Sex differences in the association between self-rated health and high-sensitivity C-reactive protein levels in Koreans: A cross-sectional study using Korea National Health and Nutrition Examination Survey (KNHANES)

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Abstract

Background

No studies have investigated the association between self-rated health (SRH) and high-sensitivity C-reactive protein (hs-CRP) in South Koreans. This study explored the association and analyzed any sex differences.

Method

Using data from the 2015-2017 Korea National Health and Nutrition Examination Survey, we analyzed the association between SRH and high group (>1.0 mg/L) in 14,544 Koreans aged ≥19 years who responded to the SRH survey and who had hs-CRP test results.

Results

The percentage of having a very poor to poor SRH was higher in the high hs-CRP level group (22.4%) than in the low level group (17.66%). Among males, the risk of a high hs-CRP level increased with worse SRH (adjusted for confounders; P for trend <0.001). After adjusting for all confounders, including chronic diseases, males with a very poor SRH showed higher odds ratio (OR) for high group than those with a very good SRH (fully adjusted OR, 1.74; 95% confidence interval, 1.04-2.90). Significant correlations were absent among females.

Conclusions

A poor SRH was correlated with low-grade inflammation (high hs-CRP level) among male Korean adults. The findings could be useful for developing health improvement programs and in goal setting at a national scale.

Background

Self-rated health (SRH) is an index utilized worldwide to summarize how patients perceive their overall health status [1]. SRH is an independent predictor of mortality and disease morbidity, even after adjusting for demographic, sociological, and medical risk factors [2]. Despite criticisms that SRH is assessed based on a single question, it is known to be a strong predictor in both healthy and unhealthy individuals. SRH is not only a predictor of previously diagnosed disease but also a predictor of reactions associated with the progression of disease in the premorbid stage; it encapsulates recent
or sporadic health issues that may be missed by one-time objective testing, and it also reflects behavioral and emotional factors [2, 3].

C-reactive protein (CRP) is produced by hepatocytes following acute tissue injury or infection. Though CRP levels are generally elevated in cases of severe inflammation, high-sensitivity C-reactive protein (hs-CRP) levels increase nonspecifically in the event of inflammation in the body. In particular, hs-CRP is used as an indicator to assess the risk of cardiovascular disease (CVD), and several studies have suggested hs-CRP as a predictor of mortality. In assessing CVD risk, the American Heart Association (AHA) and Centers for Disease Control and Prevention (CDC) defined hs-CRP levels of > 3.0 mg/L as indicating high risk, 1.0–3.0 mg/L as indicating average risk, and < 1.0 mg/L as indicating low risk [4, 5].

In South Korea, the percentage of individuals who consider their health status to be good (“very good” or “good”) is low, at 29.2% in 2017. From 1998 to 2017, this percentage has remained in the range 29–47%, indicating that less than half of the population consider themselves to be healthy. Moreover, this percentage is one of the lowest among countries of the Organization for Economic Co-operation and Development (OECD); even though South Korea maintains an objective health status similar to that of the US and Europe, South Koreans experience more subjective health anxiety [6].

Several prior studies have reported that a poor SRH is associated with a high hs-CRP level [7–9]. A poor SRH can be surmised to be related to mortality and morbidity because low-grade inflammation is related to the development of CVD, cancer, and diabetes [10, 11]. There have been studies reporting sex differences in the relationship between SRH and low-grade inflammation [8, 9, 12]; thus far, there have been no large-scale studies on this aspect in Koreans. Therefore, in this study, using data from the 2015–2017 Korea National Health and Nutrition Examination Survey (KNHANES), we aimed to investigate the correlation between SRH and hs-CRP in Koreans aged ≥ 19 years and to analyze whether the correlation showed any differences between male and female subjects.

Methods

Participants

In this study, we used raw data from KNHANES VI and VII (2015–2017). KNHANES is a nationwide
cross-sectional survey conducted by the CDC to ascertain the health and nutritional status of the Korean population. The survey extracts a representative sample of households and conducts a household member verification survey, health questionnaire survey, health examination, and nutritional survey for household members aged ≥ 1 year. In the present study, we aimed to investigate Korean adults aged ≥ 19 years. Of the 23,657 survey participants, we excluded individuals with missing measurements for hs-CRP (4871 people) and SRH (57 people), those aged < 19 years (1838 people), and those with unclear measurement values (2655 people). We also excluded individuals with hs-CRP levels ≥ 10 mg/L (866 people) as they could be considered to show acute infection, systemic inflammation, or tissue injury [13]. A total of 14,544 subjects (6281 males, 8263 females) were included in our analysis (Fig. 1).

Instruments And Procedure
SRH assessment
SRH was assessed using the question “In general, how would you rate your health?” There were five possible responses: “very good,” “good,” “fair,” “poor,” and “very poor.”

CRP measurement
hs-CRP was measured by immunoturbidimetry using a Cobas analyzer (Roche, Germany) and a Cardiac C-Reactive Protein High Sensitivity reagent (Roche, Germany). The minimum value of the specimens was 0.1 mg/L, and the maximum value was 20 mg/L. A high hs-CRP level was defined as an hs-CRP level > 1.0 mg/L.

Covariates
For the participants’ demographic characteristics, we included age; for socioeconomic characteristics, we included educational level, household income level, and marital status; for lifestyle factors, we included smoking status and alcohol consumption; and for disease and health-related factors, we included body mass index (BMI), chronic diseases, and menopausal status (females). Educational level was classified as “elementary school graduate or lower,” “middle school graduate,” “high school graduate,” or “college graduate or higher.” The household income level was classified into quartiles: “low,” “lower middle,” “upper middle,” and “high.” Marital status was classified as “married” or “unmarried.” BMI was calculated as weight (kg) divided by the square of height (m²). Smoking status
was classified as “nonsmoker,” “past smoker,” or “current smoker.” Alcohol consumption was classified as “never drinks,” “less than once a month,” “<5 times/month,” or “≥5 times/month.” For chronic diseases, we included diseases reported to be directly or indirectly associated with hs-CRP, namely hypertension, diabetes mellitus, coronary artery disease, including myocardial infarction and angina [14], dyslipidemia [15], stroke [16], and rheumatoid arthritis [17], and participants were classified as having “none,” “one,” or “two or more.”

Statistical Methods

The KNHANES applies stratified cluster sampling and weighted values to a nationally representative sample. The survey sample weights were used in all analyses. Data are presented as means ± standard error for continuous variables or as frequencies and percentages for categorical variables. The proportions of categorical variables were compared using Pearson’s chi-squared ($\chi^2$) tests. Associations between hs-CRP levels and various sociodemographic categories and SRH were explored. In addition, logistic regression analysis was used to study the relationship between hs-CRP and SRH according to sex. Results are presented as odds ratios and 95% confidence intervals. Additionally, this study investigated if there was an underlying trend in the different levels of SRH in each model (P for trend). A P-value < 0.05 was considered significant. All data analyses were performed using the statistical software package SAS version 9.4 (SAS Institute Inc., Cary, NC, USA) and IBM SPSS Statistics 25 (SPSS Inc., Chicago, IL, USA).

Results

Characteristics of participants

Table 1 shows the characteristics of the participants. Among the 14,544 participants, 6281 were male and 8263, the percentage of those with a very poor to poor SRH was higher in the high group (22.47%) than in the low group (17.66%). Likewise, for both males and females, the percentage of participants with a very poor to poor SRH was higher in the high group than in the low group (men: high, 18.1%; low, 13.6%; women: high, 26.5%; low, 20.6%), while the percentage of participants with a good to very good SRH was lower in the high group (men: high, 29.1%, low, 35.9%; women: high, 22%; low, 26.7%) (P < 0.001) (Fig. 2).

Table 1

Baseline characteristics of the study population in the 2015–2017 KNHANES
| Characteristic                  | Men                              | Women                             | P-value† | Men                              | Women                             | P-value† |
|--------------------------------|----------------------------------|-----------------------------------|----------|----------------------------------|-----------------------------------|----------|
|                                | Low hs-CRP (≤ 1.0 mg/L) (n = 4,495) | High hs-CRP (> 1.0 mg/L) (n = 1,786) |          | Low hs-CRP (≤ 1.0 mg/L) (n = 6,306) | High hs-CRP (> 1.0 mg/L) (n = 1,957) |          |
| Age (years), mean (SE)         | 45.5 (0.3)                       | 47.4 (0.3)                        | .000*    | 47.5 (0.3)                       | 49.1 (0.3)                        | .000*    |
| Educational level, n (%)       | 580 (12.9)                       | 333 (18.6)                        | .000*    | 707 (13.0)                       | 424 (24.0)                        | .000*    |
| Elementary school or lower     | 446 (9.9)                        | 205 (11.5)                        |          | 651 (10.3)                       | 203 (10.4)                        |          |
| Middle school                  | 1575 (35.0)                      | 568 (31.8)                        |          | 2011 (31.7)                      | 547 (28.0)                        |          |
| College or higher              | 1894 (42.1)                      | 680 (38.1)                        |          | 2230 (35.4)                      | 554 (28.3)                        |          |
| Marital status, n (%)          | 3536 (78.7)                      | 1487 (83.3)                       | .002*    | 5396 (85.6)                      | 1772 (90.5)                       | .000*    |
| Married                        | 959 (21.3)                       | 299 (16.7)                        | .101     | 910 (14.4)                       | 185 (9.5)                         | .009*    |
| Unmarried                      | 1130 (25.1)                      | 389 (21.8)                        | .000*    | 1742 (89.0)                      | 522 (26.7)                        | .000*    |
| Household income level, n (%)  | 1034 (23.0)                      | 457 (25.6)                        | .000*    | 5710 (90.5)                      | 1444 (22.9)                       | .000*    |
| Low                            | 1116 (25.7)                      | 435 (24.4)                        |          | 651 (10.3)                       | 1609 (25.5)                       |          |
| Lower middle                   | 1228 (27.3)                      | 430 (24.1)                        |          | 1662 (26.4)                      | 470 (24.0)                        |          |
| Upper middle                   | 1077 (24.0)                      | 464 (26.0)                        |          | 1591 (25.2)                      | 496 (25.3)                        |          |
| High                           | 1044 (23.0)                      | 457 (25.6)                        |          | 1444 (22.9)                      | 522 (26.7)                        |          |
| Weight (kg), mean (SD)         | 72.1 (0.2)                       | 58.0 (0.1)                        | .000*    | 1772 (90.5)                      | 522 (26.7)                        | .000*    |
| Height (cm), mean (SD)         | 171.5 (0.1)                      | 158.0 (0.1)                       | .000*    | 1572 (89.0)                      | 158.0 (0.1)                       | .000*    |
| BMI (kg/m²), mean (SD)         | 24.5 (0.1)                       | 23.3 (0.1)                        | .000*    | 1609 (25.5)                      | 470 (24.0)                        | .000*    |
| Smoking, n (%)                 | 1.123                            | 0.483                             |          | 0.483                            | 0.483                             |          |
| Nonsmoker                      | 1130 (25.1)                      | 389 (21.8)                        | .000*    | 5710 (90.5)                      | 1444 (22.9)                       | .000*    |
| Past smoker                    | 1926 (42.8)                      | 777 (43.5)                        |          | 522 (26.7)                       | 1609 (25.5)                       |          |
| Current smoker                 | 1439 (32.0)                      | 620 (34.7)                        | .001*    | 118 (6.0)                        | 255 (4.0)                         | .000*    |
| Alcohol consumption, n (%)     | 1.492                            | 0.019                             |          | 0.019                            | 0.019                             |          |
| Never drink                    | 196 (4.4)                        | 85 (4.8)                          |          | 916 (49.4)                       | 916 (49.4)                        |          |
| <Once/month                    | 1004 (22.3)                      | 457 (25.6)                        |          | 1009 (51.6)                      | 1009 (51.6)                       |          |
| <Five times/month              | 1691 (37.6)                      | 577 (32.3)                        |          | 496 (25.3)                       | 496 (25.3)                        |          |
| ≥Five times/month              | 1604 (35.7)                      | 667 (37.3)                        |          | 701 (11.1)                       | 701 (11.1)                        |          |
| Chronic diseases*, n (%)       | 2579 (57.4)                      | 789 (44.2)                        | .000*    | 2579 (57.4)                      | 789 (44.2)                        | .000*    |
| None                           | 1186 (26.4)                      | 590 (33.0)                        |          | 1274 (20.2)                      | 536 (27.4)                        |          |
| One                            | 1004 (22.3)                      | 457 (25.6)                        |          | 1009 (51.6)                      | 1009 (51.6)                       |          |
| Two or more                    | 370 (8.2)                        | 207 (11.5)                        | .000*    | 370 (8.2)                        | 207 (11.5)                        | .000*    |
| Self-rated health, n (%)       | 295 (6.6)                        | 89 (5.0)                          | .000*    | 295 (6.6)                        | 89 (5.0)                          | .000*    |
| Very poor                      | 80 (1.8)                         | 59 (3.3)                          |          | 80 (1.8)                         | 59 (3.3)                          |          |
| Poor                           | 532 (11.8)                       | 264 (14.8)                        |          | 532 (11.8)                       | 264 (14.8)                        |          |
| Fair                           | 2271 (50.5)                      | 943 (52.8)                        |          | 2271 (50.5)                      | 943 (52.8)                        |          |
| Good                           | 1317 (29.3)                      | 431 (24.1)                        |          | 1317 (29.3)                      | 431 (24.1)                        |          |
| Very good                      | 295 (6.6)                        | 89 (5.0)                          | .000*    | 295 (6.6)                        | 89 (5.0)                          | .000*    |
| Menopause, n (%)               | 3211 (50.9)                      | 752 (38.4)                        | .000*    | 3211 (50.9)                      | 752 (38.4)                        | .000*    |
| Yes                            | 3072 (48.7)                      | 1189 (60.8)                       |          | 3072 (48.7)                      | 1189 (60.8)                       |          |

* Chronic diseases include hypertension, diabetes, dyslipidemia, coronary heart disease (myocardial infarction or angina pectoris), stroke, or rheumatoid arthritis.
† P-value of t-test or Pearson’s chi-squared (χ²) tests for continuous and categorical variables to determine differences between groups according to high-sensitivity C-reactive protein (hs-CRP) level, p ≤ .05

KNHANES, Korea National Health and Nutrition Examination Survey; SE, standard error; SD, standard deviation; BMI, body mass index.
Correlation Between SRH And A High hs-CRP Level (overall)

Results of the logistic regression analysis to examine differences in high group according to SRH are shown in Table 2. When all participants were analyzed, in Model 1, relative to a very good SRH, the ORs for very poor, poor, and fair SRH were 2.02 (1.47–2.78), 1.82 (1.44–2.29), and 1.51 (1.22–1.87), respectively, all of which were significant. In Model 2, the ORs for very poor, poor, and fair SRH were 1.54 (1.11–2.12), 1.68 (1.32–2.13), and 1.46 (1.18–1.82), respectively, all of which also showing a significant correlation. In Model 3, the ORs for poor and fair SRH were 1.40 (1.09–1.79) and 1.34 (1.06–1.68), respectively, which were significant; in Model 4, the ORs for poor and fair SRH were 1.38 (1.08–1.77) and 1.32 (1.05–1.66), which were also significant (P < 0.05).

Table 2
Association between high hs-CRP level and SRH in all subjects

| SRH   | Model 1 |         | Model 2 |         | Model 3 |         | Model 4 |         |
|-------|---------|---------|---------|---------|---------|---------|---------|---------|
|       | OR      | 95% CI  | P-value | OR      | 95% CI  | P-value | OR      | 95% CI  | P-value |
| Very poor | 2.02   | 1.47    | 2.78    | .000*   | 1.54   | 1.11    | 2.12    | .010*   | 1.22   | 0.87    | 1.72    | .245    | 1.22   | 0.87    | 1.71    | .259    |
| Poor   | 1.82   | 1.44    | 2.29    | .000*   | 1.68   | 1.32    | 2.13    | .000*   | a.40 a.10 a.179 a.008 a.1.38 a.1.08 a.1.77 a.011 a.1.32 a.1.05 a.1.66 a.016 a.1.12 a.0.87 a.1.42 a.377 a.1.00 a.001 a.001 a.001 |
| Fair   | 1.51   | 1.22    | 1.87    | .000*   | 1.46   | 1.18    | 1.82    | .001*   | 1.34   | 1.06    | 1.68    | .013    | 1.32   | 1.05    | 1.66    | .016    a.1.12 a.0.87 a.1.42 a.377 a.1.00 a.001 a.001 a.001 |
| Good   | 1.16   | 0.92    | 1.46    | .211    | 1.17   | 0.93    | 1.47    | .183    | 1.12   | 0.88    | 1.42    | .375    | 1.12   | 0.87    | 1.42    | .377    |
| Very good (ref.) | 1.00   |         |         | 1.00    |         |         |         |         | 1.00   |         |         |         |
| P for trend | < 0.001* |        |         | < 0.001* |        |         | < 0.001* |        | < 0.001* |        |         |

Odds ratios with adjustments using logistic regression models.

Note. p ≤ .05*
Model 1: unadjusted.
Model 2: adjusted for age, educational level, marital status, and household income level.
Model 3: adjusted for Model 2 confounders + body mass index, smoking, and alcohol consumption.
Model 4: adjusted for Model 3 confounders + chronic diseases. hs-CRP, high-sensitivity C-reactive protein; SRH, self-rated health; OR, odds ratio; CI, confidence interval.

Correlation between SRH and a high hs-CRP level (male-to-female comparison)

When male participants were analyzed, in Model 1, the ORs for very poor, poor, and fair SRH were 2.69 (1.68–4.32), 1.79 (1.30–2.44), and 1.63 (1.22–2.16), respectively, which were significant. In Model 2, the ORs for very poor, poor, and fair SRH were 2.19 (1.37–3.51), 1.70 (1.23–2.35), and 1.61 (1.20–2.14), respectively, also showing significant correlations. In Model 3, the ORs for very poor, poor, and fair SRH were 1.78 (1.07–2.96), 1.43 (1.02–2.00), and 1.44 (1.06–1.96), respectively, which were significant, whereas in Model 4, the ORs for very poor and fair SRH were 1.74 (1.04–2.90) and 1.42 (1.04–1.93), which were also significant (P < 0.05) (Table 3).
Table 3
Association between high hs-CRP level and SRH in men

| SRH      | Model 1       |         |         | Model 2       |         |         | Model 3       |         |         | Model 4       |         |
|----------|---------------|---------|---------|---------------|---------|---------|---------------|---------|---------|---------------|---------|
|          | OR            | 95% CI  | P-value | OR            | 95% CI  | P-value | OR            | 95% CI  | P-value | OR            | 95% CI  | P-value |
| Very poor| 2.69          | 1.68    | 4.32    | .000*         | 2.19    | 1.37    | 3.51          | .001*   | 1.78    | 1.07    | 2.96    | .026*   |
| Poor     | 1.79          | 1.30    | 2.44    | .000*         | 1.70    | 1.23    | 2.35          | .001*   | 1.43    | 1.02    | 2.00    | .041*   |
| Fair     | 1.63          | 1.22    | 2.16    | .001*         | 1.61    | 1.20    | 2.14          | .001*   | 1.44    | 1.06    | 1.96    | .019*   |
| Good     | 1.12          | 0.83    | 1.51    | .462          | 1.14    | 0.84    | 1.54          | .396    | 1.08    | 0.78    | 1.49    | .637    |
| Very good(ref.) | 1.00    | 1.00    |         | 1.00          | 1.00    |         | 1.00          | 1.00    |         |         |         |         |
| P for trend | < 0.001*    | < 0.001* |          | < 0.001*      |         |          | < 0.001*      |         |          | < 0.001*      |         |         |

Odds ratios with adjustments using logistic regression models.
Note. p ≤ .05
Model 1: unadjusted.
Model 2: adjusted for age, educational level, marital status, and household income level.
Model 3: adjusted for Model 2 confounders + body mass index, smoking, and alcohol consumption.
Model 4: adjusted for Model 3 confounders + chronic diseases. hs-CRP, high-sensitivity C-reactive protein; SRH, self-rated health; OR, odds ratio; CI, confidence interval.

Discussion

In this study, we analyzed the relationship between SRH and hs-CRP based on large-scale, nationwide,
The AHA and CDC recommend hs-CRP cutoff points of $< 1 \text{ mg/L}$ to indicate low risk, $1-3 \text{ mg/L}$ to indicate average risk, and $> 3 \text{ mg/L}$ to indicate high risk, but these criteria were selected based on studies of Westerners, and several studies [18, 19] According to Jung et al. [20, 21] we defined the high hs-CRP level group using an hs-CRP cutoff of $> 1.0 \text{ mg/L}$.

Our findings were similar to those of previous studies that reported a correlation between a poor SRH and a high hs-CRP level ([7–9, 22]. In a study of 4049 respondent older adults without significant cognitive deficit by Szybalska et al. [23], a worse SRH was associated with increased interleukin-6 (IL-6) and CRP levels. Leshem-Rubinow et al. [7] analyzed the correlations between SRH and the inflammation-sensitive biomarkers hs-CRP and fibrinogen in 13,773 healthy individuals and observed higher biomarker levels in the group with the lowest SRH level; hs-CRP showed a correlation in both males and females, but fibrinogen only showed a correlation in males. Shanahan et al. [8] studied 13,236 young adults and reported that, when adjusting for acute/chronic diseases, medication history, and health behaviors, a lower SRH level was associated with a higher hs-CRP level, but when adjusting for BMI, the correlation in female participants was weakened, whereas the correlation in male participants remained significant. However, a study of 16,256 Japanese individuals reported a significant correlation between a poor SRH and a high hs-CRP level only in female participants [9].

Thus, while correlations between a poor SRH and a high hs-CRP level have been reported, the above studies show limitations such as restricted age of participants, including only older adults [22] or only young adults [8], and lack of consideration for diseases that could affect the relationship between SRH and CRP [9]. Moreover, there have been few studies on the relationship between SRH and CRP [7, 24] so far; there have been no such studies in Koreans.

Several studies have reported correlations between a poor SRH and pro-inflammatory cytokines, including IL-6 [19, 25]. CRP is produced by hepatocytes under the regulatory control of IL-6 and other inflammatory cytokines [26], and these pro-inflammatory cytokines cause sickness behaviors, such as weakness, depression, exaggerated pain (hyperalgesia or allodynia), and lack of appetite [27]. In other words, the relationship between a poor SRH and a high hs-CRP level can be explained by
differences caused by pro-inflammatory cytokines, and this, in turn, can explain our results. Inflammatory indices in women are known to be altered by the menstrual cycle, menopause, and hormone therapy [28], and menopause and estrogen replacement therapy have been reported to affect obesity and inflammation in women [29]. CRP levels can be presumed to change depending on the hormonal environment, and this could act as a confounding factor in the relationship between SRH and hs-CRP [30]. In our study, we were unable to investigate whether participants were taking female hormones or their stage in the menstrual cycle. Because we only accounted for female menopause, it is thought that we did not observe significant results between SRH and hs-CRP in women. Moreover, biological sex is known to affect CRP-related genetic variation [31], and according to a study by Kettunen et al. [32], allelic variants in the CRP gene are associated with CRP levels, and males and females show differences depending on the CRP genotype. Hence, the differences in genetic variation between males and females could have affected our results.

Sex differences have been reported in the relationship between CRP levels and mortality [33–36], but it is unclear why a high CRP level is only associated with an increased mortality risk in males. Zhao et al analyzed the middle-aged Chinese population; hs-CRP was associated with increased risk of developing CVD [37]. In addition, Lee JH et al. [38] studied 23,233 rural Koreans and reported that a high CRP level was more strongly associated with higher mortality in males than in females. There have been several studies reporting a stronger correlation between SRH and mortality in males than in females [36, 39]. Specifically, males with a poor SRH have been reported to show a higher risk for conditions related to mortality, such as cardiovascular disease and cancer. When assessing SRH, the subject rates their current overall health; it has been reported that men rate their own health in comparison to that of other men, and male SRH tends to mostly reflect serious and life-threatening disease, whereas female SRH tends to reflect other factors unrelated to mortality and chronic, non-life-threatening disease, resulting in a weaker correlation between SRH and mortality for women [39–41]. Moreover, in a study of Korean adults by Shin et al. [42], women tended to rate their own health more poorly than men, and in a study by Lee SY et al. [43], traditional Korean gender roles had a negative effect on women, and the risk of a poor SRH was higher among Korean women than
among women from the US. Similarly, in our study, we only observed a correlation between SRH and hs-CRP among male participants. The discrepancy between males and females could be related to the fact that CRP is more likely to reflect CVD and mortality in men than in women, and due to the fact that SRH is more likely to directly reflect health and mortality in men than in women.

In our study of Korean adults aged ≥ 19 years, when we analyzed all participants, the poor SRH group was more likely to have high group (> 1.0 mg/L) than the very good SRH group. Especially in male participants, as SRH went from very good to very poor, there was a corresponding increase in the risk of a high hs-CRP level (> 1.0 mg/L). These results can be explained by the fact that immune-related activity is associated with vague symptoms of malaise and interoceptive perception [25]. Such findings are consistent with those of a previous study of healthy adults, in which a poorer SRH was associated with increased serum inflammatory marker levels (IL-6 and CRP) [22].

Even after correcting for all sociodemographic characteristics, health-related factors, and chronic diseases known to be associated with low-level inflammation, among male participants, the very poor SRH group showed 1.74 times higher risk of a high hs-CRP level than the very good SRH group, but there was no significant relationship among female participants. This finding could be because SRH is a dynamic evaluation for judging the trajectory of health, which reflects both clinical stage and preclinical stage disease [44]. Therefore, even after correcting for chronic diseases associated with hs-CRP, we still observed a correlation in male participants.

Our study has several limitations. First, because this was a cross-sectional study, it was not possible to infer causal relationships, and we could only investigate the correlation between SRH and hs-CRP. Nevertheless, the value of this study is that we used data from the KNHANES, which is representative of the Korean population, and that it was a large-scale study of Korean adults. Second, SRH assessment was performed at specific times. Future monitoring studies are necessary to ascertain the long-term relationships between SRH and hs-CRP. Third, we only used hs-CRP as an inflammatory marker; further studies will need to investigate the correlations of SRH with other indicators (e.g., IL-6, tumor necrosis factor-alpha). Finally, because the study was based on data from a survey of South Koreans, the results could have been affected by the racial characteristics of Koreans and may thus
be difficult to apply to people of other races. Despite these limitations, our study showed a strong correlation between a poor SRH and a high hs-CRP level in male Korean adults and is valuable as the first study to examine the relationship between SRH and hs-CRP in Korean adults.

Conclusions
We investigated the relationship between SRH and hs-CRP through a survey of Korean adults. Even after correcting for factors that could affect low-grade inflammation, such as age, socioeconomic status, BMI, health-related behaviors, and chronic diseases, male adults with a poor SRH were at greater risk of having high group. This study showed a close relationship between low-grade inflammation (high hs-CRP level) and SRH, an instrument reflecting one’s own assessment of their health. Since we only observed a correlation in male participants, it suggests that there could be factors affecting the relationship between SRH and hs-CRP differently for males and females. Our findings could provide a basis for developing health improvement programs. Future studies will need to be conducted to examine sex differences in the relationship of SRH with other inflammatory markers.

List Of Abbreviations
hs-CRP, high-sensitivity C-reactive protein; SRH, self-rated health; OR, odds ratio; CI, confidence interval

Declarations
Ethics approval and consent to participate
The study was approved by the Institutional Review Board of Jaseng Hospital of Korean Medicine in Seoul, Korea (JASENG 2019-08-001).

Consent for publication
Not applicable

Availability of data and materials
All original data are publicly available free of charge from the KNHANES website (http://knhanes.cdc.go.kr) for the purposes of academic research.

Conflicts of Interest
The authors declare no conflict of interest.


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Author Contributions

Conceptualization, B.J. and S.W.P.; methodology, B.J.; software, B.J.; validation, I.H.H.; formal analysis, B.J.; investigation, E.J.K.; resources, I.H.H.; data curation, B.J.; writing—original draft preparation, B.J. and S.W.P; writing—review and editing, S.S.P., E.J.K., W.S.S. I.H.H. and B.J.; supervision, B.J.

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Figures

Figure 1

Flow diagram showing the number of included and excluded participants and the data for analysis. KNHANES, Korea National Health and Nutrition Examination Survey; hs-CRP, high-sensitivity C-reactive protein; SRH, self-rated health; BMI, body mass index.
Prevalence of self-rated health (SRH) according to sex. The percentage of participants with a very poor to poor SRH was higher in the group with a high hs-CRP level (22.47%) than in the group with a low group (17.66%) (P<0.001).