.031
MVPA		0.794	**0.660 – 0.957**
SB		1.009	**1.001 – 1.017**

(MVPA: moderate to vigorous physical activity, SB: sedentary behavior)

3.6.3 Model 3 – MVPA as a categorical variable Ⅰ

According to table 11, ten minutes of MVPA a week resulted in decreasing the risk of depression(OR: 0.592, CI: 0.375 - 0.936). Female gender was associated with the higher risk of depression than in male with the OR: 2.964 and CI: 1.649 - 5.327. Similar to other models, current smoker(OR: 2.563, CI:1.281 - 5.127), grey color worker(OR: 1.697, CI: 1.080 - 2.668), married(OR: 1.941, CI: 1.092 - 3.450) and sleep(OR: 0.997, CI: 0.995 - 0.999)were statistically significant related to the association of the depression.

Table 11. 10 minutes of MVPA a week as a categorical variable

		Odds ratio	Confidence Interval(95%)
Sex	Male		Reference
	Female	2.964	**1.649 – 5.327**
Smoking status	Never		Reference
	Former smoker	1.544	0.871 – 2.738
	Current smoker	2.563	**1.281 – 5.127**
Occupation	White		Reference
	Pink	1.494	0.797 – 2.802
	Blue	1.501	0.810 – 2.781
	Grey	1.697	**1.080 – 2.668**
Marital status	Yes		Reference
	No	1.941	**1.092 – 3.450**
Sleep		0.997	**0.995 – 0.999**
Walking		1	0.969 – 1.032
MVPA			Reference
		0.592	**0.375 – 0.936**
SB		1.008	1.000 – 1.016

(MVPA: moderate to vigorous physical activity, SB: sedentary behavior)

3.6.4 Model 4 – MVPA as a categorical variable Ⅱ

Model 4 considered the ten minutes of MVPA per day. In this model, as shown in table 12, ten minutes of MVPA a day (OR: 0.564, CI:0.338 - 0.940) was presented a protective effect on depression than those of without MVPA group. In addition, female gender(OR: 2.911, CI: 1.620 - 5.232), current smoker(OR: 2.576, CI: 1,288 - 5.151) and grey color worker(OR: 1.694, CI: 1.086 - 2.642) were significantly associated with higher risks of the depression. In other hands, sleep revealed to has a protective effect related to depression(OR: 0.997, CI: 0.995 - 0.999).

Table 12. 10 minutes of MVPA a day as a categorical variable

		Odds ratio	Confidence Interval(95%)
Sex	Male		Reference
	Female	2.911	**1.620 – 5.232**
Smoking status	never		Reference
	Former smoker	1.52	0.854 – 2.707
	Current smoker	2.576	**1.288 – 5.151**
Occuaption	White		Reference
	Pink	1.495	0.797 – 2.801
	Blue	1.495	0.814 – 2.746
	Grey	1.694	**1.086 – 2.642**
Marital status	Yes		Reference
	No	1.934	**1.091 – 3.427**
Sleep		0.997	**0.995 – 0.999**
Walking		1	0.969 – 1.032
MVPA			Reference
		0.564	**0.338 – 0.940**
SB		1.001	1.000 – 1.002

(MVPA: moderate to vigorous physical activity, SB: sedentary behavior)

3.7 Isotemporal substitution model for anemic participants

Three different types of model have been suggested in Table 13. First of all, ISM has been used for substitution the time units, for example model (a) is about replacing 10 minutes of SB to walking, MVPA each. Then the interpretation of each replacement would be as follow; Reallocating 10 minutes of SB to walking(OR: 0.993, CI: 0.961 1.025) and MVPA(OR: 0.885, CI: 0.750 – 1.044) has lower risk of depression which was indeed not significant. In model (b), substituting walking to SB revealed higher risk of depression, however it was not significant. In addition, substituting Walking to MVPA has resulted in lower risk of depression with no significance. In Model (c) as well, statistical significance has not been observed.

Partition model, present the possibility of lower risk of depression of MVPA(OR:0.58 , CI: 0.346– 0.971) whereas SB(OR: 1.001, CI: 1.000–1.002) and walking(OR: 0.734, CI: 0.502–1.074) was not significant. In Single model, which designed by one physical variable each with adjusting variable, presented significant results in walking(OR: 0.670, CI: 0.457–0.982) and MVPA(OR:0.543, CI:0.326–0.905).

3.8 Isotemporal substitution model for non-anemic participants

Table 14 also reports three different style of models. According to Model (a), replacing ten minutes of SB to walking(OR: 0.985, CI: 0.976-0.995) and MVPA(OR: 0.958, CI:0.929-0.987) are likely to have lower risk of depression. In Model (b), when Walking has been substituted by SB, higher risk of depression has been observed(OR:1.015, CI: 1.005-1.025). In other hands, depression risk was lower according to substitution to MVPA (OR:0.972, CI: 0.941-1.004), however it was not statistically significant. Model (C) suggest the result of replacement of MVPA. When reallocate ten minutes of MVPA to SB, higher odds of depression experience has been detected(OR:1.042, CI:1.012-1.074).

Next, partition model presented two physical activities' protective effect of depression. Walking showed 0.767 of odds ratio and 0.671-0.876 of confidence interval, and MVPA revealed 0.783 of odds ratio with 0.684-0.896 of confidence interval. SB looks like to have an association of increased depression risks, however it was not statistically significant. In single model, walking (OR:0.733, CI:0.641-0.838) and MVPA(OR: 0.749, CI:0.655-0.856) had an association of lower risk of depression and statistically significant.

Table 13. Time replacement effect of Physical activity and other models for anemic participants

		Sedentary behavior	Walking	Moderate to Vigorous physical activity	Total activity
Isotemporal substitution model	Substitute of SB (a)	Replaced	0.993(0.961 – 1.025)	0.885(0.750 – 1.044)	1.008(1.000 – 1.016)
	Substitute of Walking (b)	1.007(0.975 – 1.040)	Replaced	0.891(0.755 1.052)	1.001(0.970 – 1.032)
	Substitute of MVPA (c)	1.127(0.958 – 1.326)	1.118(0.950 – 1.317)	Replaced	0.894(0.761 – 1.052)
Partition model	Partition	1.001(1.000 – 1.002)	0.734(0.502 – 1.074)	**0.580(0.346 – 0.971)**	N/A
Single model	Single	1.001 (1.000 – 1.002)	**0.670(0.457 – 0.982)**	**0.543(0.326 – 0.905)**	1.001 (1.000 – 1.002)

(MVPA: moderate to vigorous physical activity, SB: sedentary behavior)

All the model has been adjusted by sex, smoking status, occupation, marital status, BMI and sleep.

Table 14. Time replacement effect of Physical activity and other models for non-anemic participants

		Sedentary behavior	Walking	Moderate to Vigorous physical activity	Total activity
Isotemporal substitution model	Substitute of SB (a)	Replaced	**0.985(0.976 – 0.995)**	**0.958(0.929 – 0.987)**	**1.005(1.002 – 1.007)**
	Substitute of Walking (b)	**1.015(1.005 – 1.025)**	Replaced	0.972(0.941 – 1.004)	**0.990(0.981 – 0.999)**
	Substitute of MVPA (c)	**1.042(1.012 – 1.074)**	1.027(0.994 – 1.060)	Replaced	**0.964(0.936 – 0.993)**
Partition model	Partition	1.001(1.000 – 1.001)	**0.767(0.671 – 0.876)**	**0.783(0.684 – 0.896)**	N/A
Single model	Single	1.001(1.000 – 1.001)	**0.733(0.641 – 0.838)**	**0.749(0.655 – 0.856)**	1.001(1.000 – 1.001)

(MVPA: moderate to vigorous physical activity, SB: sedentary behavior)
All the model has been adjusted by sex, smoking status, occupation, marital status, BMI and sleep.

4. Discussion

Depression and anemia revealed to have an association with physical activity. Effect of the physical activities was different by anemic status. Furthermore, it was also different by the types of the physical activities. Lastly, when substituting sedentary behavior to physical activities, non-anemic subjects showed protective effects on depression whereas anemic subjects were not.

The object of this study was to research the association of depression and anemia considering physical activities status. Relation of depression and anemia has been studied by researchers, and we raised the question here how to reduce the possibility of being depressive on the pathway of two diseases. With growing studies, physical activity has been suggested as a powerful method due to its protective effect on depression. With the circumstances, final research questions have been summarized as three hypotheses.

In terms of the results, several interesting findings were observed. First of all, on depression, physical activity showed a different protective effect according to its types. All the physical activity variables, VPA, MVPA, walking and muscle training presented the protective effect with statistical significance. This result is consistent with the prior studies. WHO Health Survey (WHS) data presented that lower frequency of VPA was related to higher rates of depression diagnosed among middle to older age group [32]. About the frequency

of physical activity, European study suggested group of participants with MPA and VPA at least once a week had a lower risk of depression than less than a participant group with once a week[33]. Having different health effects by different physical activity types signify that when selecting physical activity for improving health or purpose of disease prevention, more consideration is required according to what they expect for the health benefits.

Secondly, as we expected, findings were different between anemic and non-anemic patients. MPA, MVPA and Walking showed protective effect in anemic group, whereas VPA, MPA, MVPA, Walking and Muscle training were significantly effective in non-anemic group. Also, even with the same physical activity, extent of protective was differed. These results are consistent with our hypothesis. We suppose the reason of our consequence is related to the symptom of the anemia. Fatigue and powerless, one of the most prevalent symptoms of anemia, may hinder the participants from practicing vigorous activities. In that reason, anemia patients might be difficult to join in VPA and in case even if they participate, it might be hard to sustain the activity. This assumption is from actual distribution of our study which in table 5, however, since the study is based on cross-sectional design, causal inference is unknown.

In addition, About the association of anemia and physical activity several assumptions have been considered following previous studies. First, it is clear that anemic patients exercise less and spend more

time seated. Next, even when they exercise, extra caution is needed with intermittent rest. With the circumstances above and with the symptom of anemia, total physical ability of anemic patients is declined. On the other hand, however, it is also clear that physical activity is beneficial by increasing hemoglobin level which consequently leads to enhanced oxygen carrying capacity[28]. Therefore, when considering the previous study and our research, physical activity might helpful for anemic patient even though it has several difficulties in practicing.

Lastly, for practical application of the physical activity in real life, time considered refine method has been utilized. Time spent in physical activity has been changed to ten minutes unit and then, we compared the substitution effects by replacing one variable each. As a result, we could not observe significant effect from anemic subject. In contrast, we could detect statistically significant effect of time replacing from non-anemic subjects. Substitution of ten minutes of SB to Walking or MVPA showed protective effect on depression, however, when replace Walking or MVPA to SB presented the possibility of the higher risk of depression. Especially, the higher the intensity of physical activity, the higher protective effect has been shown. These trends have been observed in anemic group, even though it was not statistically significant.

What we assume about the consequence is that when exercising, people meet others for example, playing football, soccer or playing

badminton is played by teams. In other words, most of the physical activities are also social activities. Mostly, however, time spent SB is done by alone, such as reading a book, listening a music and sitting at a desk. In partition model, anemic patients also showed significant protective effect in MVPA. Therefore, effect of physical activity on depression was existed even in anemic patients however, due to their anemic status, careful consideration is needed.

According to our result, several types of physical activity showed an association with lower risk of depression. Especially moderate physical activity and moderate to severe physical activity were more effective than walking when it comes to lower risk of depression in anemic group. What we assume about the consequences is that group of anemic participants joining in exercise might have relatively strong willingness on their daily life and more likely to be interested in health improvement compare to anemic group whom without exercise. Therefore, those positive behavior might affect lower risk of depression with some other factor beyond our study. To interpret why anemic participant shows such powerful effective protection on depression in detail, however, for the underneath mechanism, further research is needed.

Our result was consisted to the United states study which indicated that moderate to vigorous physical activity has association with lower risk of depression[45]. Also for the non-anemic participants, our result was consistent with the previous study[46] in that of the

vigorous physical activity had related to lower risk of depressive symptom. Related to the time replacement, Japanese study[47] presented that only low intensity physical activity was significantly associated on lower risk of depression however, our study showed the significance in moderate to vigorous physical activity.

Our study has several limitations. First, we did not consider the sub-analysis by age group and when interpreting the result. The participant of our study is adults aged over 19 divided by anemia status. In general, however, recommendations of the physical activity types are differed by age group. Therefore, sub-analysis considering age is needed for further study. Secondly, method of physical activity measurement was a survey, not by accelerometer. The Survey is answered by participants themselves, however, since the participants depend on their memories there might be a subtle bias. KNHANES has measured the physical activity status and movement by accelerometer manufactured by ActiGraph. We also considered the use of accelerometer, however, due to the survey year difference, applicating the accelerometer results to our study was limited. Lastly, we designed the association of the key variables as figure 1 at first, however during the analysis, physical activity did not take a role as an effect modification perfectly due to its complex composition. Instead, anemia status was segmented for the analysis. Also, when considering the association of the result, it is necessary to examine the relationship of the variables in mediation context. Therefore, mediation analysis is suggested for the further

investigation.

In spite of the limitations, this study has strengths in that of the originality. The association between depression and anemia has raised by lots of study, however, their pathway has not been much studied. In a view of public health, when considering health policy on depression, perspective of anemia is also recommended. In the association of two diseases, proper physical activity could be effective prescription to lessen the prevalence. For further study, separating the depression and anemia status by its severity is required to observe the detailed results.

5. Conclusion

There was an association between anemia and depression. On the pathway of two diseases, physical activity worked as a protective factor and showed statistically significant effect. For the anemic patients, moderate to vigorous physical activities presented protective effect on depression. In other hand, for the non-anemic patients, walking and moderate to vigorous physical activities revealed significant effect. In addition, with the time-replacement approach by isotemporal substitution analysis, walking and moderate to vigorous physical activities showed significant protective effect when they substituted by SB in non-anemic group.

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요약 (국문 초록)

빈혈과 우울증의 관계와 신체활동의 등시간대체 분석법

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배경: 우울증은 2017년 여성 장애 보정 손실 수명(Years Lived with Disability, YLD)에 있어 주요한 원인 중 하나이다. 한국의 2014년 우울증 유병률은 전체 인구의 6.7%이다. 또한, 우울증은 자살의 주요 사망 원인 중 하나이다. 전 세계적으로, 빈혈은 2010년 유병률은 32.9%이다. 한국의 경우 약 7.4%가 빈혈로 인한 영향을 받고 있다. 신체활동은 신체적인 부분 뿐만 아니라, 사회적으로, 또는 심리적으로도 유익하다. 특히 단체로 하는 신체 활동은 앉아서 텔레비전을 보는 것과 같은 좌식 활동과 비교했을 때, 조직에의 참여 또는 사회활동참여의 역할을 한다. 많은 연구들은 신체활동이 우울증에 보호 효과가 있음을 제시하였다. 또한, 우울증과 빈혈의 연관성은 여러 연구에 의해 연구되어 왔다. 세 가지 주요어의 연관성에도 불구하고, 신체활동, 빈혈 그리고 우울증을 고려한 연구가 이뤄지지 않고 있다. 따라서 본 연구의 목적은 첫째, 빈혈과 우울증에 대한 신체 활동(효과 변경 인자)의 영향을 알고자 한다. 둘째, 등시간대체 분석법을 통해, 우울증에 대한 신체활동의 시간 대체 효과를 측정하고자 한다.

연구 방법: 본 연구는 한국 국민건강영양조사(KNHANES) 2014, 2016,

그리고 2018년 자료를 활용한 단면연구이다. 우울증 검사는 9가지 항목의 총합 점수를 이용하여 우울감의 여부 및 심각도를 판단하는 우울증 평가 도구(PHQ-9)에 의해 실시되었고, 신체활동은 국제신체평가도구(GPAQ)에 의해 측정되었으며, 빈혈은 헤모글로빈 수치를 고려하였다. 표본에 가중치를 적용하여 국민 전체의 대표성을 가진 결과로 분석하고자 하였다. 모든 분석에는 SAS 9.4가 활용되었다.

결과: 우울증에 대한 효과 변경 인자로서 신체활동의 역할은 빈혈의 유무에 따라 달랐다. 빈혈 환자 집단에서 10분 이상의 중강도 신체활동(OR: 0.526, CI:0.296 – 0.937), 중고강도 신체활동(OR: 0.543, CI: 0.326 – 0.905) 및 걷기(OR: 0.670, CI: 0.457 – 0.982)를 실천한 사람은 10분 미만의 중강도 신체활동, 중고강도 신체활동 그리고 걷기를 실천한 사람에 비해 우울증에 있어 통계적으로 유의한 보호효과를 보였다. 반면에, 빈혈이 없는 집단에서는 10분 이상의 중강도 신체 활동(OR: 0.746, CI: 0.0644 – 0.864)과 중고강도 신체 활동(OR: 0.749, CI: 0.655 – 0.856)과 걷기(OR: 0.733, CI: 0.641 – 0.838), 근력 운동(OR: 0.864)을 실천한 사람들이 10분 미만의 중강도 신체활동, 중고강도 신체활동, 걷기 그리고 근력 운동을 실천한 사람에 비해 우울증에 있어 통계적으로 유의한 보호효과를 나타냈다. 등시간 대체 분석의 경우, 빈혈 환자 그룹에서는 시간 대체 모델(Isotemporal substitution model, ISM) 결과가 유의하지 않았다. 반면에, 빈혈이 없는 그룹에서는 앉아서 보내는 시간(Sedentary behavior, SB)을 걷기(OR: 0.985, CI: 0.976 – 0.995) 또는 중강도 운동(OR: 0.958, CI: 0.929 – 0.987)으로 대체했을 때, 우울증에 유의미한 보호 효과를 보였다. 마지막으로, 파티션 모델(partition model) 결과에 따르면, 중강도 신체활동(OR:0.580, 0.346 – 0.971)은 빈혈 집단에 있어서 유의미한 보호 효과를 나타냈다. 빈혈이

없는 집단의 경우 걷기(OR: 0.767, CI: 0.671 – 0.876)와 중강도 신체 활동(OR: 0.783, CI:0.684 – 0.896)에 있어 우울증에 대한 보호 효과가 관찰되었다.

주요어 : 우울증, 빈혈, 신체활동, 앉아서 하는 활동, 효과 변경 인자, 등시간 대체 모델

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