Korean Journal of Health Promotion
KJHP

https://e-kjhp.org

pISSN 2234-2141
eISSN 2093-5676

Korean Journal of Health Promotion

Korean Journal of Health Promotion

KJHP

VOL. 24 / NO. 1 / March 2024

VOL. 24 / NO. 1 / March 2024

pages. 1–46

Korean Society for Health Promotion and Disease Prevention

Announcements

Original Articles

Korean Society for Health Promotion and Disease Prevention

Korean Journal of Health Promotion
KJHP

pISSN: 2234-2141 · eISSN: 2093-5676
https://e-kjhp.org

VOL. 24 / NO. 1 / March 2024

Aims and Scope

The *Korean Journal of Health Promotion (KJHP)* is an open access, multidisciplinary journal dedicated to publishing high-quality research in various areas of the medical, nursing, nutritional, physical educational, epidemiological, and public health sciences associated with health promotion and disease prevention. *KJHP*, which has been published continuously since 2001, is an official journal of the Korean Society for Health Promotion and Disease Prevention.

The aim of the *KJHP* is to advance and disseminate new knowledge and scientific information in all the areas associated with health promotion and disease prevention. KJHP publishes original articles, narrative reviews, systematic reviews and meta-analyses, letters to the editor, and perspectives in English.

Abbreviation
The correct abbreviation for abstracting and indexing purposes is *Korean J Health Promot*.

This journal is financially supported by the Korean Federation of Science and Technology Societies (KOFST) Grant funded by the Korean Government.

Open Access

Article processing charge
No review fees are charged for all the submitted articles. Article processing charges are required for publication in the *KJHP*. Publication fees for all the accepted original or review articles are 300,000 Korean Won (250 US dollars). Additionally, if the article exceeds 6 pages of the journal, additional fees (50,000 Korean Won or 40 US dollars per extra page) will be charged.

Publisher: President, Sung SUNWOO, MD, MPH, PhD
Department of Family Medicine, Asan Medical Center
Korean Society for Health Promotion and Disease Prevention

Editor-in-Chief: Seung-Kwon MYUNG, MD, PhD
Department of Family Medicine, National Cancer Center
Department of Cancer AI & Digital Health, National Cancer Center Graduate School of Cancer Science and Policy

Editorial Office
Korean Society for Health Promotion and Disease Prevention
Department of Family Medicine, Asan Medical Center, 88 Olympic-ro 43-gil, Songpa-gu, Seoul 05505, Korea
Tel: +82-2-3010-3820 Fax: +82-2-3010-3815 E-mail: kshpdp@amc.seoul.kr

Printing Office
M2PI
#805, 26 Sangwon 1-gil, Seongdong-gu, Seoul 04779, Korea
Tel: +82-2-6966-4930 Fax: +82-2-6966-4945 E-mail: support@m2-pi.com

Korean Journal of Health Promotion
KJHP

Editors

Korean Journal of Health Promotion
KJHP

Contents

VOL. 24 / NO. 1 / March 2024

Announcements

Original Articles

Announcements

Korean J Health Promot 2024;24(1):1
pISSN: 2234-2141 • eISSN: 2093-5676
https://doi.org/10.15384/kjhp.2024.00003

Korean Journal of Health Promotion
KJHP

Converting to a Journal Publishing Academic Papers Written in from English and Korean to English Only: The New Beginning toward a Journal Indexed in SCIE

Seung-Kwon MYUNG, MD, PhD[1,2,3]
Editor-in-Chief, Korean Journal of Health Promotion

[1]Department of Cancer AI & Digital Health, Graduate School of Cancer Science and Policy, National Cancer Center, 323 Ilsan-Ro, Ilsandong-Gu, Goyang, Gyeonggi-Do, 10408, Korea
[2]Cancer Epidemiology Branch, Division of Cancer Data Science, Research Institute, National Cancer Center, Goyang, Korea
[3]Department of Family Medicine and Center for Cancer Prevention and Detection, Hospital, National Cancer Center, Goyang, Korea

Received: March 27, 2024
Accepted: March 29, 2024

Corresponding author:
Seung-Kwon MYUNG, MD, PhD
Department of Cancer AI & Digital Health, National Cancer Center Graduate School of Cancer Science and Policy, 323 Ilsan-ro, Ilsandong-gu, Goyang 10408, Korea
Tel: +82-31-920-0479
Fax: +82-31-920-2606
E-mail: msk@ncc.re.kr

To all readers of the Korean Journal of Health Promotion:

I am Seung-Kwon MYUNG, Editor-in-Chief of the Korean Journal of Health Promotion (*KJHP*). *KJHP* is an open access, multidisciplinary journal dedicated to publishing high-quality research in various areas of the medical, nursing, nutritional, physical educational (kinesiological), epidemiological, and public health sciences associated with health promotion and disease prevention. *KJHP*, which is an official journal of the Korean Society for Health Promotion and Disease Prevention, has been published continuously since 2001. In order to advance and disseminate new knowledge and scientific information in all the areas associated with health promotion and disease prevention, *KJHP* has published academic papers written in English and Korean for mainly Korean researchers and readers for the past two decades.

However, in recent years, it has been strongly suggested among the members of the Korean Society for Health Promotion and Disease Prevention that *KJHP* should be indexed in the Science Citation Index Expanded in order to share and disseminate the new knowledge and scientific information related with health promotion and disease prevention for international readers as well as Korean readers. Therefore, *KJHP* has decided to reform the publication system. First, *KJHP* has converted to a journal publishing academic papers written in from English and Korean to English only from this issue, 2024. Second, we have opened the new English *KJHP* homepage and online manuscript submission system in January, this year. Last, no review (submission) fees are charged for all the submitted articles from now on. Article processing charges are required for publication in the *KJHP*. Publication fees for all the accepted original or review articles are 300,000 Korean Won (250 US dollars). Additionally, if the article exceeds 6 pages of the journal, additional fees (50,000 Korean Won or 40 US dollars per extra page) will be charged.

On behalf of the editors, I hope that all the readers and researchers submit valuable manuscripts to *KJHP* and support *KJHP*'s growth and development.

Original Article

Korean J Health Promot 2024;24(1):2-10
pISSN: 2234-2141 • eISSN: 2093-5676
https://doi.org/10.15384/kjhp.2024.00017

Korean Journal of Health Promotion
KJHP

Efficacy and Safety of Intramuscular Injections of Vitamin D3 B.O.N. on Serum Vitamin D Levels in Adults with Vitamin D Deficiency: A Prospective, Single-Center, Open-Label Study

David Samuel KWAK, MD[1], Hwa Yeon SUN, PhD[2], Byung Wook YOO, MD, PhD[1,2]

[1]Department of Family Medicine and International Healthcare Center, Soonchunhyang University Seoul Hospital, Seoul, Korea
[2]Department of Interdisciplinary Program in Biomedical Science, Soonchunhyang University, Cheonan, Korea

Abstract

Background: Vitamin D deficiency is a common challenge its consequences are studied to be related to diversity of other health concerns. The efficacy and safety in longevity of vitamin D3 B.O.N. 200,000 IU Intramuscular Injection were examined through investigator-initiated clinical trial.

Methods: One-hundred and eight subjects between ages of 19 and 65 who showed vitamin D deficiency (serum 25(OH)D<20 ng/mL) were initially injected once and were checked every 3 months for the next 12 months for serum 25(OH)D and 1,25(OH)2D levels for the drug's efficacy, and for other safety observations. The percentage of participants maintaining within the normal serum 25(OH)D range were analyzed. Participants who reduced in the serum level below 30 ng/mL during the regular visits were given additional injections.

Results: All the subjects showed similar patterns of statistically significant improvements at all times. The percentage of participants remaining in the normal range was higher in the better compliance group. No serious adverse events or severe adverse reactions occurred.

Conclusions: Treatment of the vitamin D-deficient subjects with the injection of 200,000 IU vitamin D3 B.O.N. Intramuscular Injection induced a statistically significant increase in blood vitamin D concentration for 12 months demonstrating the clinical efficacy of the intervention. The higher percentage of the better compliance group being within normal ranges strengthens the evidence of the efficacy. No new adverse events or severe adverse events were associated with the injection, demonstrating its safety. Further studies to facilitate development of appropriate guidelines for interventions using vitamin D3 intramuscular injections will be desirable.

Keywords: Vitamin D deficiency, Vitamin D, Injections, Cholecalciferol

INTRODUCTION

In modern society, individuals are prone to lacking vitamin D as they are exposed to situations that reduces vitamin D activations or supplementation such as in spending more time indoors and the scarcity of food sources that are high in the vitamin containment. As a result, vitamin D insufficiency is emerging as an important public health challenge. A study finds that possibly up to

Received: January 19, 2024; **Revised:** February 15, 2024; **Accepted:** February 21, 2024
Corresponding author: Byung Wook YOO, MD, PhD
Department of Family Medicine and International Healthcare Center, Soonchunhyang University Seoul Hospital, 59 Daesagwan-ro, Yongsan-gu, Seoul 04401, Korea
Tel: +82-2-709-9059 Fax: +82-2-709-9133 E-mail: dryoo@schmc.ac.kr

40% of Europeans are deficient in vitamin D level [1]. Based on a cutoff value of serum level 25(OH)D≤20 ng/mL, nearly 1 billion individuals worldwide would exhibit vitamin D insufficiency.

Following a study in which intake of 100 IU of vitamin D raised serum levels by around 0.7–1 ng/mL, the treatment guidelines of The United States Endocrine Society recommend that adults aged ≥19 years should take at least 1,500–2,000 IU of vitamin D each day to maintain an optimal concentration of 30 ng/mL [2,3]. Generally, in order to raise serum 25(OH)D by 10 ng/mL, an individual needs to take 1,000 IU/day of vitamin D3 for 3–4 months [3].

Vitamin D3 B.O.N. Intramuscular Injection (cholecalciferol) is a drug recommended for supplementation of vitamin D3 developed in France in 1964. It has been used for over 50 years worldwide and has been demonstrated to be safe and effective.

Prior studies investigated efficacy and safety of either a single high-dose injection of vitamin D or multiple injections to the very elderly but there have been no studies that looked over efficacy and safety of injection of vitamin D3 over a long span of time. Thus, in attempts to find out the longevity in efficacy and safety in injection supplementation of the vitamin, we conducted an investigator-initiated clinical trial and examined the efficacy and safety of regular intramuscular injections of vitamin D3 B.O.N.

We aim to evaluate efficacy and safety of regular administration of high dose intramuscular injections of vitamin D3 and establish guidelines for the regular administration of the drug.

METHODS

Participants

The study included adults aged 19–65 years with vitamin D deficiency who showed serum 25(OH)D<20 ng/mL on the screening day, and who had voluntarily signed the participant consent form after understanding the study content and goals. The recruitment of the participants was conducted openly at Soonchunhyang University Seoul Hospital.

The final participants included in the analysis consisted of 108 persons, after 74 people were screened out of 182 originally recruited, prior to commencement of trials, due to reasons such as testing above or equal to level of 20 ng/mL of serum 25(OH)D, self-cancelations of consents by the participants, concurrently participating in other clinical trial, inability to meet the planned schedules, missing of consensual authorization, and belonging to vulnerable group, in the order of prevalence of the incidents.

Of the 108 participants included, there were 59 cases that were dropped out during their trials due to reasons such as follow up loss (52 cases), self-cancelations of consents by the participants (three cases), decisions made by principal investigator to cease trial for safety (2:1 case of pregnancy, one case categorized vulnerable group), decision made by principal investigator to cease trial arbitrarily (one case of unrelated incident that caused study drug interruption) and concurrently participating in other clinical trial (one case), in the order of prevalence of the incidents (Fig. 1).

Approval and review

This study of the vitamin D clinical trial was reviewed and approved by the Institutional Review Board at Soonchunhyang University Seoul Hospital (KDBON-CPI-01). This clinical trial complied with the principles of the International Conference on Harmonization (ICH) Guidelines and the Declaration of Helsinki and was conducted in accordance with the related regulations in consideration of subject rights and safety. Written

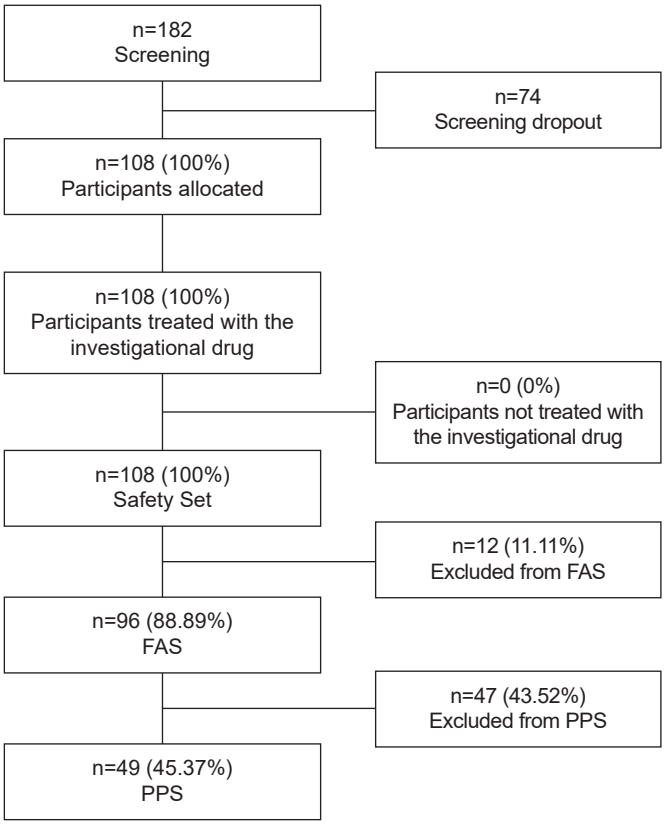

Fig. 1. Flowchart of participant registration. FAS, Full Analysis Set; PPS, Per Protocol Set.

informed consent was obtained from all subjects.

The investigational drug

Study process

The study was conducted over a period of 22 months (observation period per participant: approximately 12 months). The investigational drug (vitamin D3 B.O.N. Intramuscular Injection [cholecalciferol]) was administered via intramuscular injection at a dose of 200,000 IU in the first visit and the subjects were followed up at 3-month intervals to be checked for serum 25(OH)D levels along with other indicators including physical examinations, vital signs, serum levels of 1,25(OH)2D, and calcium concentration, urine levels of calcium and creatinine and other concurrent medications. The drug was re-administered in the subjects if serum 25(OH)D was tested to show below the normal range (30 ng/mL) during the follow up visits.

As an investigator-initiated clinical trial to examine the efficacy and safety of the drug, endpoints were set in primary and secondary efficacy, and safety. The efficacy endpoints were defined as the mean changes in serum levels of 25(OH)D (primary) and 1,25(OH)2D (secondary), each from their baselines to 3 months, from baselines to 6 months, from baselines to 9 months, and from baselines to 12 months. The percentage of participants that resulted within the normal ranges of serum 25(OH)D level (30-100 ng/mL) at 3, 6, 9, and 12 months were investigated as secondary efficacy endpoint as well. Safety endpoints consisted of physical examination, vital signs, adverse events (AEs), blood calcium concentration, and urine calcium and creatinine concentrations.

Analyses

The data obtained from the subjects of this clinical trial were analyzed in the form of FAS (Full Analysis Set), PPS (Per Protocol Set), and Safety Set. The FAS included all data obtained from subjects who were registered as trial subjects, received the investigational drug after enrollment, and had at least one primary efficacy evaluation performed after baseline. The per-protocol analysis group (PPS) was set apart within the FAS set according to the protocol compliance, given the nature of the open-label trial. The compliance refers to the minimum treatment duration, usability of measurements, and the absence of major protocol violations. PPS group included only those subjects who sufficiently adhered to the clinical trial protocol. As this clinical trial involved subjects who could have prior knowledge of the administered drug in an open-label trial, the conventional intention-to-treat principle for general randomization was not applied. The Safety Set included all data obtained from all trial subjects who received the investigational drug at least once.

In order to test the efficacy of the investigational drug for blood 25(OH)D and 1,25(OH)2D, we presented descriptive statistics for each treatment group to analyze the changes in concentration at each time point relative to baseline. We analyzed the change at each time point using either two sample t-test or Wilcoxon's rank sum test, depending on whether or not the assumption of normality was satisfied. The percentage of participants within the normal serum 25(OH)D range (30–100 ng/mL) at 3, 6, 9, and 12 months after the first dose was shown as the count and percentage of participants, and analyzed using Pearson's chi-square test or Fisher's exact test.

In order to test safety, we presented the descriptive statistics for each treatment group for AEs occurring after exposure to the investigational drug. We analyzed AEs using Pearson's chi-square test or Fisher's exact test. In addition, descriptive statistics were presented for AEs after drug administration, adverse drug reactions (ADRs), and severe adverse events (SAEs). In terms of measurements and test values, for continuous variables (physical examination, vital signs, and blood calcium concentration), descriptive statistics were presented for the baseline values, values at trial termination, and the differences between baseline and termination. The variables were analyzed using paired t-test or Wilcoxon's signed rank test. For categorical variables, contingency tables were constructed and the variables were analyzed using McNemar's test.

The results of analysis were presented in terms of odds ratios and 95% confidence interval. All data analyzes were performed using SAS ver. 9.4 (SAS Institute Inc.) with a significance level of 5%.

RESULTS

Participants' general characteristics

Ninety-six participants analysed included 23 males (23.96%) and 73 females (76.04%), with a mean age of 47.46±12.98 years, and a mean height of 161.02±7.61 cm. The detailed results are presented in Table 1.

Primary efficacy endpoint

For the 96 participants included in the FAS group, the mean

 https://doi.org/10.15384/kjhp.2024.00017

Table 1. Participant demographics characteristics (n=96)

Variable	Value
Sex	
Male	23 (23.96)
Female	73 (76.04)
Age (yr)	
Mean	47.46±12.98
Median	52 (22–64)
Age category	
20–29	9 (9.38)
30–39	26 (27.08)
40–49	11 (11.46)
50–59	25 (26.04)
Over 60	25 (26.04)
Height (cm)	
Mean	161.02±7.61
Median	160.70 (146.00–179.30)

Values are presented as number (%), mean±standard deviation, or median (range).

change in blood 25(OH)D from baseline to 3, 6, 9, and 12 months was 12.89±8.93 ng/mL, 17.96±8.51 ng/mL, 15.77±8.26 ng/mL, and 17.13±8.46 ng/mL, respectively. The changes after treatment with the investigational drug compared with baseline were statistically significant at all time points (all $P<0.0001$). The PPS group of 49 participants showed similar trends compared with the FAS group, with statistically significant changes at all time points after exposure to the investigational drug compared with baseline (all $P<0.0001$). The detailed results for blood 25(OH)D levels are shown in Table 2.

Secondary efficacy endpoint

The mean change in blood 1,25(OH)2D from baseline to 3, 6, 9, and 12 months in the 96 participants in the FAS group, was 11.36±16.42 pg/mL, 17.33±20.34 pg/mL, 20.64±21.41 pg/mL,

Table 2. Blood 25(OH)D concentration (FAS and PPS)

Item	Visit	Statistic	FAS (n=96)	PPS (n=49)
25(OH)D (ng/mL)	Baseline[a]	Number	96	49
		Mean±SD	11.51±4.32	11.86±4.51
		Median (range)	11.34 (3.52–19.39)	12.38 (3.52–19.14)
	V3 (3-mo)	Number	96	49
		Mean±SD	24.40±9.50	25.14±10.33
		Median (range)	22.44 (9.72–58.27)	24.24 (9.72–58.27)
	Change[b]	Number	96	49
		Mean±SD	12.89±8.93	13.28±9.11
		Median (range)	11.95 (–5.38 to 40.63)	11.62 (0.21 to 40.28)
		P-value	<0.0001[g]	<0.0001[g]
	V4 (6-mo)	Number	96	46[h]
		Mean±SD	29.47±8.62	31.69±6.95
		Median (range)	28.92 (8.55–58.27)	31.34 (15.25–49.82)
	Change[c]	Number	96	46[h]
		Mean±SD	17.96±8.51	19.89±6.98
		Median (range)	17.40 (2.00–40.63)	19.77 (4.57–34.54)
		P-value	<0.0001[f]	<0.0001[f]
	V5 (9-mo)	Number	96	46[h]
		Mean±SD	27.28±7.91	28.15±7.84
		Median (range)	26.92 (8.55–53.09)	29.14 (14.86–51.69)
	Change[d]	Number	96	46[h]
		Mean±SD	15.77±8.26	16.15±8.17
		Median (range)	14.95 (0.48–40.63)	15.69 (0.48–33.42)
		P-value	<0.0001[f]	<0.0001[f]
	V6 (12-mo)	Number	96	49
		Mean±SD	28.65±7.91	31.00±7.08
		Median (range)	28.06 (8.55–53.09)	31.08 (15.06–45.20)
	Change[e]	Number	96	49
		Mean±SD	17.13±8.46	19.15±8.12
		Median (range)	15.56 (–0.65 to 40.63)	20.84 (–0.65 to 35.12)
		P-value	<0.0001[f]	<0.0001[f]

FAS, Full Analysis Set; PPS, Per Protocol Set; SD, standard deviation.
[a]Values from screening (baseline) were used; [b]V3 (3-mo)–baseline; [c]V4 (6-mo)–baseline; [d]V5 (9-mo)–baseline; [e]V6 (12-mo)–baseline; [f]Paired t-test; [g]Wilcoxon signed rank test; [h]Values missing from three participants.

and 19.07±21.65 pg/mL, respectively. The changes after administering the investigational drug compared with baseline were statistically significant at all time points (all $P<0.0001$). The PPS and FAS groups showed similar trends, with statistically significant changes at all time points after treatment with the investigational drug compared with baseline (all $P<0.0001$). The results of blood 1,25(OH)2D levels are shown in Table 3.

The percentage of participants remaining in the normal serum 25(OH)D level (30-100 ng/mL) after the injection was 19 (19.79%) at 3 months after baseline, 43 (44.79%) at 6 months, 36 (37.50%) at 9 months, and 40 (41.67%) at 12 months respectively out of the 96 participants in the FAS group. The 49 participants of PPS group showed 11 (22.45%) at 3 months after baseline, 28 (57.14%) at 6 months, 20 (40.82%) at 9 months, and 26 (53.06%) at 12 months, respectively, showing higher percentage at all time points compared to that of the FAS group. The analysis is summarized in Table 4.

Safety assessment

AEs were analysed in the group of Safety Set using data collect-

Table 4. Percentage of participants in the normal range (30–100 ng/mL) for blood 25(OH)D after the injection B.O.N. Intramuscular Injection

Time point	FAS group participants in normal range (%) out of 96	PPS group participants in normal range (%) out of 49
3 mo	19.79%	22.45%
6 mo	44.79%	57.14%
9 mo	37.50%	40.82%
12 mo	41.67%	53.06%

FAS, Full Analysis Set; PPS, Per Protocol Set.

Table 3. Blood 1,25(OH)2D concentration (FAS and PPS)

Item	Visit	Statistic	FAS (n=96)	PPS (n=49)
1,25(OH)2D (pg/mL)	Baseline[a]	Number	96	49
		Mean±SD	33.38±13.56	31.34±12.94
		Median (range)	31.40 (10.44–80.05)	30.09 (11.16–76.34)
	V3 (3-mo)	Number	96	49
		Mean±SD	44.74±14.13	43.21±11.65
		Median (range)	42.78 (18.38–84.34)	41.41 (18.38–63.24)
	Change[b]	Number	96	49
		Mean±SD	11.36±16.42	11.87±15.03
		Median (range)	10.18 (–38.65 to 54.28)	13.86 (–38.60 to 37.45)
		P-value	<0.0001[f]	<0.0001[g]
	V4 (6-mo)	Number	96	45[h]
		Mean±SD	50.71±20.32	50.99±24.17
		Median (range)	48.17 (14.84–118.15)	45.48 (14.84–118.15)
	Change[c]	Number	96	45[h]
		Mean±SD	17.33±20.34	18.83±22.47
		Median (range)	17.63 (–35.81 to 94.34)	21.83 (–20.43 to 94.34)
		P-value	<0.0001[f]	<0.0001[f]
	V5 (9-mo)	Number	96	46[i]
		Mean±SD	54.02±20.61	55.32±22.36
		Median (range)	53.32 (15.60–116.06)	55.04 (15.60–116.06)
	Change[d]	Number	96	46[i]
		Mean±SD	20.64±21.41	23.52±21.89
		Median (range)	18.96 (–35.54 to 74.37)	26.49 (–21.82 to 74.37)
		P-value	<0.0001[f]	<0.0001[f]
	V6 (12-mo)	Number	96	49
		Mean±SD	52.45±18.74	52.01±18.80
		Median (range)	50.82 (19.10–110.97)	47.31 (19.10–110.97)
	Change[e]	Number	96	49
		Mean±SD	19.07±21.65	20.67±22.48
		Median (range)	15.89 (–39.23 to 99.56)	17.70 (–39.23 to 99.56)
		P-value	<0.0001[g]	<0.0001[g]

FAS, Full Analysis Set; PPS, Per Protocol Set; SD, standard deviation.
[a]Values from screening (baseline) were used; [b]V3 (3-mo)–baseline; [c]V4 (6-mo)–baseline; [d]V5 (9-mo)–baseline; [e]V6 (12-mo)–baseline; [f]Paired t-test; [g]Wilcoxon signed rank test; [h]Missing values from four participants; [i]Missing values from three participants.

 https://doi.org/10.15384/kjhp.2024.00017

ed since immediately after the informed consent (screening) until the participant's final assessment visit (the final visit in the 12 months period or by dropout).

Of the 108 participants in the Safety Set, 14 (12.96%) experienced AEs, and four (3.70%) experienced suspected ADRs. No SAEs or severe ADRs occurred during the study period. Two of the 16 cases of AEs (12.50%) exhibited ongoing symptoms, but they were both deemed unrelated to the investigational drug. The other 14 AEs (87.50%) were resolved, and no SAEs were detected during the study period.

No statistically significant changes in blood/urine calcium and creatinine concentrations were found at the end of the trial compared with baseline, and no clinically significant abnormal results were detected at any time point.

All criteria of discernment of SAEs were based on the guidelines set out by International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), which defines a serious AE (experience) or reaction as "any untoward medical occurrence that at any dose: results in death, is life-threatening, requires inpatient hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability/incapacity, or is a congenital anomaly/birth defect."

Details of the AEs are listed in Table 5.

Table 5. Summary of AEs

Variable	Total (n=108)
Number of participants experiencing AEs	14
95% CI	7.27–20.79
Number of AEs	16
Severity, n (%)	
Mild	14 (87.50)
Moderate	2 (12.50)
Severe	0 (0)
Suspected relationship with drug, n (%)	
No	
No relationship	2 (12.50)
Weak relationship	10 (62.50)
Yes	
Suspected relationship	3 (18.75)
Strong relationship	0 (0)
Clear relationship	1 (6.25)
Could not be assessed	0 (0)
Measures affecting the investigational product, n (%)	
None	15 (93.75)
Study drug interrupted	1 (6.25)
Study drug discontinued	0 (0)
Other treatment required, n (%)	
None	12 (75.00)
None	3 (18.75)
Non-drug therapies	1 (6.25)
Concomitant medications and non-drug therapies	0 (0)
Other (specify)	0 (0)
Outcomes, n (%)	
Resolved	14 (87.50)
Resolved with sequelae	0 (0)
Continuing	2 (12.50)
Fatal	0 (0)
Severe adverse event, n (%)	
No	16 (100)
Yes	0 (0)
AE details	
ADRs (n=4)	Single painful events at the injection site (n=3), injection site pruritus (n=1)
Others (n=12)	Ongoing: urinary calculus (n=1), lower limb fracture (n=1)
	Others: myalgia (n=3), dizziness (n=2), fatigue (n=1), herpes zoster (n=1), nasopharyngitis (n=1), sinusitis (n=1), gastritis (n=1)

ADR, adverse drug reaction; AE, adverse event; CI, confidence interval.

Safety assessment details

A total of 16 AEs were detected in 14 participants. These included four ADRs, with three participants experiencing a single painful event at the injection site, and a participant reporting an incident of injection site pruritus. In all, the symptoms were mild and transient and all patients recovered without further treatment.

In terms of events affecting treatment with the investigational drug, a single 'study drug interrupted' case (6.25%) was observed in relation to urinary calculus. However, the event was assessed not to be related to the drug. The patient was recommended extracorporeal shockwave lithotripsy, and based on the investigator's judgment, the patient was removed from the trial without further follow-up.

Two ongoing (12.50%) AEs, assessed as unrelated to the investigational drug, regarded a participant suffering a lower limb fracture and a participant developing urinary calculus. They were found to be ongoing after receiving concomitant medication or non-drug therapy.

When all the AEs after drug administration were classified by organ, there were three cases of injection site pain (2.78%) and one case of injection site pruritus (0.93%). However, these were confirmed to be transient AEs caused by the injection formulation.

In addition, there were three cases of myalgia (2.78%), two cases of dizziness (1.85%), and one case each of fatigue (0.93%)

and urinary calculus (0.93%), but these were not predictable AEs based on the articles of approval for the studied drug.

There was one case each of herpes zoster (0.93%), nasopharyngitis (0.93%), sinusitis (0.93%), gastritis (0.93%), and lower limb fracture (0.93%), but none of these were on going or showed any suspected association with the injection, and were resolved after appropriate treatment.

In physical examination, no participants showed clinically significant abnormalities after the injection. No statistically significant changes in systolic blood pressure were detected at the end of the trial compared with baseline. Statistically significant decreases in diastolic blood pressure, pulse rate, and body temperature at were found at the end of the trial compared with baseline, but these were not clinically significant.

DISCUSSION

There have been numerous studies that showed correlations of risks of different diseases to lower levels of serum vitamin D levels. Studies found that vitamin D deficiency increases the risk of falls and fractures in falls, as well as autoimmune disease, cardiovascular disease, infectious disease, colorectal cancer, and type 2 diabetes [4]. Individuals with low vitamin D levels or genetic variants in vitamin D receptor were reported to show higher incidence of malignant tumors such as breast cancer, colorectal cancer, and prostate cancer [5-8], hypertension [9], diabetes [10], and diseases associated with immune disorders. However, a contradicting study is also seldomly found such as in the findings, through meta-analyses of 15 randomized controlled trials, where preventive measure from high-dose supplementation of vitamin D were minimal on risk of falls and fractures [11]. They further speculated that it may even increase the risk.

Despite the disputed ideas, ample evidence suggests that vitamin D deficiency is strongly associated with multiple skeletal and non-skeletal diseases and laboratory and epidemiological studies to date indicate that appropriate vitamin D levels are essential to maintaining optimal health.

Although currently there is no consistent criteria for the determination of appropriate serum 25(OH)D concentrations, a serum level of 25(OH)D<10 ng/mL is generally defined as 'deficient', 10–30 ng/mL as 'insufficient', and ≥30 ng/mL as 'sufficient'. The World Health Organization defines <10 ng/mL as 'deficient' and ≤20 ng/mL as 'insufficient' [12].

Different academic groups suggest differing levels as being appropriate levels of serum vitamin D, such as National Academy of Medicine formerly known as the Institute of Medicine suggesting 20 ng/mL or above, yet a study by Bischoff-Ferrari et al. [13] defines appropriate serum 25(OH)D as ≥30 ng/mL. In another study, Bischoff-Ferrari et al. [14] suggest the appropriate 25(OH)D concentration recommended is 30–44 ng/mL. Precise guidelines for treating vitamin D deficiency have yet to be defined, but usually individuals with a blood vitamin D (25[OH]D) concentration <20 ng/mL are considered for treatment.

Currently, vitamin D formulations include oral formulations and injections. Based on the results of multiple studies, a daily vitamin D intake of 800–1,000 IU is recommended to prevent vitamin D insufficiency [15]. However, treating deficiency requires supplementation of a higher dose of vitamin D, which would be achieved more effectively through injections.

This study result enhances the evidence, priorly proven through studies of a single high dose injection of vitamin D in elderly or multiple injections in the regard [15], that injection is an effective and safe method for supplementation of vitamin D, and further provides information that the efficacy and safety remain valid relatively over a long period. This observance may be beneficial to people who require or prefer injections over other methods of supplementations.

The mainstay of the study was to observe efficacy and safety of the injection by seeing the serum 25(OH)D level within normal ranges, and regular repeated injections with its potential to overload the level was not considered in this study. The overlooked investigations for the number of the participants who required additional shots, the number of the shots each received, and their base serum level of 25(OH)D would have better elaborated the investigated drug's capacity to enhance the serum concentration.

The percentage of participants in the normal range (30–100 ng/mL) for blood 25(OH)D after the injection was higher in the PPS group at all time points compared to that of the FAS group, supporting the grounds, by the definition of each group, that participants who followed the protocol more strictly also more effectively gained and maintained improvements. But this can also implicate people who generally adhere better to healthy guidelines, and having better overall exposure to vitamin D, followed the protocol better.

Trials were initialized on participants regardless of the time within a year and seasonal effects on serum 25(OH)D level, such as from differing sun light exposure, might have been dis-

 https://doi.org/10.15384/kjhp.2024.00017

missed.

Even though vitamin D is known to promote calcium absorption in the small intestine and long-term high-dose vitamin D administration had been reported to have caused hypercalcemia or renal calculi [15], the lack of clinically significant abnormal results measured in blood calcium concentration and in blood/urine calcium and creatinine concentrations at any time point, along with that of any other findings in physical examination, vital signs, or AEs demonstrate the safety of the injection.

Conclusion

This clinical trial shows that treatment of vitamin D-deficient adults with B.O.N. Intramuscular Injection 200,000 IU induces a statistically significant increase in blood vitamin D concentration demonstrating the clinical efficacy of the intervention. Further, the higher percentage of the group that complied better to the guidance being within targeted normal ranges strengthens the evidence of the efficacy the drug holds. No clinically significant new AEs or SAEs were associated with the injections demonstrating its safety. Thus, administration of vitamin D3 B.O.N. Intramuscular Injection is safe and effective in vitamin D-deficient adults aged 19–65 years.

Further studies that demonstrate the role of outdoor activity and occupational categories, use of ultraviolet blockers, different age and sex groups will be desirable. Such studies may facilitate development of appropriate guidelines for interventions using vitamin D3 intramuscular injections.

ORCID

David Samuel KWAK, https://orcid.org/0000-0001-5789-5958
Hwa Yeon SUN, https://orcid.org/0000-0002-0671-1263
Byung Wook YOO, https://orcid.org/0000-0002-8753-9660

AUTHOR CONTRIBUTIONS

Dr. Byung Wook YOO had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Dr. Byung Wook YOO reviewed this manuscript and agreed to individual contributions.

Conceptualization: BWY and DSK. Data curation: HYS. Formal analysis: DSK and HYS. Funding acquisition: BWY. Investigation: DSK and HYS. Methodology: BWY and DSK. Project administration: HYS. Supervision: BWY. Visualization: DSK. Writing–original draft: DSK. Writing–Review & Editing: DSK.

CONFLICTS OF INTEREST

No existing or potential conflict of interest relevant to this article was reported.

FUNDING

This study was done with financial support from Kwang-Dong Pharmaceutical to assess injection supplemental method of vitamin D in Korean who are deficient in vitamin D.

DATA AVAILABILITY

The data presented in this study are available upon reasonable request from the corresponding author.

ACKNOWLEDGMENTS

We express sincere appreciation to the patients and medical staffs of Soonchunyang University Hospital, Seoul for all the support throughout the process.

REFERENCES

1. Cashman KD, Dowling KG, Škrabáková Z, Gonzalez-Gross M, Valtueña J, De Henauw S, et al. Vitamin D deficiency in Europe: pandemic? Am J Clin Nutr 2016;103(4):1033-44.
2. Joo NS. Clinical applications of vitamin D. Korean J Fam Pract 2014;4(1):7-14.
3. Cannell JJ, Hollis BW. Use of vitamin D in clinical practice. Altern Med Rev 2008;13(1):6-20.
4. Lee JH. Pharmacologic supplementation of vitamin D. J Korean Med Assoc 2017;60(4):330-5.
5. Grant WB. An estimate of premature cancer mortality in the U.S. due to inadequate doses of solar ultraviolet-B radiation. Cancer 2002;94(6):1867-75.
6. Giovannucci E. The epidemiology of vitamin D and cancer incidence and mortality: a review (United States). Cancer Causes Control 2005;16(2):83-95.
7. Freedman DM, Dosemeci M, McGlynn K. Sunlight and mortality from breast, ovarian, colon, prostate, and non-melanoma skin cancer: a composite death certificate based case-control study. Occup Environ Med 2002;59(4):257-62.
8. Apperly FL. The relation of solar radiation to cancer mortality in North America. Cancer Res 1941;1:191-5.

9. Rostand SG. Ultraviolet light may contribute to geographic and racial blood pressure differences. Hypertension 1997;30(2 Pt 1):150-6.
10. Mathieu C, Badenhoop K. Vitamin D and type 1 diabetes mellitus: state of the art. Trends Endocrinol Metab 2005;16(6):261-6.
11. Myung SK, Cho H. Effects of intermittent or single high-dose vitamin D supplementation on risk of falls and fractures: a systematic review and meta-analysis. Osteoporos Int 2023;34(8):1355-67.
12. World Health Organization (WHO) Scientific Group on the Prevention and Management of Osteoporosis. Prevention and management of osteoporosis: report of a WHO scientific group [Internet]. WHO; 2003 [cited Jan 18, 2024]. Available from: https://iris.who.int/handle/10665/42841
13. Bischoff-Ferrari HA, Giovannucci E, Willett WC, Dietrich T, Dawson-Hughes B. Estimation of optimal serum concentrations of 25-hydroxyvitamin D for multiple health outcomes. Am J Clin Nutr 2006;84(1):18-28.
14. Bischoff-Ferrari HA, Shao A, Dawson-Hughes B, Hathcock J, Giovannucci E, Willett WC. Benefit-risk assessment of vitamin D supplementation. Osteoporos Int 2010;21(7):1121-32.
15. Einarsdóttir K, Preen DB, Clay TD, Kiely L, Holman CD, Cohen LD. Effect of a single 'megadose' intramuscular vitamin D (600,000 IU) injection on vitamin D concentrations and bone mineral density following biliopancreatic diversion surgery. Obes Surg 2010;20(6):732-7.

 https://doi.org/10.15384/kjhp.2024.00017

Original Article

Korean J Health Promot 2024;24(1):11-19
pISSN: 2234-2141 • eISSN: 2093-5676
https://doi.org/10.15384/kjhp.2024.00010

Korean Journal of Health Promotion
KJHP

Association between Allergic Rhinitis and Osteoarthritis in the Korean Adult Population–Based on the 3rd to 8th Korea National Health and Nutrition Examination Survey

Sunmi KIM, MD, MS

Department of Family Medicine, Kangwon National University Hospital, Kangwon National University College of Medicine, Chuncheon, Korea

Abstract

Background: Recent studies reported a significant association between asthma and osteoarthritis, but the relationship between allergic rhinitis and osteoarthritis has not been studied sufficiently. This study aimed to determine the association between allergic rhinitis and osteoarthritis in adults.

Methods: Using data from the 3rd to 8th Korea National Health and Nutrition Examination Survey, multiple logistic and linear regression analyses were conducted to determine the association between allergic rhinitis and osteoarthritis with adjustment for potential confounding factors in participants aged 50 years or older.

Results: When adjusted for potential confounders, doctor-diagnosed osteoarthritis (adjusted odds ratio [OR]=1.32, 95% confidence interval [95% CI]=1.12–1.57, *P*=0.001), knee pain (adjusted OR=2.42, 95% CI=1.32–4.41, *P*=0.004), and symptomatic knee osteoarthritis (adjusted OR=2.69, 95% CI=1.10–6.57, *P*=0.030) were all significantly more frequent in participants with allergic rhinitis than in those without it.

Conclusions: These findings show an evident association between allergic rhinitis and osteoarthritis in Korean adults.

Keywords: Allergic rhinitis, Osteoarthritis, Knee

INTRODUCTION

Osteoarthritis is a common degenerative joint disease that causes pain and structural and functional damage [1]. The pathogenesis of osteoarthritis is largely unknown, and there is no treatment method to restore damaged cartilage or slow down the progression of the disease [2]. Recently, it has been reported that immunoglobulin E (IgE)-mediated activation of mast cells in the synovium may play an important role in driving the progression of osteoarthritis [3]. The IgE-mediated degranulation of mast cells is also a characteristic of allergic diseases, and recent studies have shown a genetic association between osteoarthritis and allergic diseases such as asthma and allergic rhinitis [4]. If molecular pathways related to allergic conditions play a key role in the mechanism of osteoarthritis, therapeutic agents targeting them might prevent the development or progression of osteo-

Received: January 17, 2024; **Revised:** February 14, 2024; **Accepted:** February 21, 2024
Corresponding author: Sunmi KIM, MD, MS
Department of Family Medicine, Kangwon National University Hospital, Kangwon National University College of Medicine, 156 Baengnyeong-ro, Chuncheon 24289, Korea
Tel: +82-33-258-2401 Fax: +82-33-258-2165 E-mail: arpsm800@gmail.com

arthritis. A retrospective cohort study reported that the risk of developing osteoarthritis is increased in patients with asthma or atopic dermatitis [5]. A significant association between asthma and osteoarthritis was also reported in a cross-sectional study conducted in Korea [6]. On the other hand, a Japanese study revealed ambiguous results, showing that osteoarthritis of the temporomandibular joint was not related to asthma, but related to allergies [7]. In addition, Korean studies using data from the Korea National Health and Nutrition Examination Survey (KNHANES) reported conflicting results regarding the relationship between allergic rhinitis and osteoarthritis [8,9]. However, both studies used only 3 to 4 years of the KNHANES data and included the entire population aged 19 or older [8,9]. As a result, the majority of the study subjects were in the age group where osteoarthritis is not prevalent [8,9]. Thus, this study aimed to investigate the relationship between allergic rhinitis and osteoarthritis among participants aged 50 years or older in the KNHANES from the 3rd to the 8th period.

METHODS

Study population

This study was conducted using data from the KNHANES from 2005 to 2021. The survey includes a health interview, physical examination, and laboratory tests. In 2005 to 2021, the KNHANES collected data on doctor-diagnosed osteoarthritis. In 2010 to 2013, the KNHANES included a screening survey for knee osteoarthritis. Accordingly, this study analyzed two study populations: study population 1 to confirm the association between allergic rhinitis and doctor-diagnosed osteoarthritis and study population 2 to confirm the association between allergic rhinitis and outcomes from the screening survey for knee osteoarthritis.

Study population 1 consisted of participants from 2005 to 2021. Because the prevalence of osteoarthritis is very low under 50 years of age, and the screening survey for knee osteoarthritis was conducted in participants aged 50 years or older, subjects younger than 50 years were excluded. In addition, the following subjects were excluded subsequently: those with missing data on doctor-diagnosed osteoarthritis and allergic rhinitis, and those with incomplete data on potential confounding variables. Thus, a total of 44,538 subjects were included in study population 1 (Fig. 1). Additionally, subjects without data on the screening survey for knee osteoarthritis were excluded from study population 1, and the remaining 10,729 subjects were designated as study population 2 (Fig. 1).

Variable definitions

The doctor-diagnosed osteoarthritis was determined by the following question: "Have you been diagnosed with osteoarthritis by a doctor?" [6] Allergic rhinitis was determined by whether or not the participant was diagnosed by a doctor before the age of 50. Knee pain was determined by the following question: "Have you had knee pain for 30 days or longer in the past 3 months?" If "yes", the respondents were asked the average degree of pain on a scale of 0 to 10 regardless of medication use. If "no", the knee pain score was considered as 0. The osteoarthritis screening survey included radiographic examination of the knee (SD3000 Synchro Stand; Accele Ray, Bern, Switzerland) [6]. Radiographic knee osteoarthritis was defined as a Kellgren-Lawrence Grading Scale score ≥2 [10]. Symptomatic knee osteoarthritis was defined as having both radiographic knee osteoarthritis and knee pain [11].

Age was classified as 50 to <60 years, 60 to <70 years, and 70 years or older. Education level was divided into elementary

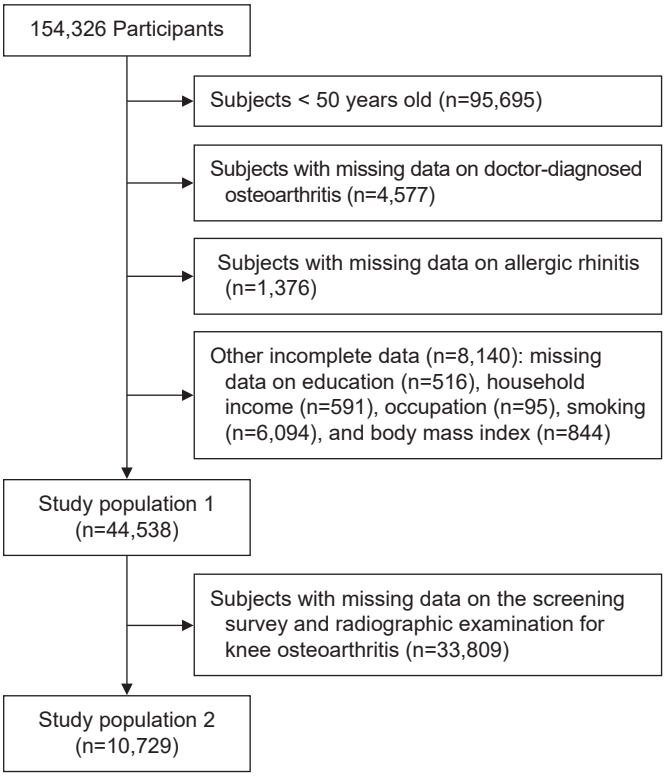

Fig. 1. Flow chart of the two study populations: study population 1 and 2.

https://doi.org/10.15384/kjhp.2024.00010

school or less, middle school, high school, and college or above. Household income was divided into four groups according to income quartile: low, mid-low, mid-high, and high. Occupation was classified based on Korean Standard Classification of Occupations as follows: group 1 (managers, professionals, and related workers); group 2 (clerks); group 3 (service and sales workers); group 4 (skilled agricultural, forestry, and fishery workers); group 5 (craft, equipment, and machine operating and assembling workers); group 6 (elementary workers); and group 7 (housewives, students, and the unemployed). In this study, groups 1, 2, 3, and 7 were merged into a single group (Group A) and groups 4, 5, and 6 were also merged (Group B) [12]. Smoking was classified as never smoked, ex-smoker, current smoker: those who smoked less than 100 cigarettes in their lifetime defined as never smoked, those who smoked in the past but do not currently smoke defined as ex-smokers, and those who currently smoked defined as current smokers [13].

Statistical analyses

Because the KNHANES used a multi-stage stratified cluster probability sampling method, the clusters, strata, and weights of the data were used to account for the complex sampling design. All statistical analyses were conducted using the statistical software package R version 4.2.3 (The R Foundation for Statistical Computing), and a two-sided *P*-value less than 0.05 was considered as statistically significant.

The proportions or means and standard deviations were estimated for demographic, socioeconomic, and clinical variables. The differences in the variables according to doctor-diagnosed osteoarthritis or allergic rhinitis were assessed using the Pearson chi-square test with Rao-Scott adjustment or design-based Wilcoxon rank-sum test for complex sample survey data.

To estimate odds ratios (ORs) of doctor-diagnosed osteoarthritis according to allergic rhinitis in study population 1, simple and multiple logistic regression analyses were performed. The multiple logistic regression model included potential confounding variables such as sex, age, education, household income, occupation, smoking, and body mass index.

To estimate ORs of knee pain, radiographic knee osteoarthritis, and symptomatic knee osteoarthritis according to allergic rhinitis in study population 2, simple and multiple logistic regression analyses were also conducted. The multiple logistic regression models included the same confounding variables as those used in study population 1.

To estimate the mean knee pain scores according to allergic rhinitis in subjects with radiographic knee osteoarthritis, simple and multiple linear regression analyses were conducted. The multiple linear regression models included the same confounding variables as those used in the multiple logistic regression models.

Ethics statement

This study was exempted from approval by the Institutional Review Board because this study was a secondary data analysis of existing data.

RESULTS

The demographic, socioeconomic, and clinical characteristics of study population 1 are summarized in Table 1. The frequency of allergic rhinitis was lower in subjects with doctor-diagnosed osteoarthritis than in those without it (proportion±standard error, 3.2%±0.2% vs. 4.2%±0.1%; *P*=0.001).

The characteristics of study population 2 are presented in Table 2. There was no significant difference in the frequencies of knee pain, radiographic knee osteoarthritis, and symptomatic knee osteoarthritis between those with and without allergic rhinitis (*P*=0.380, 0.121, and 0.845, respectively). Knee pain scores were also not significantly different between those with and without allergic rhinitis (*P*=0.471).

Without adjustment for potential confounders, the odds of doctor-diagnosed osteoarthritis were significantly lower in subjects with allergic rhinitis than in those without it (OR=0.76, 95% confidence interval [95% CI]=0.65–0.89, *P*<0.001) (Table 3). However, the multiple logistic regression analysis adjusting for confounding factors showed that the odds of doctor-diagnosed osteoarthritis were significantly higher in participants with allergic rhinitis than in those without it (adjusted OR=1.32, 95% CI=1.12–1.57, *P*=0.001) (Table 3).

Without adjustment for confounders, the odds of knee pain were not significantly different between subjects with and without allergic rhinitis (OR=1.30, 95% CI=0.72–2.33, *P*=0.381) (Table 4). However, multiple logistic regression analyses adjusting for confounders showed that the odds of knee pain were significantly higher in participants with allergic rhinitis than in those without it (adjusted OR=2.42, 95% CI=1.32–4.41, *P*=0.004) (Table 4).

The odds of radiographic knee osteoarthritis were not significantly different between subjects with and without allergic rhinitis regardless of adjustment for confounders (*P*=0.126 and 0.458 for without and with confounder adjustment, respectively) (Table 4).

Table 1. Characteristics of study population 1

Characteristic	Total (n=44,538)	Doctor-diagnosed osteoarthritis		*P*-value[a]
		No (n=34,836)	Yes (n=9,702)	
Total		80.7±0.2	19.3±0.2	
Allergic rhinitis				0.001
No	96.0±0.1	95.8±0.1	96.8±0.2	
Yes	4.0±0.1	4.2±0.1	3.2±0.2	
Sex				<0.001
Female	53.3±0.2	46.9±0.3	80.4±0.5	
Male	46.7±0.2	53.1±0.3	19.6±0.5	
Age (yr)				<0.001
50 to <60	45.8±0.4	50.9±0.4	24.3±0.6	
60 to <70	29.9±0.3	28.8±0.3	34.6±0.6	
≥70	24.3±0.3	20.3±0.3	41.1±0.6	
Education				<0.001
Elementary school or less	37.7±0.4	32.2±0.4	60.6±0.7	
Middle school	16.8±0.2	16.9±0.3	16.3±0.5	
High school	28.1±0.3	30.9±0.4	16.4±0.5	
College or above	17.5±0.4	20.0±0.4	6.8±0.3	
Household income				<0.001
Low	26.3±0.4	23.0±0.4	40.3±0.7	
Mid-low	25.3±0.3	25.1±0.3	26.3±0.6	
Mid-high	23.1±0.3	24.1±0.3	18.5±0.5	
High	25.3±0.4	27.8±0.5	14.9±0.5	
Occupation[b]				<0.001
Group A	68.4±0.4	67.4±0.4	72.8±0.6	
Group B	31.6±0.4	32.6±0.4	27.2±0.6	
Smoking				<0.001
Never smoked	57.0±0.3	52.2±0.3	77.2±0.5	
Ex-smoker	25.6±0.2	28.3±0.3	14.4±0.4	
Current smoker	17.4±0.2	19.5±0.3	8.4±0.4	
Body mass index (kg/m^2)				
Mean	24.16±0.02	23.97±0.02	24.95±0.04	<0.001
Standard deviation	3.16±0.02	3.10±0.02	3.30±0.03	

Each figure represents estimates±standard errors of percentages for categorical variables, and those of means and standard deviations for body mass index.
[a]*P*-values were obtained by Pearson chi-square test with Rao-Scott adjustment for categorical variables and by design-based Wilcoxon rank-sum test for complex sample survey data for body mass index. [b]Group A: managers, professionals, and related workers; clerks; service and sales workers; housewives, students, and the unemployed. Group B: skilled agricultural, forestry, and fishery workers; craft, equipment, and machine operating and assembling workers; elementary workers.

Without adjustment for confounders, the odds of symptomatic knee osteoarthritis were not significantly different between subjects with and without allergic rhinitis (OR=0.92, 95% CI=0.40–2.14, *P*=0.846) (Table 4). However, multiple logistic regression analyses adjusting for confounders showed that the odds of symptomatic knee osteoarthritis were significantly higher in participants with allergic rhinitis than in those without it (adjusted OR=2.69, 95% CI=1.10–6.57, *P*=0.030) (Table 4).

Without adjustment for confounders, mean knee pain scores were not significantly different between participants with and without allergic rhinitis (*P*=0.710) (Table 5). When adjusted for confounders, mean knee pain scores were also not significantly different between participants with and without allergic rhinitis (estimated marginal means 3.31 [95% CI=1.51–5.11] vs. 2.35 [95% CI=2.21–2.48], respectively; adjusted mean difference 0.96 [95% CI=–0.84 to 2.77], *P*=0.295) (Table 5, Fig. 2).

DISCUSSION

The results of this study show that there is an evident association between allergic rhinitis and osteoarthritis. When adjusted for potential confounders, doctor-diagnosed osteoarthritis, knee pain, and symptomatic knee osteoarthritis were all significantly more frequent in participants with allergic rhinitis. To

 https://doi.org/10.15384/kjhp.2024.00010

Table 2. Characteristics of study population 2

Characteristic	Total (n=10,729)	Allergic rhinitis		*P*-value
		No (n=10,657)	Yes (n=72)	
Total		99.0±0.1	1.0±0.1	
Sex				0.572[a]
Female	54.0±0.5	54.0±0.5	57.8±6.5	
Male	46.0±0.5	46.0±0.5	42.2±6.5	
Age (yr)				<0.001[a]
50 to <60	46.7±0.7	46.3±0.7	91.1±3.1	
60 to <70	28.3±0.6	28.5±0.6	7.4±3.0	
≥70	25.0±0.6	25.2±0.6	1.5±1.1	
Education				<0.001[a]
Elementary school or less	45.6±0.8	45.9±0.8	22.6±5.5	
Middle school	18.4±0.5	18.3±0.5	24.3±5.3	
High school	25.0±0.6	25.0±0.6	26.4±5.2	
College or above	11.0±0.5	10.9±0.5	26.6±6.0	
Household income				0.046[a]
Low	29.3±0.8	29.4±0.8	17.7±5.7	
Mid-low	25.7±0.7	25.8±0.7	20.0±4.6	
Mid-high	21.9±0.6	21.8±0.6	25.7±5.8	
High	23.1±0.7	23.0±0.7	36.6±6.9	
Occupation[c]				0.199[a]
Group A	65.1±0.9	65.0±0.9	73.9±6.3	
Group B	34.9±0.9	35.0±0.9	26.1±6.3	
Smoking				0.646[a]
Never smoked	56.6±0.5	56.5±0.5	62.6±6.4	
Ex-smoker	24.5±0.5	24.6±0.5	22.3±6.0	
Current smoker	18.9±0.5	18.9±0.5	15.2±4.6	
Body mass index (kg/m^2)				
Mean	24.10±0.04	24.10±0.04	23.73±0.34	0.370[b]
Standard deviation	3.13±0.03	3.13±0.03	2.73±0.28	
Knee pain				0.380[a]
No	79.2±0.5	79.3±0.5	74.7±5.6	
Yes	20.8±0.5	20.7±0.5	25.3±5.6	
Radiographic knee osteoarthritis				0.121[a]
No	64.7±0.8	64.6±0.8	75.6±6.4	
Yes	35.3±0.8	35.4±0.8	24.4±6.4	
Symptomatic knee osteoarthritis				0.845[a]
No	87.4±0.4	87.4±0.4	88.3±4.5	
Yes	12.6±0.4	12.6±0.4	11.7±4.5	
Knee pain score				
Mean	1.28±0.03	1.28±0.03	1.39±0.38	0.471[b]
Standard deviation	2.76±0.04	2.76±0.04	2.85±0.43	

Each figure represents estimates±standard errors of percentages for categorical variables, and those of means and standard deviations for continuous variables.

[a]*P*-values were obtained by Pearson chi-square test with Rao-Scott adjustment. [b]*P*-values were obtained by design-based Wilcoxon rank-sum test for complex sample survey data. [c]Group A: managers, professionals, and related workers; clerks; service and sales workers; housewives, students, and the unemployed. Group B: skilled agricultural, forestry, and fishery workers; craft, equipment, and machine operating and assembling workers; elementary workers.

the best of my knowledge, there have been no large-scale studies that investigated the relationship between allergic rhinitis and osteoarthritis in particular with analysis on the pain and radiographic findings of specific joints. Additionally, since the KNHANES data used in this study are nationally representative, the findings of this study can be extrapolated to the general Korean adult population aged 50 years or older.

There have been few studies on the relationship between allergic rhinitis and osteoarthritis, and their results were inconsistent, making it difficult to reach a clear conclusion. An et al. [8]

Table 3. Factors associated with doctor-diagnosed osteoarthritis in study population 1

	Simple logistic regression		Multiple logistic regression	
	OR (95% CI)	*P*-value	Adjusted OR (95% CI)	*P*-value
Allergic rhinitis		<0.001		0.001
No	Reference	-	Reference	-
Yes	0.76 (0.65–0.89)	<0.001	1.32 (1.12–1.57)	0.001
Sex		<0.001		<0.001
Female	Reference	-	Reference	-
Male	0.22 (0.20–0.23)	<0.001	0.25 (0.23–0.28)	<0.001
Age (yr)		<0.001		<0.001
50 to <60	Reference	-	Reference	-
60 to <70	2.51 (2.34–2.70)	<0.001	2.11 (1.94–2.28)	<0.001
≥70	4.22 (3.93–4.54)	<0.001	3.02 (2.76–3.31)	<0.001
Education		<0.001		<0.001
Elementary school or less	Reference	-	Reference	-
Middle school	0.51 (0.47–0.55)	<0.001	0.86 (0.79–0.94)	0.001
High school	0.28 (0.26–0.30)	<0.001	0.58 (0.54–0.64)	<0.001
College or above	0.18 (0.16–0.20)	<0.001	0.47 (0.42–0.53)	<0.001
Household income		<0.001		<0.001
Low	Reference	-	Reference	-
Mid-low	0.60 (0.56–0.64)	<0.001	0.88 (0.82–0.95)	0.001
Mid-high	0.44 (0.41–0.47)	<0.001	0.83 (0.76–0.90)	<0.001
High	0.31 (0.28–0.33)	<0.001	0.76 (0.69–0.84)	<0.001
Occupation[a]		<0.001		0.576
Group A	Reference	-	Reference	-
Group B	0.77 (0.72–0.82)	<0.001	1.02 (0.95–1.09)	0.576
Smoking		<0.001		0.332
Never smoked	Reference	-	Reference	-
Ex-smoker	0.34 (0.32–0.37)	<0.001	1.05 (0.94–1.17)	0.365
Current smoker	0.29 (0.26–0.32)	<0.001	0.96 (0.85–1.09)	0.553
Body mass index (kg/m^2)	1.10 (1.09–1.11)	<0.001	1.10 (1.09–1.11)	<0.001

P-values were calculated by generalized linear model for complex survey design.
CI, confidence interval; OR, odds ratio.
[a]Group A: managers, professionals, and related workers; clerks; service and sales workers; housewives, students, and the unemployed. Group B: skilled agricultural, forestry, and fishery workers; craft, equipment, and machine operating and assembling workers; elementary workers.

Table 4. Association of allergic rhinitis with knee pain, radiographic knee osteoarthritis, and symptomatic knee osteoarthritis in study population 2

	Simple logistic regression		Multiple logistic regression[a]	
	OR (95% CI)	*P*-value	Adjusted OR (95% CI)	*P*-value
Knee pain	1.30 (0.72–2.33)	0.381	2.42 (1.32–4.41)	0.004
Radiographic knee osteoarthritis	0.59 (0.30–1.16)	0.126	1.32 (0.64–2.73)	0.458
Symptomatic knee osteoarthritis	0.92 (0.40–2.14)	0.846	2.69 (1.10–6.57)	0.030

P-values were calculated by generalized linear model for complex survey design.
CI, confidence interval; OR, odds ratio.
[a]Multiple logistic regression models with adjustment for sex, age, education, household income, occupation, smoking, and body mass index.

Table 5. Association of allergic rhinitis with knee pain scores in participants with radiographic knee osteoarthritis

	Simple linear regression		Multiple linear regression[a]	
	Mean difference (95% CI)	*P*-value	Adjusted mean difference (95% CI)	*P*-value
Knee pain score	0.35 (−1.51 to 2.22)	0.710	0.96 (−0.84 to 2.77)	0.295

P-values were calculated by generalized linear model for complex survey design.
CI, confidence interval.
[a]Multiple linear regression models with adjustment for sex, age, education, household income, occupation, smoking, and body mass index.

 https://doi.org/10.15384/kjhp.2024.00010

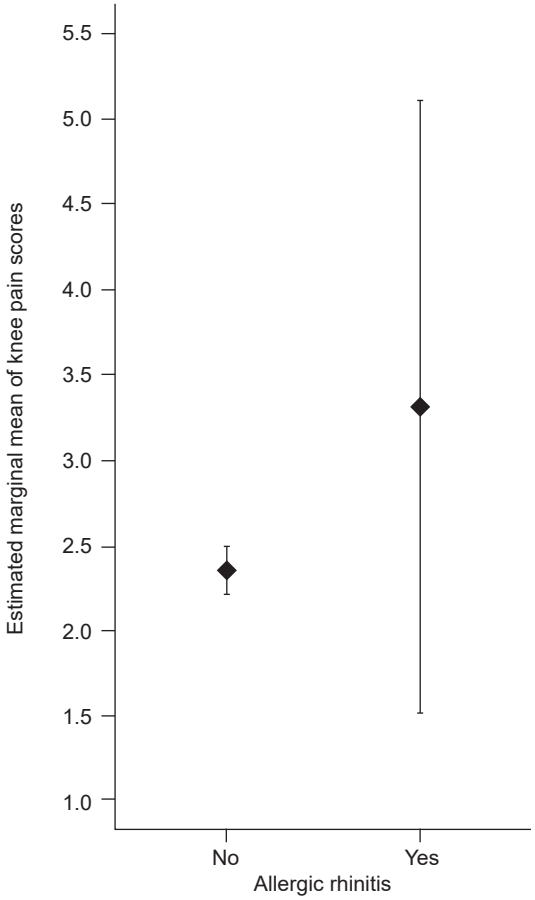

Fig. 2. Estimated marginal mean knee pain scores in participants with and without allergic rhinitis calculated by multiple linear regression analyses with adjustment for sex, age, education, household income, occupation, smoking, and body mass index. The error bars indicate 95% confidence intervals.

analyzed the KNHANES data from 2008 to 2011 and reported that there is no significant association between allergic rhinitis and osteoarthritis. On the other hand, Lee et al. [9] reported that osteoarthritis is more prevalent in those with allergic rhinitis by analyzing the KNHANES data from 2016 to 2018. Both studies covered only 3 to 4 years of the KNHANES data, and neither of the studies analyzed symptoms and radiographic findings for the knee joint. Accordingly, this study covered a total of 16 years of KNHANES data from the 3rd to the 8th period, and analyzed the osteoarthritis screening survey data from 2010 to 2013 as main outcome variables.

The association between allergic rhinitis and osteoarthritis may result from the genetic link between the two diseases. A recent study showed that those with genetic variations associated with allergic rhinitis and asthma have an increased risk of developing osteoarthritis [4]. It has also been reported that increased serum IgE levels are associated with osteoarthritis of the knee [14]. IgE may contribute to the aggravation of osteoarthritis by activating mast cells in the synovium [3]. An increase in serum IgE levels is also common in allergic conditions including allergic rhinitis, asthma, and atopic dermatitis, which might contribute to the association between osteoarthritis and the allergic conditions. Further studies would be needed to elucidate the underlying mechanisms.

The results of this study show that the adjustment for confounding variables was necessary to confirm the association between allergic rhinitis and osteoarthritis. Without adjusting for confounding factors, no significant association or even an inverse relationship was found between allergic rhinitis and osteoarthritis. However, when adjusting for confounding variables, the significant associations were confirmed between allergic rhinitis and osteoarthritis. This appears to mainly result from the confounding effect of age. The prevalence of osteoarthritis increased rapidly with age, but that of allergic rhinitis showed the opposite pattern.

In contrast with doctor diagnosis of osteoarthritis, knee pain, and symptomatic knee osteoarthritis, radiographic knee osteoarthritis was not more frequent in those with allergic rhinitis. The cause of this difference between clinical and radiological findings is unclear, but it is known that radiographic diagnosis of osteoarthritis is often discordant with clinical symptoms [15]. Thus, the diagnosis of osteoarthritis is based on clinical symptoms and signs as well as radiological findings [16], and patient's symptoms may be more meaningful related to the functional outcomes than radiological findings [17]. Furthermore, the Kellgren-Lawrence Grading Scale has been criticized on the basis of its reliability and the lack of recognition of patellofemoral arthritis [18]. When conducting epidemiological studies on osteoarthritis, one of three definitions of osteoarthritis is commonly used: subjects' self-reports, radiographic osteoarthritis, or symptomatic osteoarthritis [11]. Generally, the radiographic definition leads to higher prevalence and heterogeneous results between studies. In contrast, subjects' self-reports and symptomatic osteoarthritis result in similar prevalence estimates and show more homogeneous and consistent results across studies [11]. On the other hand, allergic rhinitis may play a role in aggravating symptoms of osteoarthritis rather than initiating the disease. Activated mast cells are known to aggravate pain in joints with osteoarthritis and their number in the synovium has a positive correlation with the disease severity [19]. The

increase in IgE, which is common in allergic rhinitis, induces mast cell activation. These mechanisms might underlie the worse osteoarthritis symptoms in subjects with allergic rhinitis observed in this study.

Among subjects with radiographic knee osteoarthritis, the mean knee pain score was numerically higher in participants with allergic rhinitis than in those without it, but the difference was not statistically significant. This statistical insignificance appears to be due to insufficient statistical power from the small number of subjects available for the analyses. Because the linear regression analyzed only subjects with radiographic knee osteoarthritis, not the entire study population 2, the number of subjects was inevitably small compared to the other analyses.

This study has several limitations. First, the cross-sectional design of the KNHANES made it possible to determine the association between allergic rhinitis and osteoarthritis, but additional studies will be needed to confirm the causality between them. Second, doctor diagnoses of osteoarthritis and allergic rhinitis may be inaccurate as they were based solely on participant reports. Third, because the KNHANES was conducted within Korea, it is difficult to directly extrapolate the results of this study to other countries.

In conclusion, this study confirmed a clear association between allergic rhinitis and osteoarthritis in Korean adults. Further studies will be needed to determine whether this association is generally observed in other populations and whether a causal relationship also exists between them.

ORCID

Sunmi KIM, https://orcid.org/0000-0002-8801-3353

AUTHOR CONTRIBUTIONS

Dr. Sunmi KIM had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Dr. Sunmi KIM reviewed this manuscript and agreed to individual contributions.

Conceptualization, Data curation, Formal analysis, Methodology, Software, Writing–original draft, Writing–review & editing: SK.

CONFLICTS OF INTEREST

No existing or potential conflict of interest relevant to this article was reported.

FUNDING

None.

DATA AVAILABILITY

The data presented in this study are available upon reasonable request from the corresponding author.

REFERENCES

1. Allen KD, Thoma LM, Golightly YM. Epidemiology of osteoarthritis. Osteoarthritis Cartilage 2022;30(2):184-95.
2. Chen D, Shen J, Zhao W, Wang T, Han L, Hamilton JL, et al. Osteoarthritis: toward a comprehensive understanding of pathological mechanism. Bone Res 2017;5:16044.
3. Ioan-Facsinay A. Initiating pain in osteoarthritis (OA): is it the mast cell? Osteoarthritis Cartilage 2018;26(1):1-3.
4. Baker MC, Robinson WH, Ostrom Q. Genetic association between atopic disease and osteoarthritis. Osteoarthritis Cartilage 2024;32(2):220-5.
5. Baker MC, Sheth K, Lu R, Lu D, von Kaeppler EP, Bhat A, et al. Increased risk of osteoarthritis in patients with atopic disease. Ann Rheum Dis 2023;82(6):866-72.
6. Koo HK, Song P, Lee JH. Novel association between asthma and osteoarthritis: a nationwide health and nutrition examination survey. BMC Pulm Med 2021;21(1):59.
7. Nishioka M, Ioi H, Matsumoto R, Goto TK, Nakata S, Nakasima A, et al. TMJ osteoarthritis/osteoarthrosis and immune system factors in a Japanese sample. Angle Orthod 2008;78(5):793-8.
8. An SY, Choi HG, Kim SW, Park B, Lee JS, Jang JH, et al. Analysis of various risk factors predisposing subjects to allergic rhinitis. Asian Pac J Allergy Immunol 2015;33(2):143-51.
9. Lee GN, Koo HYR, Han K, Lee YB. Analysis of quality of life and mental health in patients with atopic dermatitis, asthma and allergic rhinitis using a nation-wide database, KNHANES VII. Allergy Asthma Immunol Res 2022;14(2):273-83.
10. Guermazi A, Eckstein F, Hayashi D, Roemer FW, Wirth W, Yang T, et al. Baseline radiographic osteoarthritis and semi-quantitatively assessed meniscal damage and extrusion and cartilage damage on MRI is related to quantitatively defined cartilage thickness loss in knee osteoarthritis: the Multicenter Osteoarthritis Study. Osteoarthritis Cartilage 2015;23(12):2191-8.

11. Pereira D, Peleteiro B, Araújo J, Branco J, Santos RA, Ramos E. The effect of osteoarthritis definition on prevalence and incidence estimates: a systematic review. Osteoarthritis Cartilage 2011;19(11):1270-85.
12. Cheng HM, Kim S, Park GH, Chang SE, Bang S, Won CH, et al. Low vitamin D levels are associated with atopic dermatitis, but not allergic rhinitis, asthma, or IgE sensitization, in the adult Korean population. J Allergy Clin Immunol 2014;133(4):1048-55.
13. Yuan H, Kim MK. Prevalence of metabolic syndrome and related factors based on smoking status and physical activity in Korean adult men. Korean J Health Promot 2023;23(2):75-84.
14. Park S, Choi NK. Association between serum immunoglobulin E levels and knee osteoarthritis in Korean adults. Osteoarthritis Cartilage 2020;28(4):462-7.
15. Bedson J, Croft PR. The discordance between clinical and radiographic knee osteoarthritis: a systematic search and summary of the literature. BMC Musculoskelet Disord 2008;9:116.
16. Sinusas K. Osteoarthritis: diagnosis and treatment. Am Fam Physician 2012;85(1):49-56.
17. Nelson AE, Elstad E, DeVellis RF, Schwartz TA, Golightly YM, Renner JB, et al. Composite measures of multi-joint symptoms, but not of radiographic osteoarthritis, are associated with functional outcomes: the Johnston County Osteoarthritis Project. Disabil Rehabil 2014;36(4):300-6.
18. Kohn MD, Sassoon AA, Fernando ND. Classifications in brief: Kellgren-Lawrence classification of osteoarthritis. Clin Orthop Relat Res 2016;474(8):1886-93.
19. Dan J, Izumi M, Habuchi H, Habuchi O, Takaya S, Kasai Y, et al. A novel mice model of acute flares in osteoarthritis elicited by intra-articular injection of cultured mast cells. J Exp Orthop 2021;8(1):75.

Original Article

Korean J Health Promot 2024;24(1):20-28
pISSN: 2234-2141 • eISSN: 2093-5676
https://doi.org/10.15384/kjhp.2024.00024

Korean Journal of Health Promotion
KJHP

Effect of Counting Error Prevention Training on Operating Room Nurses' Counting Error Prevention Awareness and Perceptions of Patient Safety

Myung Jin JANG, RN, MS[1], Mi Kyung HONG, RN[2], Mi Jeong LEE, RN[2], Kyung A LEE, RN, MS[2], Yang Ok KIM, RN, MS[2], Jin A JEON, RN[2], Hana KO, RN, GNP, PhD[3]

[1]Incheon Regional Trauma Center, Gachon University Gil Medical Center, Incheon, Korea
[2]Operating Room, Gachon University Gil Medical Center, Incheon, Korea
[3]College of Nursing, Gachon University, Incheon, Korea

Abstract

Background: This study aimed to identify changes in counting error prevention awareness and patient safety perception through counting error prevention education to operating room nurses.
Methods: This was a one-group, pretest-posttest, quasi-experimental study. The participants were operating room nurses. A total of 46 nurses were recruited, and data was collected between October 1 and 31, 2022. Measures used for this study assessed counting error prevention awareness and patient safety perception. The data were analyzed using paired t-tests.
Results: The counting error prevention awareness of the participants increased significantly from 3.68 to 3.95 points before and after education, respectively (t=−5.07, P<0.001), while patient safety perception significantly increased from 3.95 to 4.20 points before and after training, respectively (t=−2.68, P=0.010).
Conclusions: Counting error prevention awareness and patient safety perception of operating room nurses prevent fatal damage to patients with surgeries and lower mortality. The results of this study suggest the necessity of various education methods to reduce medical accidents among surgical patients and to raise patient safety perception for operating room nurses.

Keywords: Nurses, Operating rooms, Operating room nursing, Patient safety, Surgery

INTRODUCTION

The operating room (OR) is a high-risk environment within a healthcare organization with a high incidence of errors resulting in serious injury or death to patients [1]. Furthermore, various interdisciplinary surgeries are performed in the OR, and surgical nursing care is provided here. Therefore, accurate communication with interdisciplinary team members and an understanding of equipment and supplies are required; high risk of patient safety incidents exists when these skills are lacking [2].

In the OR, verifying the type and number of items used during surgery is called "counting" and is one of the most important tasks to protect the patient from retained gauze, sutures, and surgical instruments in their body. It is also important for

Received: January 23, 2024; **Revised:** February 26, 2024; **Accepted:** March 7, 2024
Corresponding author: Hana KO, RN, GNP, PhD
College of Nursing, Gachon University, 191 Hambangmoe-ro, Yeonsu-gu, Incheon 21936, Korea
Tel: +82-32-820-4210 Fax: +82-32-820-4201 E-mail: hanago11@gachon.ac.kr

infection control, supply management, and the safety of medical personnel involved in surgery [3,4]. According to previous studies in Korea, "counting" ranked highest and second highest in the safety domain in the studies by Jang [5] and Kim and Kim [6], respectively, in terms of the importance of nursing interventions perceived by nurses working in the OR. As such, nurses in the OR consider counting to be one of the most important patient safety interventions. Nursing scholars and nurses in the field have been developing guidelines to reduce counting errors and suggesting ways to develop duty of care in the field, but counting errors still occur. Studies on OR miscounting errors have mainly addressed miscounting errors in the realm of safety management or conducted studies on factors related to miscounting errors [3,4,7], and studies on miscounting error prevention education are lacking. The standard guidelines for counting errors currently used in Korea are presented by the Korean Association of Operating Room Nurses, which is based on the standard guidelines of the American Association of Perioperative Registered Nurses and modified for Korea [8].

The importance of patient safety in the OR increases yearly, and according to a previous study, surgery-related areas recorded the highest report rate (36.9%) of medical disputes due to medical accidents in 2017 [9]. Patients undergoing surgery are unable to defend themselves due to anesthesia, and communication is difficult. Patient safety is consequently entirely the domain of the medical staff performing the surgery [2,9].

Given the importance of patient safety in the OR, the World Health Organization (WHO) has recommended the use of safety checklists, such as the WHO Surgical Safety Checklist [10], in hospitals to reduce the incidence of death and complications in surgical patients. Various outcomes have been reported, such as enhanced communication between healthcare providers, improved mobility, reduced surgical complications, and reduced readmission rates [2]. Other patient safety education programs have also been implemented, and several linear studies of nurses have reported that on-the-job training on basic skills and medication knowledge was effective in improving nurses' job confidence and medication knowledge. Furthermore, Kim et al. [11] reported positive effects on safety perception, sense of safety control, and acceptance of responsibility through patient safety-related nursing error prevention education using case studies.

The effectiveness of nurse education for patient safety has been proven by several studies. However, studies that have conducted patient safety education for OR nurses do not currently exist in Korea, and no study has measured the extent of patient safety awareness of OR nurses through counting error prevention education. Patient safety issues often arise in the OR, and these issues are related to the lives of surgical patients and complications. As such, the perception of patient safety by OR nurses is crucial, and measures to improve this perception of patient safety are needed [12].

Therefore, this study aimed to provide prevention education to OR nurses to determine the extent of prevention awareness and patient safety awareness before and after education and to provide a basis for developing an educational program for patient safety management of OR nurses.

METHODS

Study design

This study was a quasi-experimental study using a single-group pre-post design to determine the effectiveness of counting error prevention education by comparing changes in pre- and post-counting error prevention awareness and patient safety perceptions among OR nurses.

Participants

The participants of this study are nurses working in the OR of Gachon University Hospital located in Incheon City. The selection criteria for the participants were nurses with more than 3 months of work experience who had completed their initial training and were participating as disinfection or circulating nurses in the OR. Nurses working at this research organization during the study period and nurses with less than 3 months of work experience were excluded. The number of participants was calculated using the G*power 3.1.9.4 program based on a prior study by Kim et al. [13]. The power (0.8), significance level (0.05), and effect size (0.5) were calculated, and the initial sample size was 27. Considering a dropout rate of 20%, a total of 34 participants were selected. Ultimately, the analysis included all 46 participants who volunteered to attend training at a single study site.

Procedures: education to prevent counting errors

The educational materials for the prevention of counting errors used in this study were developed by seven medical staff working in the OR (three head nurses and four nurses with over 10 years of clinical experience in the OR) and one professor of nursing, who modified and supplemented the previously used

educational materials for OR nurses by referring to the 2013 article "Development of a guideline to prevent errors of surgical counts in the operating room at a university hospital" by Park and Jang [4].

The educational content consisted of the purpose of OR counting, OR counting guidelines (sponge counting guidelines, sharps counting guidelines, instrument counting guidelines, OR specimen counting guidelines, and guidelines for counting discrepancies), and OR counting records (surgical nursing record sheet guidelines, computerized surgical nursing record guidelines).

To enhance the content validity of the educational program, it was validated by six experts (two nurses with more than 10 years of experience in the OR, two nurses with more than 5 but less than 10 years of experience, one surgeon, and one nurse dedicated to OR education). As a result of the validation, the content validity of the education program was >0.8 for each component, and the training was conducted without further modifications.

The existing counting-error prevention education provided new nurses in the OR with approximately 10 minutes of education time and a surgical nursing guideline with a brief explanation during a 1 month-long curriculum. The counting-error prevention education developed in this study used a lecture-style education and presented counting-error cases to allow participants to discuss the problem. The education program comprised 40 minutes of lecture and 20 minutes of case-based discussions, focusing on specific examples of counting errors that can occur before, during, and following surgery. The sessions were conducted in person by the researcher, and due to the challenges posed by the nature of nurses' shift work, the training was divided into three sessions.

Measurements

General characteristics

The demographic characteristics investigated in this survey included sex, age, education level, total years of experience, years in the OR, position, work type, experience counting errors, and need for counting error education.

Cause of counting errors

We asked subjects what they thought were the causes of counting errors. After a preliminary survey of nurses working in the OR, we were able to collect the following items: 'time constraints,' 'pressure from the doctor,' 'insufficient knowledge,' 'burden to make mistakes,' and 'excessive work,' which we presented to the participants.

Awareness of counting error prevention

A tool developed by Park and Jang [4] and modified and supplemented by Lee [14] was used to measure the awareness of preventing counting errors. The tool consisted of 29, 94, and 13 questions before, during, and after surgery, respectively, totaling 136 questions in three subsections. The tool used a 4-point Likert scale ranging from 0 for "not at all important" to 4 for "very important," and the distribution of scores ranged from a minimum of 0 to a maximum of 544, with higher scores indicating greater awareness of preventing counting errors. The reliability of the tool was not published when it was developed, thus the exact reliability could not be confirmed. The Cronbach α was 0.99 in this study.

Patient safety perception

The patient safety perception measurement tool was the Hospital Survey on Patient Safety developed by the Agency for Health Research and Quality [15], a healthcare management organization in the United States, translated by Kim et al. [16], and modified by Park et al. [17]. The instrument consisted of 25 questions with five subscales: hospital environment (four questions), departmental work environment (eleven questions), communication and procedures (five questions), immediate supervisor/manager attitude (four questions), and departmental patient safety (one question). The tool used a 5-point Likert scale ranging from 1 ("not at all") to 5 ("very much so"), and the distribution of scores ranged from 25 to 125, with higher scores indicating higher levels of patient safety awareness. The reliability of the tool at the time of development was Cronbach α=0.82, and the reliability in this study was Cronbach α=0.94.

Data collection

The data collection period of this study was from October 1 to October 31, 2022. The pre-questionnaire was distributed in an envelope after completing the voluntary participation agreement, and the questionnaire was returned in the envelope after completion. The post-training questionnaire was also distributed in an envelope, which was returned in a sealed envelope after being filled out.

Data analysis

The collected data were analyzed using the IBM SPSS/WIN 25.0

https://doi.org/10.15384/kjhp.2024.00024

(IBM Corp.) program, and the specific analysis methods are as follows.

1) The general characteristics of the participants were analyzed using means, standard deviations, frequencies, and percentages.
2) The scores of the participants counting error prevention awareness and patient safety awareness were analyzed using the mean and standard deviation.
3) The paired t-test was used to compare the difference between pre- and post-education awareness and patient safety awareness.

Ethical considerations

The study was conducted after ethical review approval (No. GBIRB2021-480) from the research ethics committee of Gachon University Hospital located in Incheon City. Participants were informed of the relevance, purpose, benefits, and risks of the study; their autonomy to discontinue the study; the time required for training and questionnaire completion; and confidentiality of information. Participants were asked for their consent to participate in the study, and those who completed the questionnaire were provided with a token.

All participant information used in this study was anonymized with alphabetic and numeric characters. To enhance participant privacy, collected data were stored only on the personal computer of the principal investigator and encrypted so that only the principal investigator could access it. The data from this study were used only for the study and will be stored for 3 years after the completion of the study report before being destroyed to protect personal information.

RESULTS

General characteristics

The general characteristics of the participants are shown in Table 1. The average age of the participants was 26.93 years, and most were female (91.3%). In terms of education, 43 (93.5%) were 4-year graduates, and 30 (65.2%) were nurses with less than 3 years of overall clinical experience. Regarding OR experience, 33 (71.7%) had less than 3 years; generalist nurses were the most common with 42 (91.3%). Most nurses—42 (91.3%)—worked shifts, and 25 (54.3%) had experience with counting errors. When asked about the need for miscount training, 30 (65.2%) responded that it was very necessary and 16 (34.8%) responded that it was necessary.

Causes of counting errors according to the participants

Table 2 shows the causes of counting errors according to the participants. Among the causes of counting errors, 20 participants (43.5%) indicated "time constraints," followed by "pressure from the doctor (nine participants, 19.6%)," "insufficient knowledge (seven participants, 15.2%)," "burden to make mistakes (five participants, 10.9%)," and "excessive work (five par-

Table 1. General characteristics of participant (n=46)

Characteristic	Value
Age (yr)	26.93±5.74
Sex	
Female	42 (91.3)
Male	4 (8.7)
Level of education	
College	3 (6.5)
BSN	43 (93.5)
Total career (yr)	
<3	30 (65.2)
3–5	8 (17.4)
6–9	3 (6.5)
>9	5 (10.9)
Experience of operation room (yr)	
<3	33 (71.7)
3–5	6 (13.0)
6–9	3 (6.5)
>9	4 (8.7)
Position	
Staff nurse	42 (91.3)
Charge nurse	4 (8.7)
Duty type	
Rotation duty	42 (91.3)
Mid duty	4 (8.7)
Experience of counting error	
Yes	25 (54.3)
No	21 (45.7)
Need for counting error education	
Very necessary	30 (65.2)
Necessary	16 (34.8)

Values are presented as mean±standard deviation or number (%). The sum of the percentages does not equal 100% because of rounding.
BSN, bachelor of science in nursing.

Table 2. The cause of counting error in operating room nurses opinion (n=46)

Category	Value
Time shortage	20 (43.5)
Burden to make mistakes	5 (10.9)
By the pressure of the doctor	9 (19.6)
Insufficient of knowledge	7 (15.2)
Excessive work	5 (10.9)

Values are presented as number (%). The sum of the percentages does not equal 100% because of rounding.

ticipants, 10.9%)."

Awareness of counting errors prevention and perception of patient safety before and after education

The pre- and post-training awareness and patient safety perceptions of the participants are shown in Table 3. The total score of the participants' awareness of preventing counting errors before and after the training significantly increased from 500.76±51.56 (mean 3.68±0.38) before the training to 537.11±16.13 (mean 3.95±0.12) after the training (t=–5.07, *P*<0.001). Considering the differences in the subscale of awareness of preventing counting errors, the preoperative item increased significantly from 106.07±11.52 (rating mean 3.66±0.40) before education to 114.15±3.58 (rating mean 3.94±0.12) after training (t=–5.02, *P*<0.001), and the intraoperative items increased significantly from 345.20±37.74 (mean 3.67±1.30) before training to 371.00±11.03 (mean 3.95±0.12) after training (t=–4.95, *P*<0.001). The postoperative item significantly increased from 49.50±5.38 (mean 3.81±0.41) pre-training to 51.96±2.30 (mean 4.00±0.18) post-training (t=–2.80, *P*=0.007).

Participants' perception of patient safety increased significantly from 98.80±13.58 (mean 3.95±0.54) before the training to 104.91±14.36 (mean 4.20±0.57) after the training (t=–2.68, *P*=0.010).

DISCUSSION

Counting errors in the OR still occur, albeit less frequently than in the past, and are a medical error that can adversely affect patient outcomes. However, the exact incidence and cases of medical errors, including counting errors, are not shared due to hospital evaluation, patient safety concerns, and blame on individuals [18], and effective education on counting errors remains lacking. Therefore, to reduce the incidence of these errors and increase awareness of patient safety, this study was conducted to develop an education program on the prevention of counting errors and to determine its effectiveness after applying it to OR nurses.

The results of this study showed a significant increase in the participants' awareness of counting error prevention before and after training and a significant increase in each subdomain. Patient safety awareness also increased significantly from pre- to post-training. Based on these findings, this study indicates that the education of OR nurses on counting error prevention is beneficial for positive changes in awareness of counting error prevention and patient safety perceptions.

Given that the error prevention education used in this study was developed and applied by the developers, referring to the guidelines for error prevention in the OR by Park and Jang [4], direct comparison is difficult due to the lack of previous studies. That said, this study shall be compared to previous studies on error prevention activities for OR nurses and studies that measured patient safety awareness among nurses.

The participants' awareness of counting error prevention was 3.68±0.38 before training, which was somewhat lower than the mean of 3.89±0.20 in a study by Lee [14] that measured the awareness of counting error prevention among OR nurses. This difference may be due to the difference in clinical experience since only 28.2% of the nurses in the previous study had less than 3 years of experience, compared to 65.2% in this study. As such, education on counting error prevention should be specialized by years of experience, and education should be focused on those with less than 3 years of experience.

The participants' awareness of preventing counting errors increased significantly from 3.68±0.38 points before the training to 3.95±0.12 points after the training. Although accurate comparisons are difficult to make due to the lack of studies in Korea verifying the effectiveness of preventing counting errors, this study likely proved the effectiveness of preventing counting errors. Miscalculation is a medical error that causes fatal complications and deaths in surgical patients, thus subsequent studies should be conducted to verify the effectiveness of improving awareness of miscalculation prevention through education, as well as the reduction in the actual incidence of miscalculation

Table 3. Differences of counting error prevention awareness, patient safety perception before and after education (n=46)

Variable	Pre-education	Post-education	t (*P*)
Counting error prevention awareness	500.76±51.56 (3.68±0.38)	537.11±16.13 (3.95±0.12)	−5.07 (<0.001)
Preoperation	106.07±11.52 (3.66±0.40)	114.15±3.58 (3.94±0.12)	−5.02 (<0.001)
Intraoperation	345.20±37.74 (3.67±1.30)	371.00±11.03 (3.95±0.12)	−4.95 (<0.001)
Postoperation	49.50±5.38 (3.81±0.41)	51.96±2.30 (4.00±0.18)	−2.80 (0.007)
Patient safety perception	98.80±13.58 (3.95±0.54)	104.91±14.36 (4.20±0.57)	−2.68 (0.010)

Values are presented as mean±standard deviation of total score (mean score).

https://doi.org/10.15384/kjhp.2024.00024

through various education programs [4].

Furthermore, since this study was conducted only in one medical center and the education was delivered in a lecture format by the researcher, the effectiveness of education for the prevention of counting errors must be verified through various educational formats using simulations and multicenter studies in the future.

When looking at the difference in scores by subsection of the awareness of counting error prevention by training, the preoperative item had the largest difference in score. This suggests that there was a lack of training on the steps to verify the counting of pre-operative items and pre-operative preparation in general. As such, education must be provided to OR nurses focusing on preoperative nursing care, counting, and overall surgical preparation, and further studies should be conducted to verify the effectiveness of education in preventing preoperative counting errors.

The biggest problem with OR counting errors is the complications associated with retained foreign bodies in the body cavity. According to previous studies, it takes an average of 2.2 years for a foreign body to be detected after surgery, and the main complications are intestinal adhesions, abscesses, and fistula formation, and the mortality rate associated with foreign body retention is reported to be 11% to 35% [19,20]. Based on these previous studies, changes in the awareness of counting error prevention among OR nurses are directly related to patient safety issues, which are also linked to patient prognosis and survival. Therefore, although many hospitals in Korea conduct training, various societies and organizations, including the Hospital Surgical Nurses Association, should strive to improve the knowledge and awareness of OR nurses on counting error prevention through improved guidelines and regular education on counting error prevention.

In this study, we investigated the patient safety awareness of the participants, and the mean patient safety awareness before the training was 3.95±0.54. This was higher than the score of 3.33±0.39 in the study by Park et al. [17] on OR nurses, and higher than the score of 3.42±0.30 in the study by Kim and Kim [21] on general hospital nurses. Comparing the results of the present study with the two previous studies, educational levels differed, although the clinical experience was similar; 69.5% of the nurses in Park et al.'s study [17] were 3-year graduates, and 61.2% in Kim and Kim's study [21] were 3-year graduates, compared to 6.5% in this study. However, given that the educational level of the participants in the previous study was reported as 3.23±0.22 by Im and Park [22], where 36.1% were 4-year graduates and 63.9% had a master's degree or higher, distinguishing between 3 and 4 years of education is complicated. Further research is needed to identify factors that affect patient safety perceptions by controlling these variables.

The patient safety awareness of the participants increased significantly from 3.95±0.54 before training to 4.20±0.57 after training, indicating that patient safety awareness was improved by the prevention of counting errors. Considering that previous studies have reported that counting and counting error prevention are crucial for patient safety [9,23,24], the counting error prevention education conducted in this study may have improved the patient safety awareness of OR nurses.

Previous studies that measured patient safety awareness by providing nurses with medication education for patient safety and education on nursing error cases have shown that various topics can positively change nurses' patient safety awareness [11,13]. However, education on the topic of patient safety awareness is lacking. As such, further research on developing such a curriculum and verifying its effectiveness is required.

In a systematic review of patient safety-related educational programs to improve patient safety awareness on nursing students, Seo et al. [25] recommended that patient safety education should include content on adverse events, safety risks, coping, communication, safety culture, teamwork and cooperation, clinical safety, safety systems or informatics, and other knowledge related to patient safety. Various educational methods—such as lectures, simulations, problem-based learning, small group lectures, group discussions, and watching video cases—were also recommended. A previous study that developed a practical education program on patient safety for surgical nurses reported that education in six practical areas, including medication knowledge, suctioning, drainage tube management, oxygen administration, etc., contributed to enhancing awareness of patient safety [13]. There was no research conducted on educating OR nurses about patient safety in Korea. However, in other countries, there was an emphasis on improving patient safety through enhancing teamwork with surgeons [26]. In another previous study, education on four different areas, including safe surgical techniques, industrial safety, safety management theory, and medical information security, was conducted using various methods such as lectures, case-based learning, and group discussions. This study reported that a duration of 4 to 8 hours of education was considered appropriate [27]. Based on these previous studies, developing a systematic education

program for patient safety targeting OR nurses, considering various topics, educational delivery methods, and appropriate timing, is recommended.

This study asked the OR nurses who participated in the study about the causes of counting errors in their opinion, and the most common cause was "Time shortage" (43.5%), followed by "Due to pressure from the doctor" (19.6%) and "Insufficient of knowledge" (15.2%). These results indicate that time to perform pre-operative, intra-operative, and post-operative counts is insufficient compared to the recent increase in the number of surgeries. Medical centers should consider Providing ample time for surgeries and ensuring that counts are performed efficiently to ensure patient safety and prevent coding errors. Furthermore, in a previous study by Kwon et al. [28] that compared physicians' and nurses' perceptions of miscalculation and patient safety, the nurses' perception of miscalculation was significantly higher than the physicians' perception of miscalculation. This result suggests that perceptions of miscalculations can be enhanced through communication and cooperation between nurses and physicians.

Given that this study was conducted in a single medical institution using convenience sampling, the results of the study cannot be generalized. Furthermore, since the method of education involved lecturing by the researchers, it was difficult to assess and evaluate the participants' understanding of the educational contents and its practical applicability in real-world settings. Additionally, since the education was provided in one session that was about 60 minutes long, it was difficult to gauge the appropriateness of the duration of the education. Therefore, verifying the effectiveness of error-prevention education with more than one session using various educational methods, including repeated sessions, simulations, practical training, and multi-institutional research, rather than a single institution for future follow-up studies is imperative. Because this was a single-group study without a control group, observing differences in the effect of education between groups. Therefore, future follow-up studies should consider establishing control groups to explore ways to assess the effectiveness of education objectively. Additionally, although this study focused solely on education regarding error prevention among OR nurses, future research should consider developing education programs for error prevention, as well as enhancing patient safety awareness. Such an approach could have a positive impact on patient safety and outcomes.

Finally, the results of this study showed that both the level of awareness of prevention of counting errors and patient safety awareness were significantly improved before and after the prevention education. The causes of counting errors were investigated, and the main causes were discussed. However, there are several limitations that impact the generalizability of the study findings. Firstly, limitations due to the single-arm pre-post study design are present. Therefore, an randomized controlled trial study design should be considered for further evaluation of effectiveness. Secondly, this study did not measure the long-term effects of a single training session. Therefore, measuring the long-term effects of various training methods is crucial.

ORCID

Myung Jin JANG, https://orcid.org/0000-0001-5059-0385
Mi Kyung HONG, https://orcid.org/0009-0000-1054-6195
Mi Jeong LEE, https://orcid.org/0009-0008-4729-5340
Kyung A LEE, https://orcid.org/0009-0005-5333-7664
Yang Ok KIM, https://orcid.org/0009-0003-4391-0688
Jin A JEON, https://orcid.org/0009-0004-6414-406X
Hana KO, https://orcid.org/0000-0001-9726-5926

AUTHOR CONTRIBUTIONS

Dr. Hana KO had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Dr. Hana KO reviewed this manuscript and agreed to individual contributions.

Conceptualization: all authors. Data curation: MKH, MJL, KAL, YOK, and JAJ. Formal analysis: MJJ and HK. Investigation: MKH, MJL, KAL, YOK, and JAJ. Methodology: MJJ and HK. Software: MJJ. Validation: MJJ and HK. Writing–original draft: MJJ and HK. Writing–review & editing: all authors.

CONFLICTS OF INTEREST

No existing or potential conflict of interest relevant to this article was reported.

FUNDING

None.

DATA AVAILABILITY

The data presented in this study are available upon reasonable

request from the corresponding author.

ACKNOWLEDGMENTS

We would like to thank the Gachon University Gill Medial Center operating room nurses for their help in collecting the data and the older adults who participated in this study.

REFERENCES

1. Ahn S, Lee NJ. Experience of communication for patient safety by perioperative nurses. J Korean Acad Nurs Adm 2019;25(4):329-39.
2. Kwon KN, Hwang SY. Impact of perception of patient safety culture and safety control on patient safety management activities among perioperative nurses in university hospitals. J Korean Acad Nurs Adm 2022;28(3):285-96.
3. Jeon HS, Choi CS, Kim UG, Kim SR, Han MA, Nam JH, et al. A study on the cause of sponge, sharpe, and instrument's count error operating nurses experienced. J Korean Clin Nurs Res 2001;7(2):159-73.
4. Park H, Jang KS. Development of a guideline to prevent errors of surgical counts in the operating room at a university hospital. Chonnam J Nurs Sci 2013;18(1):89-107.
5. Jang HY. Analysis of core nursing interventions according to the importance and the performance perceived by operating room nurses [master's thesis]. Seoul University; 2007. Korean.
6. Kim JS, Kim JS. Importance awareness and compliance on patient safety for nurses working in operating rooms. J Korea Acad Ind Coop Soc 2011;12(12):5748-58.
7. Jun JY, Lee NJ. Perioperative nurse's experience of nursing errors and emotional distress, coping strategies, and changes in practice. J Korean Acad Nurs Adm 2014;20(5):481-91.
8. AORN Recommended Practices Committee. Recommended practices for sponge, sharps, and instrument counts. AORN J 2006;83(2):418, 421-6, 429-33.
9. Kwon EY, Park KY. Perception of patient safety culture, intra-organizational communication satisfaction and factors influencing patient safety nursing activities among operating room nurses in small- and medium-sized hospitals. Health Soc Welf Rev 2019;39(1):428-52.
10. Lepänluoma M, Takala R, Kotkansalo A, Rahi M, Ikonen TS. Surgical safety checklist is associated with improved operating room safety culture, reduced wound complications, and unplanned readmissions in a pilot study in neurosurgery. Scand J Surg 2014;103(1):66-72.
11. Kim KK, Song MS, Lee JS, Kim YS, Yoon SY, Back JE, et al. Effects of an education program on prevention of malpractice using precedent cases related to patient safety in safety perception, safety control, autonomy and accountability in clinical nurses. J Korean Acad Nurs Adm 2012;18(1):67-75.
12. Lee KH, Lee YS, Park HK, Rhu JO, Byun IS. The influences of the awareness of patient safety culture on safety care activities among operating room nurses. J Korean Clin Nurs Res 2011;17(2):204-14.
13. Kim YM, You MS, Cho YH, Park SH, Nam SN, Park MO, et al. Development and evaluation of a patient safety-focused inservice education program for surgical nurse. J Korean Acad Nurs Adm 2010;16(2):152-61.
14. Lee YM. The recognition and performance of nurses upon preventing count error in the operating room [master's thesis]. The Catholic University of Korea; 2011. Korean.
15. Agency for Health Research and Quality. Hospital survey on patient safety [Internet]. Agency for Health Research and Quality; 2004 [cited Sep 15, 2023]. Available from: https://www.ahrq.gov/sops/surveys/hospital/index.html
16. Kim JE, Kang MA, An KE, Sung YH. A survey of nurses' perception of patient safety related to hospital culture and reports of medical errors. Clin Nurs Res 2007;13(3):169-79.
17. Park SJ, Choi EH, Lee KS, Chung KA. A study on perception and nursing activity for patient safety of operating room nurses. J Korea Acad Ind Coop Soc 2016;17(11):332-9.
18. Park KS. Development of a tool for risk of nursing errors in the operating room and nurses' experience [master's thesis]. Kyungpook National University; 2010. Korean.
19. Pelter MM, Stephens KE, Loranger D. An evaluation of a numbered surgical sponge product. AORN J 2007;85(5):931-6, 938-40.
20. Lauwers PR, Van Hee RH. Intraperitoneal gossypibomas: the need to count sponges. World J Surg 2000;24(5):521-7.
21. Kim HY, Kim HS. Effects of perceived patient safety culture on safety nursing activities in the general hospital nurse's. J Korean Acad Nurs Adm 2011;17(4):413-22.
22. Im SA, Park MJ. The effects of patient safety culture perception and organizational commitment on patient safety management activities in general hospital nurses. J Digit Converg 2018;16(6):259-70.
23. Duggan EG, Fernandez J, Saulan MM, Mayers DL, Nikolaj M, Strah TM, et al. 1,300 Days and counting: a risk model approach to preventing retained foreign objects (RFOs). Jt Comm J Qual

Patient Saf 2018;44(5):260-9.
24. Bubric KA, Biesbroek SL, Laberge JC, Martel JA, Litvinchuk SD. Prevalence and characteristics of interruptions and distractions during surgical counts. Jt Comm J Qual Patient Saf 2021;47(9):556-62.
25. Seo EJ, Seo YS, Hong EH. Systematic review on the patient safety education for the improvement of patient safety competency of nursing students. J Korea Entertain Ind Assoc 2020;14(5):255-66.
26. Makary MA, Sexton JB, Freischlag JA, Holzmueller CG, Millman EA, Rowen L, et al. Operating room teamwork among physicians and nurses: teamwork in the eye of the beholder. J Am Coll Surg 2006;202(5):746-52.
27. Zhang P, Liao X, Luo J. Effect of patient safety training program of nurses in operating room. J Korean Acad Nurs 2022;52(4):378-90.
28. Kwon E, Kim YW, Kim SW, Jeon S, Lee E, Kang HY, et al. A comparative study on patient safety attitude between nurses and doctors in operating rooms. J Int Med Res 2020;48(4):300060519884501.

 https://doi.org/10.15384/kjhp.2024.00024

Original Article

Korean J Health Promot 2024;24(1):29-36
pISSN: 2234-2141 • eISSN: 2093-5676
https://doi.org/10.15384/kjhp.2024.00038

Korean Journal of Health Promotion
KJHP

Mediating Effect of Loneliness on Anxiety and Smartphone Overdependence among Korean Adolescents: Based on the 16th Korea Youth Risk Behavior Survey

Jaeyoung LEE, PhD, RN

Department of Nursing Science, College of Life and Health Sciences, Kyungsung University, Busan, Korea

Abstract

Background: This study aimed to determine the mediating role of loneliness in the relationship between anxiety and smartphone overdependence among Korean adolescents.
Methods: This national cross-sectional secondary study used data from the 16th (2020) Korea Youth Risk Behavior Survey. The sample comprised 54,948 adolescents in middle and high schools. The mediating effects were analyzed using the procedure of Baron and Kenny and the Sobel test.
Results: Anxiety impacted both loneliness and smartphone overdependence (P<0.001). Additionally, loneliness was identified as a factor influencing smartphone overdependence (P<0.001). Loneliness demonstrated a statistically significant mediating effect in the relationship between anxiety and smartphone overdependence (P<0.001).
Conclusions: It was concluded that smartphone overdependence increases with the heightened maladaptive emotions of adolescents, such as anxiety and loneliness. These findings confirmed the mediating role of loneliness in the relationship between anxiety and smartphone overdependence.

Keywords: Loneliness, Anxiety, Internet addiction disorder, Adolescent health, Problem behavior

INTRODUCTION

Background

South Korea had a very high smartphone penetration rate in 2023, with 95.7% of Korean adolescents owning smartphones [1]. Adolescents have low control and high impulsivity, making them vulnerable to addiction, and their risk of smartphone overdependence is 40.1%, higher than that of adults and children [2].

Smartphone overdependence poses more severe problems in adolescents than in adults. Using smartphones for a long time in poor postures leads to unbalanced physical growth [3]. Furthermore, it affects brain development, causing distractions, lack of attention, and impulsive behavior [4]. There is also a high risk of exposure to harmful stimuli such as pornography and dangerous situations such as cyberbullying [5]. Individuals with addiction are more likely to be addicted to another behavior if they are addicted to one behavior [6,7].

Received: January 27, 2024; **Revised:** February 24, 2024; **Accepted:** March 8, 2024
Corresponding author: Jaeyoung LEE, PhD, RN
Department of Nursing Science, College of Life and Health Sciences, Kyungsung University, 309 Suyeong-ro, Nam-gu, Busan 48434, Korea
Tel: +82-51-663-4865 Fax: +82-51-663-4865 E-mail: leejy@ks.ac.kr

Anxiety is highly associated with overdependence and addiction [8,9]. Studies have shown that individuals with high levels of anxiety use smartphones to check social media feeds more frequently and that the emotional state of adolescents is a risk factor for smartphone addiction [5,10]. Thus, it can be expected that individuals with high anxiety levels are using smartphones excessively to alleviate anxiety, unlike those with low anxiety levels [11]. Therefore, gaining a comprehensive understanding of the variables affecting smartphone overdependence and identifying various ways to prevent smartphone overdependence of adolescents with high anxiety are possible by investigating the mediators between anxiety and smartphone overdependence.

Loneliness is an emotion that most individuals experience as a lack of belonging in social relationships [12]. However, as with anxiety, anyone experiencing more loneliness is likely to be dependent on or addicted to something [13]. In the life cycle, adolescence is a period in which there is a very high need for belonging and intimacy [14], which are not all fulfilled; therefore, one experiences much loneliness [15]. Because one can interact with others anytime and anywhere using smartphones, adolescents use smartphones to build and maintain social relationships [16]. Therefore, it can be assumed that adolescents use smartphones as a medium to overcome loneliness, and loneliness can be expected to amplify smartphone overdependence even more.

However, in prior studies that explored loneliness, anxiety, and smartphone overdependence among adolescents, only connections among these variables were recognized. Finding studies that systematically examined the mediating role of loneliness in the relationship between anxiety and smartphone overdependence is difficult [8-11,16]. Therefore, this study aimed to contribute to the conception of specific and expanded prevention and intervention strategies for smartphone addiction in adolescents by examining the effect of anxiety on smartphone overdependence through loneliness as a mediator.

Conceptual framework of the research

Based on the mediating effect model [17], the conceptual framework of this study was developed with the assumption that anxiety in adolescents affects their smartphone overdependence through the mediating role of loneliness (Fig. 1).

METHODS

Research design

This descriptive analysis used secondary data from the 16th (2020) Korea Youth Risk Behavior Survey (KYRBS) [18] to examine the mediating effects of loneliness on the association between anxiety and smartphone overdependence among Korean adolescents.

Participants

The KYRBS is an anonymous, self-administered online survey conducted among middle to high school students to gain insights into the health behavior of Korean youth. This government-approved statistical survey (approval number: 117058) has been conducted annually since 2005. The 16th KYRBS [18] was conducted involving students from 400 middle schools and 400 high schools. In total, 54,948 students from 793 schools (398 middle schools and 395 high schools) were surveyed (response rate=94.9%). Among the sample students, long-term absences, children with special needs who could not participate in the survey independently, and students with text-reading disabilities were excluded. The data collection period was from August 2020 to November 2020.

Measures

Smartphone overdependence

The smartphone overdependence scale was used to assess the degree of smartphone overdependence among the adolescent

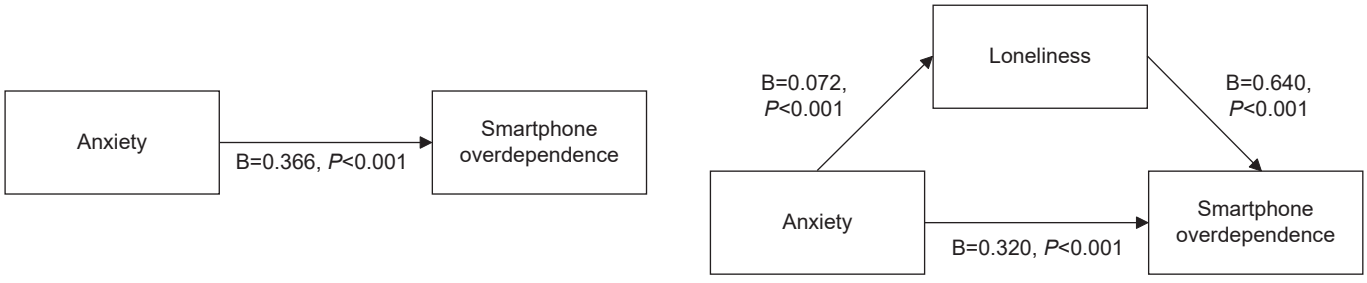

Fig. 1. Mediation model for anxiety, loneliness, and smartphone overdependence in Korean adolescents.

 https://doi.org/10.15384/kjhp.2024.00038

participants. A questionnaire was developed to measure smartphone overdependence among South Korean youth, adults, and seniors [19-21]. The questionnaire comprises 10 items. Responses are based on a 4-point scale: 1="strongly disagree" to 4="strongly agree." The total scores ranged from 10 to 40. The higher the score, the more severe the overdependence on smartphones [19]. Cronbach's α during survey development was 0.84 [21], and 0.92 in this study.

Anxiety

The Generalized Anxiety Disorder-7 (GAD-7) comprises a self-report questionnaire that allows for the rapid detection of GAD [22]. The subjects were asked whether they were bothered by anxiety-related problems over the past 2 weeks by answering seven items on a 4-point scale. The total scores ranged from 0 to 21 [22]. Cronbach's α was 0.92 in the previous study [22] and 0.90 in this study.

Loneliness

The question "How often have you felt lonely during the last 12 months?" was answered on a 5-point scale (5=always feeling lonely to 1=not feeling lonely at all).

Covariates

Twelve covariates were included in the analysis, including socioeconomic status, problem behavior, and mental health variables [23-27].

1) Socioeconomic variables included sex, age, perceived economic status, perceived academic performance, and body mass index (BMI) (kg/m^2).
2) Problem behavior variables included drug, drinking, and smoking experiences.
3) Mental health variables included perceived stress, sleep satisfaction, depressive symptoms, and suicidal ideation.

Data analysis

The KYRBS comprises complex data, which were analyzed based on complex sampling design and strata, cluster, weight, and finite population correction provided by the Korea Disease Control and Prevention Agency (KDCA) [18]. The analysis was performed using IBM SPSS Statistics 25.0 (IBM Corp.). A *P*-values <0.05 were used to denote statistical significance.

Data were analyzed according to the following steps. First, anxiety, loneliness, and smartphone overdependence were analyzed using complex sample descriptive statistics. Second, the relationship among the respondents' anxiety, loneliness, and smartphone overdependence was analyzed using the complex sample general linear model. Third, the mediating effects of loneliness on the relationship between anxiety and smartphone overdependence were analyzed using the three-step mediated effect validation procedure of Baron and Kenny [28] and the Sobel test [29] with the complex sample general linear model. The analysis was adjusted for covariate variables.

Ethical considerations

The KYRBS is a government-approved statistical survey conducted annually in Korea since 2005 (approval no. 117058) [18]. This study obtained data from the survey website (https://www.cdc.go.kr/yhs) according to the regulations of the KDCA. This study involved secondary data analysis and, therefore, was exempt from institutional review board approval.

RESULTS

General characteristics

Table 1 shows the general characteristics of the study participants included in this study. The study included 51.9% males and 48.1% females, with a mean age of 15.19 years. The mean BMI was 21.50 kg/m^2. Regarding economic status, 47.5% were medium. Regarding subjective academic performance, 30.1% were medium. Furthermore, 0.8% of the students had drug experience, 33.4% had drinking experience, and 10.2% had smoking experience. Depressive symptoms were reported by 25.2% of the respondents, and suicidal ideation was reported by 10.9%. Regarding sleep satisfaction, 33.7% were medium, and regarding perceived stress, 44.4% were medium.

Anxiety, loneliness, and smartphone overdependence

The anxiety score was 3.94, the loneliness score was 2.41, and the smartphone overdependence score was 18.60. The risk of anxiety was 11.2%. The risk of smartphone overdependence was 25.5% (Table 2).

Relationship between anxiety, loneliness, and smartphone overdependence

Anxiety showed a significant association with loneliness (B=0.13, *P*<0.001); loneliness (B=1.52, *P*<0.001) and anxiety (B=0.45, *P*<0.001) both affected smartphone overdependence (Table 3).

Table 1. General characteristics in Korean adolescents (N=54,948)

Variable	Category	Subject (n)	Weighted %	Mean	SE
Sex	Males	28,353	51.9		
	Females	26,595	48.1		
Age (yr) (n=54,809)				15.19	0.023
Body mass index (kg/m^2) (n=53,534)				21.50	0.029
Perceived economic status	Very high	6,039	11.3		
	High	15,300	28.6		
	Middle	26,397	47.5		
	Low	5,937	10.4		
	Very low	1,275	2.2		
Subjective academic performance	Very high	6,736	12.2		
	High	13,410	24.7		
	Middle	16,585	30.1		
	Low	12,684	23.0		
	Very low	5,533	10.0		
Drug experience	No	54,543	99.2		
	Yes	405	0.8		
Drinking experience	No	36,591	66.6		
	Yes	18,357	33.4		
Smoking experience	No	49,318	89.8		
	Yes	5,630	10.2		
Depressive symptoms	No	41,108	74.8		
	Yes	13,840	25.2		
Suicidal ideation	No	48,969	89.1		
	Yes	5,979	10.9		
Sleep satisfaction	Very satisfied	5,582	9.9		
	Satisfied	11,242	20.4		
	Neutral	18,656	33.7		
	Dissatisfied	13,481	24.8		
	Very dissatisfied enough	5,987	11.2		
Perceived stress	Very low	2,018	3.6		
	Low	9,889	17.8		
	Middle	24,379	44.4		
	High	14,059	25.9		
	Very high	4,603	8.3		

SE, standard error.

Table 2. Anxiety, loneliness, and smartphone overdependence in Korean adolescents (N=54,948)

Variable	Category (score)	n (weighted %)	Mean	SE	Range
Anxiety			3.94	0.031	0–21
	Risk group (10–21)	6,099 (11.2)			
	Low risk group (0–9)	48,849 (88.8)			
Loneliness			2.41	0.007	1–5
Smartphone overdependence			18.60	0.043	10–40
	Overdependence group (23–40)	13,775 (25.5)			
	Normal group (0–22)	41,173 (74.5)			

SE, standard error.

Mediating effect of loneliness on the relationship between anxiety and smartphone overdependence

In this study, the independent variable was anxiety, the mediator was loneliness, and the dependent variable was smartphone overdependence. Twelve control variables were used to adjust for differences in smartphone overdependence according to the respondents' general characteristics (Table 4, Fig. 1).

The assumption of the regression analysis was verified by

 https://doi.org/10.15384/kjhp.2024.00038

Table 3. Relationship between anxiety, loneliness, and smartphone overdependence in Korean adolescents (N=54,948)

Variable		R^2	Wald F (*P*)	B	SE	t (*P*[a])
Independent	Dependent					
Anxiety	Loneliness	0.282	12,433.10 (<0.001)	0.13	0.001	111.50 (<0.001)
Loneliness	Smartphone overdependence	0.067	3,292.42 (<0.001)	1.52	0.027	57.38 (<0.001)
Anxiety	Smartphone overdependence	0.096	3,986.59 (<0.001)	0.45	0.007	63.14 (<0.001)

SE, standard error.
[a]Complex sample general linear model.

Table 4. Mediating effect of loneliness on the relationship between anxiety and smartphone overdependence (N=54,948)

Variable	B	SE	t (*P*[a])	R^2	Wald F (*P*)
Step 1. Anxiety → loneliness	0.072	0.001	54.89 (<0.001)	0.371	1,913.07 (<0.001)
Step 2. Anxiety → smartphone overdependence	0.366	0.009	41.16 (<0.001)	0.124	464.66 (<0.001)
Step 3. Anxiety, loneliness → smartphone overdependence					
1) Anxiety → smartphone overdependence	0.320	0.009	35.58 (<0.001)	0.131	458.44 (<0.001)
2) Loneliness → smartphone overdependence	0.640	0.032	19.98 (<0.001)		
Sobel test			Z=19.270, *P*<0.001		

SE, standard error.
[a]Complex sample general linear model with the following covariates: sex, age, perceived economic status, perceived academic performance, body mass index, drug/drinking/smoking experiences, perceived stress, sleep satisfaction, depressive symptoms, suicidal ideation.

multiple regression before verifying the mediating effect, and the effect of the independent variable, parameter, and control variables on smartphone overdependence was analyzed.

The first step of the analysis showed that anxiety had a significant effect on loneliness (B=0.072, *P*<0.001). The results of the second step showed that anxiety had a significant effect on smartphone overdependence (B=0.366, *P*<0.001). The third step showed that loneliness had a significant effect on smartphone overdependence (B=0.640, *P*<0.001). Furthermore, anxiety had a significant mediating effect on smartphone overdependence (B=0.320, *P*<0.001), with a partial mediating effect. Moreover, the Sobel test had a statistically significant result (Z=19.270, *P*<0.001).

DISCUSSION

This study established and verified the relationship between anxiety and smartphone overdependence mediated by loneliness as a theoretical model.

Anxiety and loneliness affected smartphone overdependence. These findings are consistent with those of previous research, which found that various emotions experienced during adolescence, such as anxiety and loneliness, affect the problematic use of media such as smartphones. Individuals with psychological issues, such as anxiety or loneliness, overuse cyber media or technological devices such as smartphones [30,31]. These addictions to media and technology cause other problems, such as physical injury or cognitive impairment, leading to dangerous health consequences, such as suicidal ideation [31,32]. In several studies, users with high smartphone dependence showed increased anxiety, nervousness, and depression when separated from smartphones [30,33]. Thus, if adolescents' maladaptive emotions are not resolved and lead to smartphone overdependence, it could result in a vicious cycle that leads to other health problems and increased maladaptive emotions such as anxiety and restlessness. Therefore, a system that can closely monitor the emotional state of adolescents should be established.

During the COVID-19 (coronavirus disease-19) pandemic, psychological and emotional problems, including anxiety, loneliness, and depression caused by COVID-19, increased among adolescents [34]. Negative emotions, such as anxiety and loneliness, may have persisted for many years because of social distancing, which may have further increased smartphone dependence. Therefore, identifying the potential risk group expected to have a high degree of anxiety and loneliness is necessary. Smartphone overdependence risk groups should also be screened. In South Korea, diagnostic tests are currently being performed for the early detection of mental health problems in children and adolescents. However, the tests are conducted only in some mental health centers and mainly for individuals suspected to be at a high risk, which is hardly considered a comprehensive solution [35]. Therefore, accessible school-wide

screenings must be established to identify potential risk groups for mental health issues and smartphone use among adolescents.

In this study, adolescents' anxiety affected smartphone overdependence through the mediation of loneliness. In particular, the higher the anxiety, the greater the loneliness, and the higher the level of smartphone overdependence. This result suggests that when assisting adolescents suffering from anxiety, closely examining their loneliness levels and exploring the effects of the degree of loneliness on smartphone overdependence are necessary. Anxiety is a psychological response that protects an individual against danger and threat and a personality trait that forms over many years from the beginning of life [36,37]. During adolescence, anxiety is frequent because of sudden physical changes and development, and decreasing anxiety levels in adolescents through short-term intervention or counseling is challenging [36-38]. In contrast, loneliness is relatively easier to manage through emotional reflection and counseling relationships than anxiety [39]. Improving unstable family or peer relationships and reducing the loneliness of adolescents during the time in life when one is most dependent on peers are possible [40].

The results of this study suggest that if adolescents complaining of smartphone overdependence experience anxiety, seeking specific interventions and solutions that can alleviate loneliness along with measures to intervene for anxiety is practical. The findings indicate that managing anxiety in adolescents with smartphone overdependence necessitates specific interventions directed at alleviating both loneliness and anxiety. This comprehensive approach can guide practical solutions for adolescents dealing with smartphone overdependence.

This study has limitations and suggests directions for future research. First, the cross-sectional nature of the data prevents the establishment of clear causal relationships between variables [41]. Longitudinal analyses in subsequent studies are essential to determine significant causal directions. Second, breaking down maladaptive emotions for a more detailed examination is recommended. Anxiety [42] and loneliness [43] can manifest in various forms. Therefore, future studies should perform a nuanced evaluation of emotions to identify specific aspects of anxiety and loneliness associated with smartphone addiction.

Despite its limitations, this study can help establish a psychological framework to predict smartphone overdependence among adolescents. This study offers insights into the risk factors associated with smartphone overdependence in this age group. This study confirmed that the maladaptive emotions of adolescents, such as anxiety and loneliness, are associated with smartphone overdependence. Furthermore, because loneliness mediates anxiety in adolescents, it was established that loneliness should be mediated together when intervening in smartphone overdependence of adolescents with high anxiety levels in the future.

ORCID

Jaeyoung LEE, https://orcid.org/0000-0002-5516-8199

AUTHOR CONTRIBUTIONS

Dr. Jaeyoung LEE had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. The author reviewed this manuscript and agreed to individual contributions.

Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Software, Validation, Writing–original draft, Writing–review & editing: JL.

CONFLICTS OF INTEREST

No existing or potential conflict of interest relevant to this article was reported.

FUNDING

None.

DATA AVAILABILITY

The data presented in this study are available upon reasonable request from the corresponding author.

REFERENCES

1. Korea Information Society Development Institute. 2023 Korean Media Panel Survey [Internet]. Korean Information Society Development Institute; 2024 [cited Mar 19, 2024]. Available from: https://stat.kisdi.re.kr/kor/tblInfo/TblInfoList.html?vw_cd=MT_ATITLE&siteGb=SITE002&sub_div=E
2. Jeong IS. Smartphone overdependence has also decreased, except for teenagers [Internet]. The Hankyoreh; 2023 [cited Jan

27, 2024]. Available from: https://www.hani.co.kr/arti/economy/it/1084819.html
3. Jung SI, Lee NK, Kang KW, Kim K, Lee DY. The effect of smartphone usage time on posture and respiratory function. J Phys Ther Sci 2016;28(1):186-9.
4. Wilmer HH, Sherman LE, Chein JM. Smartphones and cognition: a review of research exploring the links between mobile technology habits and cognitive functioning. Front Psychol 2017;8:605.
5. Bozzola E, Spina G, Agostiniani R, Barni S, Russo R, Scarpato E, et al. The use of social media in children and adolescents: scoping review on the potential risks. Int J Environ Res Public Health 2022;19(16):9960.
6. Alavi SS, Ferdosi M, Jannatifard F, Eslami M, Alaghemandan H, Setare M. Behavioral addiction versus substance addiction: correspondence of psychiatric and psychological views. Int J Prev Med 2012;3(4):290-4.
7. Konkolÿ Thege B, Hodgins DC, Wild TC. Co-occurring substance-related and behavioral addiction problems: a person-centered, lay epidemiology approach. J Behav Addict 2016;5(4):614-22.
8. Lee YS, Joo JH, Shin J, Nam CM, Park EC. Association between smartphone overdependence and generalized anxiety disorder among Korean adolescents. J Affect Disord 2023;321:108-13.
9. Ge J, Liu Y, Zhang A, Shu T. The relationship between anxiety and smartphone addiction in the context of Covid-19: the mediating effect of attentional control and executive dysfunction. Heliyon 2023;9(2):e13273.
10. Abi-Jaoude E, Naylor KT, Pignatiello A. Smartphones, social media use and youth mental health. CMAJ 2020;192(6):E136-41.
11. Pourafshari R, Rezapour T, Rafei P, Hatami J. The role of depression, anxiety, and stress in problematic smartphone use among a large sample of Iranian population. J Affect Disord Rep 2022;10:100436.
12. Yanguas J, Pinazo-Henandis S, Tarazona-Santabalbina FJ. The complexity of loneliness. Acta Biomed 2018;89(2):302-14.
13. Hosseinbor M, Yassini Ardekani SM, Bakhshani S, Bakhshani S. Emotional and social loneliness in individuals with and without substance dependence disorder. Int J High Risk Behav Addict 2014;3(3):e22688.
14. Shulman S, Laursen B, Kalman Z, Karpovsky S. Adolescent intimacy revisited. J Youth Adolesc 1997;26(5):597-617.
15. Achterbergh L, Pitman A, Birken M, Pearce E, Sno H, Johnson S. The experience of loneliness among young people with depression: a qualitative meta-synthesis of the literature. BMC Psychiatry 2020;20(1):415.
16. Yue H, Yue X, Zhang X, Liu B, Bao H. Exploring the relationship between social exclusion and smartphone addiction: the mediating roles of loneliness and self-control. Front Psychol 2022;13:945631.
17. Hayes AF. Beyond Baron and Kenny: statistical mediation analysis in the new millennium. Commun Monogr 2009;76(4):408-20.
18. Korea Disease Control and Prevention Agency (KDCA). The 16th Korea Youth Risk Behavior Survey [Internet]. KDCA; 2020 [cited Jan 27, 2024]. Available from: http://www.kdca.go.kr/yhs/
19. Ministry of Science and ICT (MSIT) & National Information Society Agency (NIA). 2020 the survey on smartphone overdependence [Internet]. MSIP & NIA; 2021 [cited Jan 27, 2024]. Available from: https://www.iapc.or.kr/mediaView.do?idx=28&article_id=ICCART_0000000113023&type=A1#this
20. Ministry of Science, ICT and Future Planning (MSIP) & National Information Society Agency (NIA). 2016 the survey on internet overdependence [Internet]. MSIP & NIA; 2016 [cited Jan 27, 2024]. Available from: http://library.nia.or.kr/search/detail/CATTOT000000027783?mainLink=/search/tot&briefLink=/search/tot/result?st=KWRD_A_q=2016+%EC%9D%B8%ED%84%B0%EB%84%B7+%EA%B3%BC%EC%9D%98%EC%A1%B4+%EC%A1%B0%EC%82%AC_A_si=TOTAL_A_x=0_A_y=0
21. National Information Society Agency (NIA). 2016 Digital Culture Forum Policy Research Report [Internet]. NIA; 2016 [cited Jan 27, 2024]. Available from: http://library.nia.or.kr/search/detail/CATTOT000000027760
22. Seo JG, Park SP. Validation of the Generalized Anxiety Disorder-7 (GAD-7) and GAD-2 in patients with migraine. J Headache Pain 2015;16:97.
23. Kang JW. Relationship between smartphone use time, depression and suicide in adolescents. J Korean Assoc Soc Psychiatry 2019;24(2):48-57.
24. Kim JY. The relationship among loneliness, stress, and smartphone addiction of adolescents in the era of digitalization. J Digit Converg 2017;15(9):335-43.
25. Kim HJ, Min JY, Kim HJ, Min KB. Association between psychological and self-assessed health status and smartphone overuse among Korean college students. J Ment Health 2019;28(1):11-6.
26. Pereira FS, Bevilacqua GG, Coimbra DR, Andrade A. Impact of problematic smartphone use on mental health of adolescent students: association with mood, symptoms of depression, and physical activity. Cyberpsychol Behav Soc Netw 2020;23(9): 619-

26.
27. Fischer-Grote L, Kothgassner OD, Felnhofer A. Risk factors for problematic smartphone use in children and adolescents: a review of existing literature. Neuropsychiatr 2019;33(4):179-90.
28. Baron RM, Kenny DA. The moderator-mediator variable distinction in social psychological research: conceptual, strategic, and statistical considerations. J Pers Soc Psychol 1986;51(6):1173-82.
29. Lee IH. EasyFlow regression analysis. Hannarae Publishing Co.; 2016. p. 281-317.
30. Busch PA, McCarthy S. Antecedents and consequences of problematic smartphone use: a systematic literature review of an emerging research area. Comput Human Behav 2021;114:106414.
31. Hussain Z, Griffiths MD. The associations between problematic social networking site use and sleep quality, attention-deficit hyperactivity disorder, depression, anxiety and stress. Int J Ment Health Addict 2021;19:686-700.
32. Sohn SY, Rees P, Wildridge B, Kalk NJ, Carter B. Prevalence of problematic smartphone usage and associated mental health outcomes amongst children and young people: a systematic review, meta-analysis and GRADE of the evidence. BMC Psychiatry 2019;19(1):356.
33. Cheever NA, Rosen LD, Carrier LM, Chavez A. Out of sight is not out of mind: the impact of restricting wireless mobile device use on anxiety levels among low, moderate and high users. Comput Human Behav 2014;37:290-7.
34. Guessoum SB, Lachal J, Radjack R, Carretier E, Minassian S, Benoit L, et al. Adolescent psychiatric disorders during the COVID-19 pandemic and lockdown. Psychiatry Res 2020;291:113264.
35. Ministry of Health and Welfare. 2023 Mental health program guide [Internet]. Ministry of Health and Welfare; 2023 [cited Jan 27, 2024]. Available from: https://www.ncmh.go.kr/ncmh/board/boardView.do?no=9334&fno=106&gubun_no=9&menu_cd=04_02_02_04&bn=newsView&search_item=&search_content=&pageIndex=1#
36. Steimer T. The biology of fear- and anxiety-related behaviors. Dialogues Clin Neurosci 2002;4(3):231-49.
37. Twenge JM. The age of anxiety? Birth cohort change in anxiety and neuroticism, 1952-1993. J Pers Soc Psychol 2000;79(6):1007-21.
38. Beesdo K, Knappe S, Pine DS. Anxiety and anxiety disorders in children and adolescents: developmental issues and implications for DSM-V. Psychiatr Clin North Am 2009;32(3):483-524.
39. Pearce E, Myles-Hooton P, Johnson S, Hards E, Olsen S, Clisu D, et al. Loneliness as an active ingredient in preventing or alleviating youth anxiety and depression: a critical interpretative synthesis incorporating principles from rapid realist reviews. Transl Psychiatry 2021;11(1):628.
40. Schwartz-Mette RA, Shankman J, Dueweke AR, Borowski S, Rose AJ. Relations of friendship experiences with depressive symptoms and loneliness in childhood and adolescence: a meta-analytic review. Psychol Bull 2020;146(8):664-700.
41. Enez Darcin A, Kose S, Noyan CO, Nurmedov S, Yılmaz O, Dilbaz N. Smartphone addiction and its relationship with social anxiety and loneliness. Behav Inf Technol 2016;35(7):520-5.
42. Zinbarg RE, Anand D, Lee JK, Kendall AD, Nuñez M. Generalized anxiety disorder, panic disorder, social anxiety disorder, and specific phobias. In: Blaney PH, Krueger RF, Millon T, editors. Oxford textbook of psychopathology. 3rd ed. Oxford University Press; 2014. p. 133-62.
43. DiTommaso E, Spinner B. Social and emotional loneliness: a re-examination of weiss' typology of loneliness. Pers Individ Dif 1997;22(3):417-27.

Original Article

Korean J Health Promot 2024;24(1):37-46
pISSN: 2234-2141 • eISSN: 2093-5676
https://doi.org/10.15384/kjhp.2024.00031

Korean Journal of Health Promotion
KJHP

Factors Affecting Perceived Stress-Cortisol Responses in Young Adults

Shinae SEO, PhD(c), RN[1,2], Chun-Ja KIM, PhD, RN[2], Hee Sun KANG, PhD, RN[3], Elizabeth A. SCHLENK, PhD, RN, CNL, FAAN[4]

[1]School of Nursing, University of Virginia, Charlottesville, VA, USA
[2]College of Nursing and Research Institute of Nursing Science, Ajou University, Suwon, Korea
[3]Red Cross College of Nursing, Chung-Ang University, Seoul, Korea
[4]School of Nursing, University of Pittsburgh, Pittsburgh, PA, USA

Abstract

Background: This study examined the distribution of stress-cortisol responses and risk factors affecting perceived stress and cortisol responses among 187 university students in South Korea.
Methods: Perceived stress, depressive symptoms, and health-promoting lifestyle were assessed using structured questionnaires. Blood analyses and anthropometrics were used to determine cortisol and cardiometabolic risks. Multinomial logistic regression analysis was used to examine the factors affecting stress-cortisol responses.
Results: Four groups of stress-cortisol responses were found, including normal (39.0%), high stress (34.8%), high stress-cortisol (13.9%), and high cortisol group (12.3%). Age, systolic blood pressure, high-density lipoprotein cholesterol, depressive symptoms, and physical activity were associated with stress-cortisol responses.
Conclusions: Multidimensional interventions are needed to reduce stress levels and promote normal stress-cortisol responses.

Keywords: Cardiometabolic risk factors, Cortisone, Depression, Life style, Subjective stress

INTRODUCTION

University students experience acute and chronic stress during their developmental transition to adulthood [1,2], including academic pressure, peer influence, financial concerns, time management, and interpersonal relationships [3-6]. Stress during college or early adulthood has been linked to physical and mental health problems [7-9].

One response to stress is the secretion of cortisol from the adrenal cortex at the end of the hypothalamic-pituitary-adrenal (HPA) axis, the pathway of the stress-hypothalamus-pituitary-adrenal cortex. This pathway is a major stress response system that maintains homeostasis during stress [10,11]. Cortisol is a major steroid hormone essential for human survival and a well-known key indicator of stress [12]. The results of previous studies on stress-cortisol responses have been inconsistent, and it remains unclear how cortisol responds to stress in different situations [13,14]. In light of the results from previous studies that stress-cortisol responses appear differently depending on physical, psychological, and lifestyle factors, this study con-

Received: January 23, 2024; **Revised:** March 8, 2024; **Accepted:** March 13, 2024
Corresponding author: Chun-Ja KIM, PhD, RN
College of Nursing and Research Institute of Nursing Science, Ajou University, 164 World cup-ro, Yeongtong-gu, Suwon 16499, Korea
Tel: +82-31-219-7017 Fax: +82-31-219-7020 E-mail: ckimha@ajou.ac.kr

sidered how these factors may affect stress-cortisol responses among university students.

Background

Cardiometabolic risks can lead to cardiovascular diseases and type 2 diabetes [15]. Increased stress and cortisol levels are significantly linked to cardiometabolic risk factors for cardiovascular diseases and metabolic syndrome. Dysregulation of the HPA axis increases cortisol levels in the blood, resulting in increased glucose and insulin levels, the emergence of insulin resistance, and the promotion of dyslipidemia, hypertension, and visceral adiposity [10,16-18]. While cardiometabolic risks may be related to stress-cortisol responses in university students, scarce information exists on the relationship between stress-cortisol responses and cardiometabolic risks among university students.

Depressive symptoms are the predominant mental health problem among university students, where about 30% to 40% experience depressive symptoms [19], and the prevalence of depressive symptoms are increasing [20]. Stress is a well-known risk factor for depressive symptoms [7,21], which predicts steeper cortisol reactivity and recovery [22]. Several studies on the relationships between cortisol levels, perceived stress, and depressive symptoms have used hair or salivary cortisol [23,24]. However, few studies have discussed the relationship between stress-cortisol responses and depressive symptoms among university students using plasma cortisol.

Stress-cortisol responses might differ depending on individuals' health-related lifestyle behaviors. For example, young adults, transitioning to university life, often adopt unhealthy habits [25] such as poor dietary choices [26-28], alcohol consumption, and smoking [29,30]. These maladaptive health behaviors in young adults are related to stress [31]. Moreover, psychological stress was associated with healthy lifestyle behaviors among university students [32,33]. However, little is known about the association between stress-cortisol responses and healthy lifestyle behaviors, such as health responsibility, physical activity, nutrition, stress management, interpersonal relationships, and spiritual growth.

While stress and its health implications garner scientific interest, most studies on stress-cortisol responses have focused on acute stress based on laboratory stimuli [13] and primarily focused on the linear relationship between stress and cortisol. It is essential to capture the subtle interplay more accurately between stress and cortisol responses. To enhance specificity, therefore, this study examined (a) the distribution of perceived stress and cortisol responses among university students, and (b) physical (cardiometabolic risks), psychological (depressive symptoms), and lifestyle (health-promoting lifestyle behaviors) factors affecting stress-cortisol responses (Fig. 1).

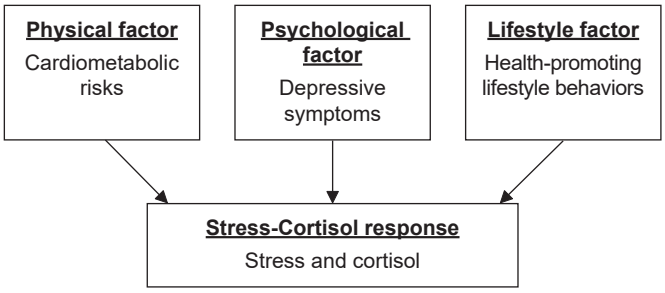

Fig. 1. Conceptual framework of this study.

METHODS

Design

This study was a secondary analysis of survey data conducted during the general health check-up for Korean college students.

Sample and setting

The setting was the Ajou University Hospital in Suwon, South Korea. Recruitment of participants occurred through a notice posted on a university healthcare center bulletin board from March 2015 to February 2017 [2]. Participants were instructed to avoid consuming caffeine, alcohol, or dairy products after 7 PM on the day before cortisol sampling. Clinical laboratory measurements and questionnaires were used to collect the data. Using the G*Power version 3.1.9.7 (Heinrich Heine University, Düsseldorf, Germany), a sample size of 208 was required based on a medium effect size (odds ratio=1.5) and a power of 80% using 95% confidence interval (CI) tests for logistic regression analysis. Among the 208 eligible students, data from 187 students were included in the analyses. Twenty-one individuals who had been prescribed medications to lose weight and those with chronic morbidity or major depression were excluded.

Measures

Stress (subjective and objective)

Perceived stress

The 10-item Perceived Stress Scale (PSS) [34] was used to assess the global level of stressful life situations and circumstances

 https://doi.org/10.15384/kjhp.2024.00031

during the past month. The PSS measures the degree to which respondents find their lives overwhelming, uncontrollable, and unpredictable by asking them to respond on a 5-point Likert scale ranging from 0 (never) to 4 (very often), with higher scores indicating greater psychological stress. Total scores range from 0 to 40 and are calculated by summing the scores of all items. Items 4, 5, 7, and 8 are reverse scored. PSS scores >20 were considered as the high stress group. Cronbach's alpha coefficient was 0.83.

Cortisol

Clinical laboratory measurement of afternoon cortisol was evaluated through ethylenediaminetetraacetic acid-plasma at the central laboratory of a university-affiliated hospital. Cortisol levels were assessed by electro-chemiluminescence immunoassay using an automatic analyzer (Toshiba TBA 200FR; Toshiba Medical Systems Co. Ltd., Tokyo, Japan). In this study, normal values of plasma cortisol were considered as 1.8–12.7 μg/dL.

Cardiometabolic risk

Cardiometabolic risk was assessed using blood sample analysis and anthropometrics. Overnight fasting blood samples were collected from the antecubital veins. Fasting plasma glucose (FPG) was assessed through the enzymatic reference method with hexokinase, and lipid profiles, including triglycerides (TGs) and high-density lipoprotein cholesterol (HDL-C), were assessed by enzymatic colorimetric assay using an automatic analyzer (COBAS C702 Auto Analyzer; Roche Diagnostics Systems Ltd., Basel, Switzerland). A trained nurse gauged waist circumference (WC) at the central position between the 12th rib and the iliac crest. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared (kg/m^2). Blood pressure (BP) was measured after a 5-minute rest in a sitting position using an automatic sphygmomanometer (HEM-7210; OMRON, Kyoto, Japan).

Depressive symptoms

Depressive symptoms were assessed using the Center for Epidemiologic Studies Depression Scale (CES-D) [35]. The CES-D is a self-report 20-item scale that asks respondents to rate how often, over the past week, they have experienced depressive symptoms such as restless sleep, poor appetite, and feeling lonely. Items are responded to using a 4-point Likert scale ranging from 0 (rarely or none) to 3 (most or all the time, 5–7 days). Total scores range from 0 to 60 and are generated by summing the scores of all items. Higher scores indicate higher levels of depressive symptoms. A CES-D cutoff score of 16 has been used to indicate significant depressive symptomatology [36]. Cronbach's alpha coefficient was 0.90.

Health-promoting lifestyle behaviors

The Korean version of the Health Promoting Lifestyle Profile II (HPLP II) [37,38] was used to measure health-promoting lifestyle behaviors. The six subscales include interpersonal relationships, nutrition, health responsibility, physical activity, stress management, and spiritual growth. The HPLP II consists of 52 items with response options on a 4-point Likert scale ranging from 1 (never) to 4 (routinely). The total score is the mean of the responses to the 52 items, with a possible range of 1–4; higher scores indicate higher health-promoting lifestyle performance. Cronbach's alpha coefficients ranged from 0.71 to 0.88 for the subscales and 0.94 for the total scale.

Sociodemographic factors

Sociodemographic factors (age, gender, education level, current smoking status, and drinking status) were collected using a self-administered questionnaire.

Ethical considerations

This study was approved by the Ajou University Hopistal Institutional Review Board (No. AJOUIRB-MDB-2021-016). All participants provided informed consent upon registration for a general health checkup at Ajou University Hospital and participants' confidentiality was preserved.

Statistical analysis

Data were analyzed using IBM SPSS Statistics (ver. 22.0; IBM Corp.) and Stata/BE (ver. 17; StataCorp LLC). Descriptive analyses were performed using frequencies and percentages for categorical variables and means and standard deviations (SDs) for continuous variables. Participants were classified into one of four stress-cortisol response groups using cortisol levels (normal cortisol range: 1.8–12.7 μg/dL) and perceived stress scores (high levels of stress: PSS scores>20) as follows: normal group (PSS scores≤20, cortisol level<12.7 μg/dL), high stress-cortisol group (PSS scores>20, cortisol level≥12.7 μg/dL), high cortisol group (PSS scores≤20, cortisol level≥12.7 μg/dL), and high stress group (PSS scores>20, cortisol level<12.7 μg/dL). The cardiometabolic risks are considered as elevated WC (≥85 cm for women, ≥90 cm for men), elevated BP (≥130/85 mmHg), elevated TG (≥150

mg/dL), decreased HDL-C (≤50 mg/dL for women, ≤40 mg/dL for men), and elevated FPG (≥100 mg/dL). Pearson's chi-square test, Fisher's exact test, and Analysis of Variance (ANOVA) were used to examine bivariate associations between sociodemographic factors, cardiometabolic risks, depressive symptoms, health-promoting lifestyle behaviors, and stress-cortisol response groups. Post-hoc analyses with ANOVA were conducted using Bonferroni multiple-comparison tests. Multinomial logistic regression analysis was used to examine risk factors associated with the stress-cortisol responses. The strength of association was estimated using relative risk ratios (RRRs) and the 95% CI. All subcategories of the HPLP II were included in the multinomial logistic regression along with other variables with significant relationships at $P<0.05$ (alpha of 5%) in the bivariate analyses.

RESULTS

General characteristics

Table 1 presents the participants' general, physical, psychological, and lifestyle characteristics. The mean age was 23.97 years (SD=3.38), and 54.0% of the participants were women. Approximately 70% of the participants were undergraduates; most were non-smokers (n=169, 90.4%) and did not drink alcohol (n=120, 64.2%). The mean score for perceived stress was 20.02 (SD=5.52), within a possible range of 0–40. The mean cortisol level was 10.81 μg/dL (SD=4.08). The numbers of participants in each cardiometabolic risk factor group were 45 (24.1%) with high BP, 33 (17.6%) with high WC, 17 (9.1%) with high TG, 5 (2.7%) with low HDL-C, and 7 (3.7%) with high FPG. The mean depressive symptom score was 19.10 (SD=9.36), within a range of 0–60, with 115 (61.5%) participants scoring 16 or higher. The lowest score on the HPLP II subscales was for physical activity (1.83/4.00).

The distribution of stress–cortisol response groups

Fig. 2 shows the distribution of the stress-cortisol response groups. The results indicated 73 participants (39.0%) were in the normal group (PSS scores≤20, cortisol level<12.7 μg/dL), 26 (13.9%) were in the high stress-cortisol group (PSS scores>20, cortisol level≥12.7 μg/dL), 65 (34.8%) were identified as being in the high stress group (PSS scores>20, cortisol level<12.7 μg/dL), and 23 (12.3%) were in the high cortisol group (PSS scores≤20, cortisol level≥12.7 μg/dL).

Table 1. General characteristics, depressive symptoms, cardiometabolic risks, and health-promoting lifestyle behaviors (N=187)

Variable	Category	Value
Age (yr)		23.97±3.38
Gender		
Women		101 (54.0)
Men		86 (46.0)
Education		
Undergraduate		132 (70.6)
Graduate		55 (29.4)
Current smoking		
No		169 (90.4)
Yes		18 (9.6)
Drinking		
No		120 (64.2)
Yes		67 (35.8)
Perceived stress		20.02±5.52
Cortisol (μg/dL)		10.81±4.08
Cardiometabolic risks		
BP (mmHg)		121.50±10.48
	High (≥130/85)	45 (24.1)
Waist circumference (cm)		80.21±8.07
	High[a]	33 (17.6)
TG (mg/dL)		81.14±70.58
	High (≥150)	17 (9.1)
HDL-C (mg/dL)		62.75±14.71
	Low[b]	5 (2.7)
FPG (mg/dL)		88.44±6.66
	High (≥100)	7 (3.7)
BMI (kg/m^2)		22.24±3.11
Depressive symptoms		19.10±9.36
	Significant (≥16)	115 (61.5)
Health-promoting lifestyle behaviors	Total	2.23±0.44
Subscales	Interpersonal relationships	2.82±0.52
	Nutrition	2.01±0.57
	Health responsibility	1.94±0.61
	Physical activity	1.83±0.71
	Stress management	2.25±0.50
	Spiritual growth	2.49±0.63

Values are presented as mean±standard deviation or number (%).
BMI, body mass index; BP, blood pressure; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; TG, triglyceride.
[a]≥85 cm for women, ≥90 cm for men. [b]≤40 mg/dL for men and ≤50 mg/dL for women.

Univariate analysis across stress–cortisol response groups

Table 2 shows the results of the univariate analyses for the differences in the general characteristics according to stress-cortisol response groups. Among the sociodemographic variables, gender ($P<0.001$) was significantly associated with stress-cortisol response groups. Among the cardiometabolic risk factors, systolic blood pressure (SBP) ($P<0.01$), HDL-C ($P=0.03$), and BMI ($P=0.02$) were significantly associated with stress-cortisol response groups. Depressive symptoms were also significantly associated

https://doi.org/10.15384/kjhp.2024.00031

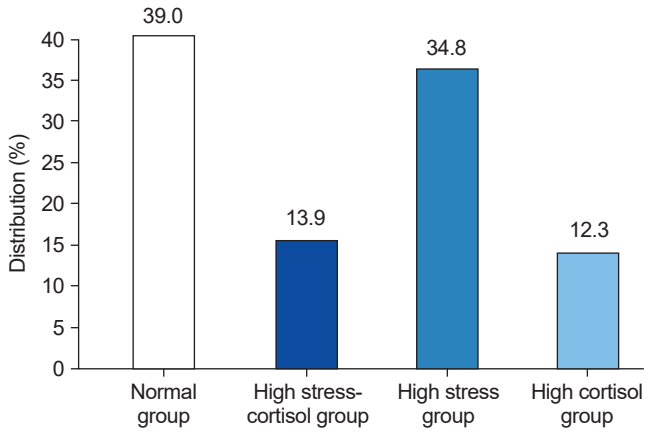

Fig. 2. Distribution of stress-cortisol response groups (N=187).

with stress-cortisol response groups (P<0.001). Significant associations were found between stress-cortisol response groups and four HPLP II subscales, including interpersonal relationships (P<0.001), nutrition (P<0.01), stress management (P<0.01), and spiritual growth (P<0.001).

Risk factors for stress-cortisol response groups

The normal group, consisting of participants who exhibited normal ranges of perceived stress and cortisol, served as a reference group in the multinomial logistic regression analysis. Table 3 presents the risk factors associated with stress-cortisol responses based on the multinomial logistic regression analysis. Participants of higher ages were relatively less likely to belong

Table 2. Univariate analyses across stress-cortisol response groups (N=187)

	Normal group[a] (n=73)	High stress-cortisol group[b] (n=26)	High stress group[c] (n=65)	High cortisol group[d] (n=23)	*P*-value	Post hoc
Age (yr)	24.40±3.81	23.35±2.48	23.34±3.28	23.13±2.72	0.07	
Gender					<0.001	
Women	33 (45.2)	11 (42.3)	50 (76.9)	7 (30.4)		
Men	40 (54.8)	15 (57.7)	15 (23.1)	16 (69.6)		
Education					0.44	
Undergraduate	53 (72.6)	18 (69.2)	48 (73.8)	13 (56.5)		
Graduate	20 (27.4)	8 (30.8)	17 (26.2)	10 (43.5)		
Current smoking					0.81	
No	65 (89.0)	24 (92.3)	60 (92.3)	20 (87.0)		
Yes	8 (11.0)	2 (7.7)	5 (7.7)	3 (13.0)		
Drinking					0.67	
No	30 (41.1)	9 (34.6)	21 (32.3)	7 (30.4)		
Yes	43 (58.9)	17 (65.4)	44 (67.7)	16 (69.6)		
Perceived stress	15.81±3.34	24.04±3.03	24.77±3.16	15.43±3.93	<0.001	a,d<b,c
Cortisol (μg/dL)	9.34±2.27	16.26±3.46	8.58±2.66	15.60±2.94	<0.001	a,c<b,d
Cardiometabolic risks						
SBP (mmHg)	121.82±9.27	125.65±12.10	118.22±9.59	125.09±12.10	<0.01	c<b,d
Waist circumference (cm)	80.83±8.04	79.66±7.88	79.05±7.29	82.17±10.25	0.36	
TG (mg/dL)	95.27±10.11	89.38±46.24	64.69±31.59	73.48±41.58	0.07	
HDL-C (mg/dL)	59.14±13.45	67.15±20.71	65.26±13.31	62.17±12.22	0.03	
FPG (mg/dL)	88.74±7.60	89.85±6.99	86.83±5.33	90.48±5.84	0.06	
BMI (kg/m^2)	22.52±3.05	22.07±3.17	21.50±2.96	23.69±3.24	0.02	c<d
Depressive symptoms	13.33±6.06	22.54±7.39	25.98±8.61	14.04±7.16	<0.001	a,d<b,c
Health-promoting lifestyle behaviors						
Interpersonal relationships	3.03±0.60	2.61±0.50	2.68±0.53	2.82±0.55	<0.001	b,c<a
Nutrition	2.11±0.54	1.68±0.49	1.99±0.60	2.13±0.54	<0.01	b<a,d
Health responsibility	2.03±0.66	1.69±0.44	1.93±0.60	1.99±0.60	0.10	
Physical activity	1.89±0.74	1.62±0.54	1.75±0.67	2.12±0.77	0.05	
Stress management	2.41±0.54	2.06±0.37	2.15±0.47	2.21±0.46	<0.01	b,c<a
Spiritual growth	2.75±0.62	2.14±0.54	2.32±0.56	2.52±0.60	<0.001	b,c<a

Values are presented as mean±standard deviation or number (%). *P*-values by Pearson's chi-square and Fisher's exact test, and Analysis of Variance. Post-hoc analyses were conducted using Bonferroni multiple-comparison tests.

BMI, body mass index; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; SBP, systolic blood pressure; TG, triglyceride.

[a]Normal group indicates normal stress, normal cortisol. [b]High stress-cortisol group indicates high stress, high cortisol. [c]High stress group indicates high stress, normal cortisol. [d]High cortisol group indicates normal stress, high cortisol.

Table 3. Multinomial logistic regression model across stress-cortisol response groups (N=187)

	High stress group[a]			High cortisol group[b]			High stress-cortisol group[c]		
	RRR±SE	*P*-value	95% CI	RRR±SE	*P*-value	95% CI	RRR±SE	*P*-value	95% CI
Age	0.82±0.08	0.03	0.68–0.98	1.06±0.08	0.46	0.91–1.23	0.81±0.10	0.10	0.64–1.04
Women[d]	2.12±1.39	0.25	0.59–7.66	1.04±0.71	0.95	0.26–3.94	0.57±0.44	0.47	0.13–2.60
Cardiovascular risk factors									
BMI	1.07±0.10	0.46	0.89–1.29	1.17±0.12	0.11	0.96–1.42	1.04±0.12	0.70	0.84–1.30
SBP	1.00±0.03	0.85	0.95–1.06	1.03±0.03	0.31	0.97–1.09	1.07±0.04	0.04	1.00–1.14
HDL-C	1.04±0.02	0.07	1.00–1.08	1.03±0.02	0.18	0.99–1.07	1.06±0.02	0.02	1.01–1.10
Depressive symptoms	1.33±0.07	<0.001	1.21–1.47	0.99±0.05	0.89	0.90–1.09	1.28±0.07	<0.001	1.15–1.42
Health-promoting lifestyle behaviors									
Interpersonal relationships	1.23±0.76	0.74	0.36–4.16	1.10±0.79	0.90	0.27–4.53	2.89±2.20	0.17	0.65–12.87
Nutrition	1.05±0.58	0.93	0.35–3.13	1.27±0.75	0.68	0.40–4.02	0.44±0.31	0.24	0.11–1.73
Health responsibility	0.99±0.53	0.98	0.35–2.82	0.92±0.54	0.89	0.29–2.92	0.65±0.47	0.55	0.16–2.67
Physical activity	1.60±0.76	0.32	0.64–4.04	3.49±1.89	0.02	1.20–10.11	1.53±0.94	0.48	0.46–5.09
Stress management	0.52±0.34	0.32	0.14–1.89	0.24±0.20	0.09	0.05–1.25	0.51±0.43	0.43	0.10–2.68
Spiritual growth	0.64±0.42	0.50	0.18–2.30	0.39±0.28	0.19	0.09–1.62	0.26±0.19	0.07	0.06–1.09

The reference group is the normal group (normal stress, normal cortisol). *P*-values by multinomial logistic regression analysis.
BMI, body mass index; CI, confidence interval; HDL-C, high-density lipoprotein cholesterol; RRR, relative risk ratio; SBP, systolic blood pressure; SE, standard error.
[a]High stress group indicates high stress, normal cortisol. [b]High cortisol group indicates normal stress, high cortisol. [c]High stress-cortisol group indicates high stress, high cortisol. [d]The reference group for gender is men.

to the high stress group (RRR 0.82, 95% CI 0.68–0.98) than to the normal group. Participants who were at risk of having depressive symptoms (RRR 1.33, 95% CI 1.21–1.47) were more likely to be in the high stress group. Participants who reported engaging in high levels of physical activity were relatively more likely to belong to the high cortisol group (RRR 3.49, 95% CI 1.20–10.11). In addition, individuals with higher SBP (RRR 1.07, 95% CI 1.00–1.14), higher HDL-C levels (RRR 1.06, 95% CI 1.01–1.10), and those at risk of experiencing depressive symptoms (RRR 1.28, 95% CI 1.15–1.42) were more likely to be categorized in the high stress-cortisol group compared to the normal group.

DISCUSSION

The present study investigated the distribution of four types of stress-cortisol responses and risk factors associated with stress-cortisol responses in university students. We found that age, cardiometabolic risk factors (e.g., SBP, HDL-C), depressive symptoms, and lifestyle factors (e.g., physical activity) predicted stress-cortisol responses to naturally occurring stress in university students.

We identified four groups: a normal group (39.0%), a high stress-cortisol group (13.9%), a high stress group (34.8%), and a high cortisol group (12.3%). Thus, over 60% of the participants were at risk of stress. Other studies have also explored the distribution of stress-cortisol response groups [39,40]. Dalile et al. [39] classified stress-cortisol responses into four classes: mild (11.5%), moderately low (34.2%), moderately high (35.9%), and hyper-responders (18.5%). Paananen et al. [40] identified three cortisol response patterns in young adults using the Trier Social Stress Test: an intermediate-responsive group (47% women, 54% men), a hyporesponsive group (34% women, 21% men), and a hyperresponsive group (18% women, 21% men). It should be noted that these studies [39,40] used trajectory modeling based on longitudinal data. However, our study identified stress-cortisol response groups based on normal cortisol levels and naturally accruing stress with no artificial stimuli. Nevertheless, all these results, including findings of this study, support the importance of monitoring stress-cortisol responses to promote health.

We found that participants with high SBP and HDL-C levels were more likely to belong to the high stress-cortisol group than to the normal group. High SBP and low HDL-C levels are well-known risk factors for cardiovascular diseases. The relationship between HPA axis activity and cardiometabolic diseases is well-documented [10,16-18]. In addition, stress elevates glucocorticoid output, which can cause elevated cholesterol and BP levels [18]. Prolonged exposure to stressful situations can increase the risk of cardiovascular diseases [41]. In the context of this study, experiencing naturally occurring stress, we can assume that university students who belong to the high

 https://doi.org/10.15384/kjhp.2024.00031

stress-cortisol group may have repeated exposure to everyday stressors. This study indicates that special attention and early intervention are essential for this group.

In our study, the participants who showed high levels of depressive symptoms had a higher probability of belonging to the high stress and high stress-cortisol groups than to the normal group. This finding indicates that university students with high levels of depressive symptoms may experience high levels of psychological stress with varying cortisol levels; likewise, stress is a well-known risk factor for depressive symptoms [42]. Our findings align with previous studies linking stress-cortisol responses to depression [22,43]. These results indicate that depression is associated with higher stress levels.

Participants who reported high levels of physical activity were more likely to belong to the high cortisol group than to the normal group. Previous studies found that physical activity reduces perceived stress [44,45]. Unlike our result, a review of the literature revealed that physical exercise could have beneficial effects on lowering cortisol levels [46]. Further investigation is needed to determine whether physical activity itself is a stressor activating the HPA axis and whether cortisol level recovery to baseline is associated with physical activity.

Notably, among the sociodemographic factors in our study, there was a significant difference in the gender ratio among the stress-cortisol response groups although gender had no significant effect on those groups. The percentage of men students was much higher in the high cortisol group (69.6%) and high stress-cortisol group (57.7%), whereas the rate of women students was much higher in the high stress group (76.9%). A study found gender differences in perceived stress (higher levels of stress in women college students) and more utilization of emotion-focused coping strategies in women than men students [47]. These results imply that gender is a contributing factor in the experience of stress and therefore healthcare providers should consider gender when developing and implementing health promotion interventions.

The probability of being in the high stress group decreased with a one-year increase in age. This result is consistent with a previous study that reported higher levels of stress in younger students [48], suggesting that younger students need more support. However, it remains unclear whether aging is accompanied by changes in the HPA axis function [13]. Furthermore, all participants in this study were young adults aged 19–39 years, an age range that may be too narrow to consider the effects of age on stress-cortisol responses.

Contrary to expectations, BMI and aspects of health-promoting lifestyle behaviors, including interpersonal relationships, nutrition, health responsibility, stress management, and spiritual growth, did not emerge as significant contributors to stress-cortisol responses. Possible explanations for these non-significant findings may be rooted in the multifaceted nature of stress-cortisol interactions. It is conceivable that the influence of these factors is moderated by unexplored variables not accounted for in our study. Further exploration into the reasons for these outcomes is warranted.

The study's findings suggest delivering customized health promotion interventions for university students, addressing the factors affecting stress-cortisol responses, and acknowledging the adverse impact of high stress and cortisol levels on health. According to a previous study, university students with low resilience showed higher scores in perceived stress [49]. Furthermore, mindfulness meditation was significantly effective in decreasing serum cortisol levels and perceived stress [50]. Therefore, providing programs focused on resilience and mindfulness meditation could be beneficial for students, particularly those who experience high stress.

Limitations

The participants in this study were limited to healthy university students recruited using convenience sampling at a single university in Korea. Thus, a limitation is the generalizability of the results to other student populations. Future research should use a larger and more diverse sample to improve generalizability. Furthermore, the present study employed a cross-sectional design and therefore could not investigate the potential fluctuations and trajectories of cortisol responses to stress. Studies using a longitudinal design are required to better understand these relationships.

ORCID

Shinae SEO, https://orcid.org/0000-0002-9922-1692
Chun-Ja KIM, https://orcid.org/0000-0002-7594-5418
Hee Sun KANG, https://orcid.org/0000-0003-3808-306X
Elizabeth A. SCHLENK, https://orcid.org/0000-0001-7361-1951

AUTHOR CONTRIBUTIONS

Conceptualization: SS, CJK, and HSK. Data curation: SS and CJK. Formal analysis: SS, CJK, and HSK. Investigation: CJK.

Resources: SS and CJK. Software: SS and CJK. Supervision: CJK. Validation: CJK, HSK, and EAS. Visualization: CJK. Writing–original draft: SS and CJK. Writing–review & editing: all authors.

CONFLICTS OF INTEREST

No existing or potential conflict of interest relevant to this article was reported.

FUNDING

This work was partly supported by the National Research Foundation of Korea grant funded by the Korea government (MSIT) (No. 2021R1A2C2007858). The funder did not play any role in the conduct or publication of the study.

DATA AVAILABILITY

The data are not publicly available due to further analyses.

ACKNOWLEDGMENTS

The authors acknowledge with gratitude the most competent assistance of Drs. MA YOO, EJ SEO and B-T KIM, MD and the cooperation of the study participants and clinical staff of outpatient clinics in Ajou University Hospital.

REFERENCES

1. Asif S, Mudassar A, Shahzad TZ, Raouf M, Pervaiz T. Frequency of depression, anxiety and stress among university students. Pak J Med Sci 2020;36(5):971-6.
2. Seo EJ, Ahn JA, Hayman LL, Kim CJ. The association between perceived stress and quality of life in university students: the parallel mediating role of depressive symptoms and health-promoting behaviors. Asian Nurs Res 2018;12(3):190-6.
3. Al Omari O, Wynaden D, Alkhawaldeh A, Alhalaiqa F, Al Dameery K, Roach EJ, et al. Jordanian University students' lived experience of misusing amphetamine (Captagon): a qualitative study. J Addict Nurs 2022;33(1):20-6.
4. Cornwall J, Mayland EC, van der Meer J, Spronken-Smith RA, Tustin C, Blyth P. Stressors in early-stage doctoral students. Stud Contin Educ 2019;41(3):363-80.
5. Kappner N, Lang J, Berthold A, Gaum PM. The moderating effect of social resources on the link between study-related stressors and depressive symptoms among medical students in North Rhine-Westphalia, Germany: a cross-sectional study. BMC Psychiatry 2022;22(1):524.
6. Khademian F, Aslani A, Ravangard R, Nami M, Abbasi S, Bastani P. Iranian University students' stressors and coping strategies: a qualitative study. J Educ Health Promot 2021;10:244.
7. Acharya L, Jin L, Collins W. College life is stressful today: emerging stressors and depressive symptoms in college students. J Am Coll Health 2018;66(7):655-64.
8. Pascoe MC, Hetrick SE, Parker AG. The impact of stress on students in secondary school and higher education. Int J Adolesc Youth 2020;25(1):104-12.
9. Ribeiro ÍJS, Pereira R, Freire IV, de Oliveira BG, Casotti CA, Boery EN. Stress and quality of life among university students: a systematic literature review. Health Prof Educ 2018;4(2):70-7.
10. Chu B, Marwaha K, Sanvictores T, Ayers D. Physiology, stress reaction. In: StatPearls [Internet]. StatPearls Publishing; 2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK541120/
11. Dunlavey CJ. Introduction to the hypothalamic-pituitary-adrenal axis: healthy and dysregulated stress responses, developmental stress and neurodegeneration. J Undergrad Neurosci Educ 2018;16(2):R59-60.
12. Sherman GD, Mehta PH. Stress, cortisol, and social hierarchy. Curr Opin Psychol 2020;33:227-32.
13. Zänkert S, Bellingrath S, Wüst S, Kudielka BM. HPA axis responses to psychological challenge linking stress and disease: what do we know on sources of intra- and interindividual variability? Psychoneuroendocrinology 2019;105:86-97.
14. Špiljak B, Vilibić M, Glavina A, Crnković M, Šešerko A, Lugović-Mihić L. A review of psychological stress among students and its assessment using salivary biomarkers. Behav Sci (Basel) 2022;12(10):400.
15. Grundy SM. Metabolic syndrome update. Trends Cardiovasc Med 2016;26(4):364-73.
16. Bouillon-Minois JB, Dutheil F. Biomarker of stress, metabolic syndrome and human health. Nutrients 2022;14(14):2935.
17. Gebreab SZ, Vandeleur CL, Rudaz D, Strippoli MF, Gholam-Rezaee M, Castelao EL, et al. Psychosocial stress over the lifespan, psychological factors, and cardiometabolic risk in the community. Psychosom Med 2018;80(7):628-39.
18. Iob E, Steptoe A. Cardiovascular disease and hair cortisol: a novel biomarker of chronic stress. Curr Cardiol Rep 2019;21(10):116.
19. Li W, Zhao Z, Chen D, Peng Y, Lu Z. Prevalence and associated factors of depression and anxiety symptoms among college stu-

dents: a systematic review and meta-analysis. J Child Psychol Psychiatry 2022;63(11):1222-30.
20. Jiang L, Wang Y, Zhang Y, Li R, Wu H, Li C, et al. The reliability and validity of the Center For Epidemiologic Studies Depression Scale (CES-D) for Chinese university students. Front Psychiatry 2019;10:315.
21. Hirsch JK, Rabon JK, Reynolds EE, Barton AL, Chang EC. Perceived stress and suicidal behaviors in college students: conditional indirect effects of depressive symptoms and mental health stigma. Stigma Health 2019;4(1):98-106.
22. Fiksdal A, Hanlin L, Kuras Y, Gianferante D, Chen X, Thoma MV, et al. Associations between symptoms of depression and anxiety and cortisol responses to and recovery from acute stress. Psychoneuroendocrinology 2019;102:44-52.
23. Holding AC, Moore E, Moore A, Verner-Filion J, Ouellet-Morin I, Koestner R. When goal pursuit gets hairy: a longitudinal goal study examining the role of controlled motivation and action crises in predicting changes in hair cortisol, perceived stress, health, and depression symptoms. Clin Psychol Sci 2021;9(6):1214-21.
24. Leung C, Kyung M. Associations among perceived stress, cortisol, and adolescent depressive symptoms. J Pediatr Health Care 2022;36(4):397-8.
25. Jao NC, Robinson LD, Kelly PJ, Ciecierski CC, Hitsman B. Unhealthy behavior clustering and mental health status in United States college students. J Am Coll Health 2019;67(8):790-800.
26. Abraham S, Noriega BR, Shin JY. College students eating habits and knowledge of nutritional requirements. J Nutr Hum Health 2018;2(1):13-7.
27. Ramón-Arbués E, Gea-Caballero V, Granada-López JM, Juárez-Vela R, Pellicer-García B, Antón-Solanas I. The prevalence of depression, anxiety and stress and their associated factors in college students. Int J Environ Res Public Health 2020;17(19):7001.
28. Yun TC, Ahmad SR, Quee DKS. Dietary habits and lifestyle practices among university students in Universiti Brunei Darussalam. Malays J Med Sci 2018;25(3):56-66.
29. Haardörfer R, Windle M, Fairman RT, Berg CJ. Longitudinal changes in alcohol use and binge-drinking among young-adult college students: analyses of predictors across system levels. Addict Behav 2021;112:106619.
30. Krieger H, Young CM, Anthenien AM, Neighbors C. The epidemiology of binge drinking among college-age individuals in the United States. Alcohol Res 2018;39(1):23-30.
31. Dalton ED, Hammen CL. Independent and relative effects of stress, depressive symptoms, and affect on college students' daily health behaviors. J Behav Med 2018;41(6):863-74.
32. Ramón-Arbués E, Granada-López JM, Martínez-Abadía B, Echániz-Serrano E, Antón-Solanas I, Jerue BA. Factors related to diet quality: a cross-sectional study of 1055 university students. Nutrients 2021;13(10):3512.
33. Moriarty T, Bourbeau K, Fontana F, McNamara S, Pereira da Silva M. The relationship between psychological stress and healthy lifestyle behaviors during COVID-19 among students in a US Midwest University. Int J Environ Res Public Health 2021;18(9):4752.
34. Cohen S, Kamarck T, Mermelstein R. A global measure of perceived stress. J Health Soc Behav 1983;24(4):385-96.
35. Radloff LS. The CES-D scale: a self-report depression scale for research in the general population. Appl Psychol Meas 1977;1(3):385-401.
36. Lewinsohn PM, Seeley JR, Roberts RE, Allen NB. Center for Epidemiologic Studies Depression Scale (CES-D) as a screening instrument for depression among community-residing older adults. Psychol Aging 1997;12(2):277-87.
37. Yun SN, Kim JH. Health-promoting behaviors of the women workers at the manufacturing industry: based on the Pender's health promotion model. Korean J Occup Health Nurs 1999;8(2):130-40.
38. Walker SN, Hill-Polerecky DM. Psychometric evaluation of the Health-Promoting Lifestyle Profile II. Unpublished manuscript. University of Nebraska Medical Center; 1996. Available from: https://www.unmc.edu/nursing/faculty/HPLPII_Abstract_Dimensions.pdf
39. Dalile B, La Torre D, Verbeke K, Van Oudenhove L, Vervliet B. When the mind says one thing, but the HPA axis says another: lack of coherence between subjective and neuroendocrine stress response trajectories in healthy men. Psychoneuroendocrinology 2022;139:105692.
40. Paananen M, O'Sullivan P, Straker L, Beales D, Coenen P, Karppinen J, et al. A low cortisol response to stress is associated with musculoskeletal pain combined with increased pain sensitivity in young adults: a longitudinal cohort study. Arthritis Res Ther 2015;17:355.
41. Osborne MT, Shin LM, Mehta NN, Pitman RK, Fayad ZA, Tawakol A. Disentangling the links between psychosocial stress and cardiovascular disease. Circ Cardiovasc Imaging 2020;13(8):e010931.
42. Da Costa D, Danieli C, Abrahamowicz M, Dasgupta K, Sewitch M, Lowensteyn I, et al. A prospective study of postnatal depressive symptoms and associated risk factors in first-time fathers. J Affect Disord 2019;249:371-7.

43. Ahmad MH, Rizvi MA, Fatima M, Mondal AC. Pathophysiological implications of neuroinflammation mediated HPA axis dysregulation in the prognosis of cancer and depression. Mol Cell Endocrinol 2021;520:111093.
44. González-Valero G, Gómez-Carmona CD, Bastida-Castillo A, Corral-Pernía JA, Zurita-Ortega F, Melguizo-Ibáñez E. Could the complying with WHO physical activity recommendations improve stress, burnout syndrome, and resilience? A cross-sectional study with physical education teachers. Sport Sci Health 2023;19:349-58.
45. Vogel EA, Zhang JS, Peng K, Heaney CA, Lu Y, Lounsbury D, et al. Physical activity and stress management during COVID-19: a longitudinal survey study. Psychol Health 2022;37(1):51-61.
46. De Nys L, Anderson K, Ofosu EF, Ryde GC, Connelly J, Whittaker AC. The effects of physical activity on cortisol and sleep: a systematic review and meta-analysis. Psychoneuroendocrinology 2022;143:105843.
47. Graves BS, Hall ME, Dias-Karch C, Haischer MH, Apter C. Gender differences in perceived stress and coping among college students. PLoS One 2021;16(8):e0255634.
48. Hitches E, Woodcock S, Ehrich J. Building self-efficacy without letting stress knock it down: stress and academic self-efficacy of university students. Int J Educ Res open 2022;3:100124.
49. García-León MÁ, Pérez-Mármol JM, Gonzalez-Pérez R, García-Ríos MDC, Peralta-Ramírez MI. Relationship between resilience and stress: perceived stress, stressful life events, HPA axis response during a stressful task and hair cortisol. Physiol Behav 2019;202:87-93.
50. Alhawatmeh HN, Rababa M, Alfaqih M, Albataineh R, Hweidi I, Abu Awwad A. The benefits of mindfulness meditation on trait mindfulness, perceived stress, cortisol, and C-reactive protein in nursing students: a randomized controlled trial. Adv Med Educ Pract 2022;13:47-58.

 https://doi.org/10.15384/kjhp.2024.00031

Instructions for Authors

Korean Journal of Health Promotion
KJHP

Revised in January, 2024 (6th)
Revised in January, 2016 (5th)
Revised in June, 2011 (4th)
Revised in June, 2009 (3rd)
Revised in June, 2007 (2nd)
Revised in March, 2003 (1st)
Enacted in March, 2001

The Korean Journal of Health Promotion (KJHP) is an open access, multidisciplinary journal dedicated to publishing high-quality research in various areas of the medical, nursing, nutritional, physical educational, epidemiological, and public health sciences associated with health promotion and disease prevention.

The manuscript should be prepared according to the "ICMJE Recommendations for the Conduct, Reporting, and Publication of Scholarly Work in Medical Journals" (2023) (https://www.icmje.org/recommendations/). Matters unspecified in this document will follow the general principles of writing and editing of biomedical publication.

1. MANUSCRIPT SUBMISSION

All manuscripts must be submitted online via the online manuscript submission and review system for *KJHP* (https://submit.e-kjhp.org/)

Editor-in-Chief
Prof. Seung-Kwon MYUNG, MD, PhD
Department of Family Medicine, National Cancer Center
Department of Cancer AI & Digital Health, National Cancer Center Graduate School of Cancer Science and Policy

Editorial Office
Department of Family Medicine, Asan Medical Center, 88 Olympic-ro 43-gil, Songpa-gu, Seoul 05505, Korea

Tel: +82-2-3010-3820
Tel: +82-2-3010-3815
E-mail: kshpdp@amc.seoul.kr
For manuscript submission, please visit https://submit.e-kjhp.org/

2. CATEGORIES OF ARTICLES

KJHP publishes original articles, review articles (narrative reviews and systematic reviews without meta-analyses), letters to the editor, letters in reply, editorials, and viewpoints.

*Summary of Article Types

Article Type	Description	Requirements
Original Article	Cross-sectional study Case-control study Cohort study Clinical trial Meta-analysis Qualitative research Survey research Other observational or original research	• ≤3,500 words • ≤10 tables and/or figures • Structured abstract, ≤300 words • Key Points: Question, Findings, and Meaning, ≤100 words • ≤50 references • Title Page including Key Points • Manuscript text: Title, Abstract, Keywords, Introduction, Methods, Results, Discussion, Acknowledgments, Author Contributions, References, Figure Legends, and Tables • Figures uploaded separately • Cover letter
Review Article	Narrative review (general review) Systematic review without meta-analysis	• ≤3,500 words • ≤10 tables and/or figures • Structured abstract, ≤300 words • Key Points: Question, Findings, and Meaning, ≤100 words • ≤50 references • Subtitle should be 'A Narrative Review or A Systematic Review' • Title Page including Key Points • Manuscript text: Title, Abstract, Keywords, Introduction, Methods, Results, Discussion, Acknowledgments, Author Contributions, References, Figure Legends, and Tables • Figures uploaded separately • Cover letter

Letter to the Editor	Letters discussing a recent article in this journal should be submitted within 4 weeks of the article's publication in print.	• ≤1,000 words • ≤5 references • ≤3 authors • No abstract required
Letter in Reply	Replies by authors of original articles to letters from readers.	• ≤1,000 words • ≤5 references • ≤3 authors • No abstract required
Editorial	An opinion or a view of a member of the editorial board or any senior or reputed faculty written in a journal	• ≤1,000 words • 1 author • No abstract required
Viewpoint	A short opinion which focuses on some of the key topics, issues, or developments in health promotion and disease prevention	• ≤1,500 words • ≤10 references • ≤3 authors • Unstructured abstract, ≤150 words

3. MANUSCRIPT PREPARATION AND SUBMISSION REQUIREMENTS

1) Original Article and Review Article

Manuscript Style

Manuscripts should be prepared in accordance with the ICMJE Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals (https://icmje.org/recommendations) and written in proper and clear English.

Manuscript Components

The authors should prepare at least 3 files such as a cover letter, title page (with author details), manuscript text (no author identifiers), and as appropriate, figures. Start each of these sections on a new page, numbered consecutively. Tables should be included in the manuscript text, and figures should be uploaded as separate files (individual or combined figure files) and not included in the manuscript text. Also, a copyright transfer form should be signed by a corresponding author on behalf of all authors and submitted (a link for downloading the form should be inserted here).

Manuscript File Formats

For submission and review, please submit the manuscript as a Word document (e.g., Microsoft Office Word). Do not submit your manuscript in PDF format. For submission of drawings, photos, graphs, or combined figures, PPT and PDF formats are acceptable.

Use 12-point font size, double-space text, and leave both margins justified.

Cover Letter (≤200 words)

Prepare a cover letter. This is a great opportunity to highlight to the journal editor what makes your research new and important. The cover letter should explain why your work is perfect for the *KJHP* and why it will be of interest to our readers. The cover letter should have a maximum of 200 words and include complete contact information for the corresponding author (affiliation, postal/mail address, email address, and telephone number) and whether the authors have published, posted, or submitted any related papers from the same study.

Title Page (≤300 words)

The title page should include an article title; running head; type of study design; the full names, academic degrees, and affiliations of all authors (if an author's affiliation has changed since the work was done, the new affiliation also should be listed); name and complete contact information for corresponding author; word count of the abstract and manuscript text (not including title, abstract, acknowledgment, references, tables, and figure legends); total number of tables; total number of figures; number of references; funding sources; declaration of conflict of interests; and key points.

Provide ORCID IDs for all authors. Titles should be concise, specific, and informative. Limit the length of titles to 30 words. A running head or running title is a short version of the article title, which should consist of no more than 10 words.

The key points is a short structured summary of the findings of your manuscript (required only for research and review manuscripts), following 3 key points: Question, Findings, and Meaning. Limit to 100 words or less.

<Example>

Key Points

Question: Is intermittent high-dose vitamin D supplementation effective in the prevention of falls and fractures?

Findings: In this meta-analysis of 15 randomized controlled trials, intermittent high-dose vitamin D supplementation showed no beneficial effect in the prevention of falls and fractures and even showed a harmful effect in the high-quality trials.

Meaning: Our findings support that intermittent high-dose vitamin D supplementation for the prevention of falls and fractures should be discouraged.

Manuscript Text

A manuscript text should be prepared in the following sequence: title, abstract, keywords, introduction, methods, results, discussion, acknowledgments, author contributions, references, figure legends, and tables. The full text containing introduction, methods, results, and discussion should not exceed 3500 words.

Title (≤30 words)

An article title should be inserted at the top of the first page of the manuscript text file.

Abstract (≤300 words) and Keywords

An abstract should briefly summarize the content of the manuscript in a structured format and should not exceed 300 words. The abstract should be structured as follows: Background, Methods, Results, and Conclusions. Three to six keywords should be listed after the abstract.

Introduction (≤500 words)

Desribe a brief background and purpose of the study and elaborate on its significance. Summarize the rationale and include only strictly pertinent references.

Methods (≤1,000 words)

Identify the methods. Describe study participants, controls, or laboratory animals clearly and identify procedures in sufficient details to allow other researchers to reproduce the results. Identify the apparatus or reagents used by giving the product's name, followed by the name of the product company in parentheses. Give references to established methods, including statistical methods. Provide references and brief descriptions for methods that have been published but are not well known or substantially modified, and give reasons for using them and evaluate their limitations.

Describe statistical methods with enough details to verify the reported results. Whenever possible, quantify findings and present them with appropriate indicators of measurement error or uncertainty (such as confidence intervals). Avoid relying solely on statistical hypothesis testing, such as the use of *P*-values, which fails to convey important quantitative information. When the results of the data in the text are given, provide details specifically in terms of average, proportion, or correlation coefficient to describe the difference between study groups or the relevant size and direction of variables. Specify statistical software used for statistical analysis.

Results (≤1,000 words)

Present the findings and results in logical sequence in the text, tables, and figures. Do not repeat in the text all data in the tables or figures, but describe important points and trends.

Discussion (≤1,000 words)

Emphasize the new and important aspects of the study and the conclusions that follow from them. Do not repeat in detail data or other materials given in the Introduction or the Results section. Include the implications of the findings and their limitations, including implications for future research. Link the conclusions with the purpose of the study by discussing and comparing the relevant results of other research data. Avoid unqualified statements and conclusions not completely supported by the data. Propose new hypotheses when warranted and recommendations, when appropriate, may be included.

Acknowledgments

If necessary, persons who have contributed to the article but whose contributions do not meet authorship standards may be appreciated through acknowledgment section. Clearly state their contributing role for acknowledgement. For example, data collection, financial support, statistical analysis, analysis of experiment, and so forth. Authors should notify that their names will be in the Acknowledgement and are responsible for obtaining permission from persons acknowledged.

Author Contributions

What authors have done for the study should be described in this section. To qualify for authorship, all contributors must meet at least one of the seven core contributions by CRediT (conceptualization, methodology, software, validation, formal analysis, investigation, data curation), as well as at least one of the writing contributions (original draft preparation, review, and editing).

The submitting author is responsible for completing this information at submission, and it is expected that all authors will have reviewed, discussed, and agreed to their individual contributions ahead of this time.

<Example>

Dr. MYUNG had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. All authors reviewed this manuscript and agreed to individual contributions.

Conceptualization: SKM.
Data curation: SWO and YJC.
Formal analysis: YJC.
Methodology: SKM, SWO, and YJC.
Software: SKM and YJC.
Writing - original draft: YJC.
Writing - review & editing: SKM, SWO, and YJC.

References

Authors are responsible for the accuracy and completeness of their references and for correct text citation. In the text, references should be cited with Arabic numerals in brackets, numbered in the order cited. In the references section, the references should be numbered and listed in order of appearance in the text. If there is more than one reference cited coincidentally, then a comma separates the numbers and only the last number is closed with a right bracket. If a consecutive number of references is cited together, then a hyphen '-' should be used between the first and the last number.

List all authors and/or editors up to 6; if more than 6, list the first 6 followed by "et al." Journal references should include the issue number in parentheses after the volume number. Reference styles are as follows:

Journal articles

Name(s) of author(s). Title of article. Abbreviated journal name. Year of publication;Volume number (Issue number):Page numbers.

<Example> Myung SK, Oh SW, Choi YJ. How to use the KJHP's online manuscript submission system. Korean J Helath Promot 2024;24(1):123-7.

Books

Name(s) of author(s). Title of publication: subtitle. Edition. Publisher; Year of publication. p. Page numbers.

Name(s) of the chaptor's author(s). Title of chapter. In: Name(s) of the editor(s). Title of publication. Edition. Publisher; Year of publication. p. Page numbers.

Conference proceedings

Name(s) of author(s). Title of conference proceedings. Title of conference; Date of conference; Place of conference. Publisher; Year of publication.

Dissertations

Name of author. Title of thesis [dissertation]. Name of university; Year when degree was given. Language of dissertation.

Journal articles in electronic media

Name(s) of author(s). Title of article. Abbreviated title of journal [Internet]. Year of publication;Volume number (Issue number):Page numbers. Name of source URL:

Website or online sources

Name(s) of author(s). Title of web page [Internet]. Name of publisher; Year of publication [Date of citation]. Available from: available URL

Figure Titles and Legends (Captions)

After references, include a title for each figure. The figure title should be a brief descriptive phrase, preferably no longer than 10 to 15 words. A figure legend (caption) can be used for a brief explanation of the figure or markers if needed and expansion of abbreviations.

Tables

All tables should be inserted after figure legends in the manuscript text. Restrict tables and figures to those needed to explain and support the argument of the article and to report all outcomes identified in the Methods section. Number each table and figure and provide a descriptive title for each. Every table and figure should have an in-text citation. Verify that data are consistently reported across text, tables, figures, and supplementary material. The number of tables and /or figures should not exceed 10.

Within a table, if an abbreviation is used or a description may be necessary, then list them under annotation below. Use the alphabet in the order of a, b, c by superscript on the right side of the part that needs explanation and the annotation should be recorded according to the symbols listed below the table. For each annotation marked, the first letter of the first word should be capitalized. The *P* of the *P*-value should also be capitalized. The title of the table should be on the top placed at the right end of the table. The title of the figure should also be on the top placed at the right end of the figure. The numbering of the table or figure should be in the order of entry in the main text, and Arabic numeral should be used after a space of the word 'Table (Figure)' followed by a period. The first letter of the first word should be capitalized. In making a table, the average and standard deviation, the number of participants and other figures should be given and on the annotated part of the table, the ap-

plied statistical method should be noted. For ratio, the number of responders and the ratio, and for correlation coefficient, the value of correlation coefficient should be given, respectively.

Figures

Number all figures (graphs, charts, photographs, and illustrations) in the order of their citation in the text. When illustrating a figure, use a bar or a line graph for average or proportion, and list measures using standard deviation or standard error and must show their *P*-values. Identify the applied statistical methods at the footnote of each figure. Primary outcome data should not be presented in figures alone. Exact values with measure of variability should be reported in the text or table as well as in the abstract. All symbols, indicators (including error bars), line styles, colors, and abbreviations should be defined in a legend. Each axis on a statistical graph must have a label and units of measure should be labeled. Error bars should be included in both directions, unless only 1-sided variability was calculated.

Acceptable file formats are .jpg, .tif, .pdf, .ppt, .psd, and .eps. Required minimum resoultion for publication is 300 ppi.

Abbreviations

Overindulgence with the use of abbreviations is forbidden, and the use of abbreviations must be minimized. Only standardized abbreviations may be used and abbreviations should not be used in titles or abstracts. With the exception of measurement units, abbreviation should be specified when first introduced in the text and then may be used independently.

Units of Measurement

Laboratory values are expressed using conventional units of measure, with relevant Systeme International (SI) conversion factors expressed secondarily (in parentheses) only at first mention. Figures and tables should use conventional units, with conversion factors given in legends or footnotes. The metric system is preferred for the expression of length, area, mass, and volume.

Names of Drugs, Devices, and Other Products

Generic names should be used. When proprietary brands are used in research, include the brand name and the name of the manufacturer in parentheses after the first mention of the generic name in the Methods section.

Generic Names, Numbers, and Measurement Units

Personal, geographical and generic names must be written in original language, if possible, and numbers must be written in Arabic numerals. The measurement units such as length, height, mass and volume should be indicated in the metric system (meter, kilogram, liter etc). Temperature must be indicated in centigrade and blood pressure in mmHg. Units for blood and clinical laboratory test measurements should be expressed in the ordinary scale or by International Units (SI). A space is required between a measured value and its unit.

Supplementary Materials

Supplementary materials for online-only publication can be submitted, when there is insufficient space to include the materials in the manuscript text or figures. Because supplementary materials are not edited or formatted after publication, authors are responsible for the accuracy and presentation of these materials.

Reporting Sex/Gender

The term sex (male, female) should be used when reporting biological factors and gender (man, woman) should be used when reporting gender identity or psychosocial/cultural factors. The methods used to obtain information on sex, gender, or both (e.g., selfreported, investigator observed or classified, or laboratory test) should be explained in the Methods section. If only one sex is reported, or included in the study, the reason the other sex is not reported or included should be explained in the methods section, except for studies of diseases/disorders that only affect males (e.g., prostate disease) or females (e.g., ovarian disease). The sex distribution of study participants or samples should be reported in the results section, including for studies of humans, tissues, cells, or animals. Study results should disaggregate and report all outcome data by sex.

2) Letters to the Editor, Letters in Reply, Editorials, and Viewpoints

For preparation of Letters to the Editor, Letters in Reply, Editorials, and Viewpoints, refer to 'Summary of Article Types' in the categories of articles secction.

4. REPORTING GUIDELINES FOR SPECIFIC STUDY DESIGNS

Authors should be aware of the information that must be in-

cluded in the contents of the research according to the study design and must reflect them in their articles. Authors should refer to STROBE (http://www.strobe-statement.org) for observational studies, CONSORT (http://www.consort-statement.org) for randomized controlled trials, STARD (http://www.stard-statement.org) for studies of diagnostic accuracy, and PRISMA (https://www.equator-network.org/reporting-guidelines/prisma/) and MOOSE (https://www.equator-network.org/reporting-guidelines/meta-analysis-of-observational-studies-in-epidemiology-a-proposal-for-reporting-meta-analysis-of-observational-studies-in-epidemiology-moose-group/) for systematic reviews and meta-analyses.

5. MANUSCRIPT REVIEW AND PUBLICATION

Upon submission of a manuscript, the Editorial Committee will review the article whether its contents meet the objectives of the Journal, and the article can be rejected at this initial review process. The Editorial Committee will entrust two or more experts with review of articles and will decide their acceptance for publication with the help of experts' recommendations. Based on comments from reviewers and editors, authors may be asked to revise their manuscripts. Authors are required to submit a revised manuscript and a letter of explanation regarding how they have dealt with all comments and questions raised by reviewers and editors through the electronic submission system. The Editorial Committee or the editor-in-chief may entrust an statistical expert with statistical review of articles at the final stage of review, and ask authors to revise their manuscripts, if necessary.

The acceptance for publication is decided by the Editorial Committee after its thorough review process, and the editor-in-chief will deliver an official approval of acceptance for publication.

6. COPYRIGHT

Once publication of the manuscript has been decided, the copyright will be deferred to the Korean Society for Health Promotion and Disease Prevention, and the copyright of the manuscript published will belong to the Society. The Society is entitled to publish, distribute and print a manuscript in the journal or other media. As the time of submission, a corresponding author, on behalf of all authors, must sign and submit the 'copyright transfer agreement form', which must be downloaded from the homepage, to confirm that its copyright is assigned.

7. ETHICAL REGULATIONS

Review and handling procedures related to all research ethics including ethics regulations and plagiarism, duplicate publication, and research misconduct will be followed according to the 'Good Publication Practice Guidelines for Medical Journals (http://kamje.or.kr/)' stipulated by the Korean Association of Medical Journal Editors (KAMJE).

1) Ethical Review and Informed Consent

If the research involves human participants, it must comply with the ethical standards of the Declaration of Helsinki (adopted in 1964; amended in 2008; https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/) and in principle must undergo scrutiny of an independent Institutional Review Board (IRB) or Research Ethics Committee (REC) which reviews the ethical issues of the human experiment. However, in clinical studies, the approval of the IRB or ERC and participant's consent must be received and specified in the text.

2) Privacy and Confidentiality

Every author must protect privacy and confidentiality of study participants. The personal information regarding the identity of a study participant must not be disclosed in any form: article, photo or pedigree. However, if a study participant's personal information is indispensable as scientific information, it must be explained to the study participant or his/her legal guardian, written informed consent should be obtained from him/her before publication, and his/her approval must be specified in a published article. At the time of explanation, a manuscript to be published, including photos, must be offered to a study participant and be approved by him/her. Description materials including photographs should not disclose study participant's name, english initials, and hospital identification number.

3) Redundant Publication/Duplicate Submission

An article that has been already reported in another journal or is being reviewed by another journal, and an article that has a redundant material previously published in the journal will be rejected. If the article contains similar work that has already been reported in another publication or has been published in the journal, the author should include copies of such material along with the submitted article. The Editorial Committee will decide on the matter of secondary publication of the submitted

article and then consider for its acceptance. Also, the author can not submit a published article to another journal without authorization. Only under the conditions for secondary publication stipulated in the 'Uniform Requirements for Manuscripts Submitted to Biomedical Journals' this may be allowed.

4) Authorship and Contributorship

Every author must meet the authorship standards set forth in the 'Uniform Requirements for Manuscripts Submitted to Biomedical Journals'. He/she has a duty of verifying that his/her article has not yet been published and is not the same as any existing one. All persons designated as authors must fulfill all three conditions that they had contributed to 1) conception and design, acquisition of data, or analysis and interpretation of data, 2) drafting the article or revising it critically for important intellectual content, and 3) final approval of the version to be published. All contributors participating in the research not meeting the authorship standards must be listed in 'Acknowledgments' section after receiving their permission. After a manuscript has been submitted, no author could not be added.

5) Conflicts of Interest and Financial Disclosures

Each author has a duty to disclose direct or indirect conflicts of interest in the subject matter discussed in the submitted article. All authors must reveal all possible conflicts of interest that related to research such as consultation fees and stocks when submitting their article and should provide all of their personal signatures to verify that they have revealed so. A financial grant or support received for research purposes should be disclosed at the bottom of the title page, and all conflicts of interest such as consulting fees and stocks associated with study should also be disclosed at the bottom of the title page or in acknowledgment section. The corresponding author is required to confirm whether his/her or his/her co-authors have any conflict of interest to declare, and to provide appropriate details to the Editorial Committee.

8. RESUBMISSION

The resubmission period for a manuscript sent to its author for revision must be three months, and if three months are exceeded, the manuscript must be judged again as a new manuscript.

9. PAGE PROOFS

Page proofs will be sent to corresponding authors by the Editorial Committee. Authors must send them back within 48 hours after reading them carefully and revising them if necessary. The revision of page proofs must be limited to the errors of typesetting, and it is prohibited to change or to add new contents to the article. Authors are responsible for the contents of page proofs.

10. ARTICLE PROCESSING CHARGE

No review fees are charged for all the submitted articles. Article processing charges are required for publication in the *KJHP*. Publication fees for all the accepted original or review articles are 300,000 Korean Won (250 US dollars). Additionally, if the article exceeds 6 pages of the journal, additional fees (50,000 Korean Won or 40 US dollars per extra page) will be charged.

11. CORRECTIONS

If necessary, requests to publish corrections should be sent to the Editorial Committee within one month of journal publication. Corrections are reviewed by editors and authors and published in the next issue of the journal.

Copyright Transfer Agreement

Manuscript Title: _____

_____

_____

Authors: _____

_____

_____

On behalf of all authors of the manuscript entitled as above, I, as a corresponding author, certify that this article is an original work and that none of the material in the manuscript has been published previously or will be published. The authors warrant that they have obtained permission from the copyright holder to reproduce any materials and media including printed and electronic forms not owned by the authors, and that they have acknowledged the source.

Also, all the authors of this manuscript declare that there is no commercial association (e.g., financial interest, stock ownership, consultancy, patent and licensing agreement, etc.) that might pose a conflict of interest in relation to the submitted manuscript.

On behalf of all the authors, I hereby transfer, convey, and assign all copyrights in the Article to the *Korean Journal of Health Promotion* (*KJHP*). Also, the copyright to the Contribution identified above is transferred to the *KJHP*. The copyright transfer covers the right to print, publish, distribute, and sell throughout the world the said Contribution and parts thereof, including all revisions or versions and future editions, in all forms and media expression – such as in its electronic form (offline, online) – now known or developed in the future, as well as to translate, print, publish, distribute, and sell the Contribution in any foreign languages and throughout the world.

Name of Corresponding Author: _____

Signature of Corresponding Author on behalf of All Authors: _____

Date: _____/_____/_____